END OF STUDY REPORT

[21/01/2016]

[Femoral Nerve Block Intervention in Neck of Femur Fracture]

Protocol Number	V6.0 27/Sep/2013
Chief Investigator	Professor Opinder Sahota
EudraCT Number	2010-023871-25
REC Reference Number	10/H0408/113
Sponsor Reference Number	10HC005
Study Start Date	06/Jan/2012
Study End Date	05/Jan/2015
Funder(s)	NIHR-RfPB
Sponsor(s)	Nottingham University Hospitals NHS Trust

Name of Test Drug / Investigational Product	Chirocaine. Ropivacaine
Indication Studied	Nerve block in proximal femoral fracture

Report Author: Martin Rowlands — Date: 01-02-2016.

Dr Martin Rowlands, Research Fellow — DD-MMM-YYYY

Chief Investigator Authorisation: Signature — 29.01.2016

Prof Opinder Sahota, Professor of Orthogeriatric Medicine — DD-MMM-YYYY

Sponsor Authorisation: Signature — Date: 4th FEB 2016

Maria Koufali, Deputy Director of R&I — DD-MMM-YYYY

This study was carried out in compliance with International Conference on Harmonisation (ICH) Good Clinical Practices (GCP) and Nottingham University Hospitals NHS Trust (NUH) Research and Innovation (R&I) Procedures

EudraCT Number: 2010-023871-25
REC Reference Number: 10/H0408/113
Sponsor Reference Number: 10HC005

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List of Abbreviations and Definition of Terms

AE	Adverse Event
AMT	Abbreviated mental test
AR	Adverse reaction
CAS	Cumulative ambulation score
CI	Chief Investigator
CRA	Clinical Research Associate
CRF	Case report form
CRO	Contract research organisation
CT	Clinical Trials
CTA	Clinical Trials authorisation
EC	Ethics Committee
ED	Emergency Department
FNB	Femoral Nerve Block
GCP	Good clinical practice
GP	General Practitioner
IB	Investigators brochure
ICF	Informed consent form
IMP	Interventional Medicinal Products
IV	Intra-venous
Kg	Kilogramme
PFF	Proximal femoral fracture (Hip fracture)
Pt	Patient
q.d.s.	Quarter die summendus (four times a day)
QMC	Queen's Medical Centre
MHRA	Medicines and healthcare products Regulatory Agency
mg	milligram
mls	millilitres
NHS	National Health Service
NCTU	Nottingham Clinical Trials Unit
#NOF	Fractured neck of femur

PI	**Principle Investigator**
PIL/PIS	**Patients information Leaflet/Sheet**
R+D	**NHS Trust R+D Department**
REC	**Research Ethics Committee**
SAE	**Serious Adverse Event**
SAR	**Serious Adverse Reaction**
SmPC/SPC	**Summary of Product Characteristics**
SOP	**Standard Operating Procedure**
SUSAR	**Suspected Unexpected Serious Adverse Reaction.**
TMF	**Trial Master File**
VAS	**Visual Analogue Score**

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Summary of Study

Hip fractures are very painful leading to lengthy hospital stays. Conventional methods of treating pain are limited. Non-steroidal anti-inflammatories are relatively contraindicated and opioids have significant side effects. Regional anaesthesia holds promise but results from these techniques are inconsistent. Trials to date have been inconclusive with regard to which blocks to use and for how long. Inter-patient variability remains a problem.

This was a single centre pragmatic, parallel arm randomised controlled trial to compare early femoral nerve block using catheters with standard analgesia in patients with proximal femoral fracture. It was conducted at Queen's Medical Centre, Nottingham between 06/Jan/2012 and 05/Jan/2015.

Patients were eligible if:-

1) Aged >70,
2) Resident in their own home or warden aided flat,
3) Cognitively intact, (AMT>7),
4) Had a prior fracture New Mobility Score of 3 or more,
5) Willing and able to give informed consent,
6) Not participating in another clinical trial.

Patients were excluded if:-

1) Prefracture hospitalisation,
2) Contraindications to femoral nerve block analgesia,
3) Regular prefracture opioid or glucocorticoid therapy,
4) Alcohol or substance abuse,
5) Morphine intolerance,
6) Postoperative surgical restrictions for ambulation,
7) Any other disease/disorder which, in the opinion of the investigator, may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study.

Objectives

The aims of this study were to:

1) Evaluate the effects of femoral nerve block compared to standard analgesic care upon pain in the acute and post-operative phase and post-operative rehabilitation.
2) Estimate the cost effectiveness of femoral nerve block, compared to usual care from an NHS perspective.
3) Examine issues of compliance, acceptability to staff and patients and systems implementation (content and process fidelity) to enable replication of the findings of this study to other hospital settings.

Ethical Review

The study received Ethics committee approval on 28/Jan/2011 from Nottingham Research Ethics Committee 2. All staff who worked on the study were trained in GCP principles and had up to date GCP certification. The study was carried out in accordance with GCP and NUH processes.

Investigational Plan

Patients were screened in ED by a member of the investigational team. Patients presenting with history suggestive of PFF were attended and inclusion/exclusion criteria were checked. If patients were eligible then initial verbal consent was obtained.
Randomisation was via web-based computer generated concealed tables (service provided by Nottingham University Clinical Trials Unit). Due to the nature of the intervention it was not possible to blind patients to their group allocation. It was not considered ethical to administer a sham block so there was no placebo group.

In patients randomised to the active group, initial FNB was then established in ED using portable ultrasound guidance and 0.5mls/kg of 0.25% Levo-bupivacaine (Chirocaine).
In control patients analgesia was obtained using IV morphine titrated to a VAS pain score of 5.
It was initially intended to randomise 150 participants but this did not prove possible in the time frame. Overall 141 participants were randomised; 71 into the active group and 70 into the control group.

Active patients were then given a femoral nerve catheter on transfer to the ward. Study participation was for three post-operative days. Final follow up, made by phone call occurred 30 days post operatively.

Selection of Study Population

Inclusion criteria were:-

- Aged 70yrs and over,
- Resident in their own home or warden aided flat,
- Cognitively intact [as defined by a score of seven or more on the Abbreviated 10 point Mental Test Score,
- Have a prior fracture New Mobility Score of 3 or more (indicating independent indoor ambulation),
- Willing and able to give informed consent.

Exclusion criteria were:-

- Pre-fracture hospitalisation,
- Contraindications to femoral nerve block analgesia,
- Regular pre-fracture opioid use,
- Alcohol or substance abuse,
- Morphine allergy or sensitivity,
- Any other disease/disorder which, in the opinion of the investigator, may either put the participants at risk because of participation of the study, or may influence the result of the study, or the participant's ability to participate in the study,
- Participants participating in another research study.

Study Settings

The study was conducted entirely on Queen's Medical Centre campus of Nottingham University Hospitals NHS Trust, Nottingham.
CI - Professor Opinder Sahota.
Investigators - Dr Iain Moppett, Dr Martin Rowlands, Dr Gerrie van de Walt, Dr Jim Bradley.
Statistician - Dr Sarah Armstrong.

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Research Nurses - Wendy Sheldon, Ellie Tsvetely, Alison Watson.

Interventions

Due to the nature of the intervention for this study it was not possible to blind either participants or researchers to the study allocation.
Administration of sham block was considered unethical and therefore there was no placebo arm for this study.
On randomisation to the study patients in the control group received IV morphine titrated to a pain score of 5 or less out of ten before being sent to x-ray. This was obtained via the ED drug supply and administered by the research fellow.
Patients in the active group received initial femoral nerve block performed under ultrasound guidance and using 0.5 mls/kg of 0.25% (2mg/ml) Levo-bupivacaine local anaesthetic (Chirocaine™, Abbott) up to a maximum amount of 30 mls total volume. This dose was selected as it allows for reasonable volume and intensity of block whilst remaining well within safe dose limits. This block was performed in the ED department before transfer of the patient to x-ray.

Patients in the control group received standard analgesia according to hospital protocols. Regular paracetamol 1g q.d.s. and regular Tramadol 50-100mg q.d.s. with oral morphine solution 10-20mg every 2 hours as required for breakthrough pain. These drugs were prescribed on the standard hospital drug chart and administered by ward nursing staff.

Patients in the active group received regular paracetamol 1g q.d.s. with oral morphine for breakthrough analgesia. In addition they had a femoral nerve catheter which infused 5mls/hour of 0.2% ropivacaine (Naropin™, Astrazeneca) via an elastomeric pump (Surefusor+ 250™, NIPRO). This was inserted under ultrasound guidance by the research fellow on transfer of the patient from ED to hospital ward. Femoral nerve catheters were inserted under aseptic conditions in the operating theatre complex of QMC (see
13-picture of pump insitu).
Local anaesthetic drugs were administered through Trials pharmacy at QMC and stored in a locked cupboard in the theatre complex for use when needed. A strict log of trial local anaesthetic was maintained as per clinical trials pharmacy practices. The local anaesthetics used were the standard local anaesthetics in use at QMC at the time and from the same supplier.

Continuous nerve block via femoral catheter was maintained until 48 hours post-surgery for repair of PFF. In the event of catheter dislodgement for a pragmatic approach catheters were replaced if less than 24 hours post-surgery but were not replaced if greater than 24 hours. This represents local practice at QMC, and reasonably practice nationally.

Changes in the Protocol from Initial Approval

Table 1: Protocol amendments

Previous protocol version	Previous protocol date	New protocol version	New protocol date	Brief summary of changes
Version 3.0	18/Jan/2011	Version 4.0	03/May2011	1) Use of pump changed to continue for 48 hours after operation 2) Additional block assessments to be performed at 60 min and 180 min post operatively 3) Dynamic pain assessments clarified; to be performed at 30 min, 60 min and 180 min post block 4) Clarification that a continuous infusion of local anaesthetic will be given for 48 hours post operatively
Version 4.0	03/May/2011	Version 5.0	21/Dec/2011	The type of pump changed from Accufusor to Elastomeric to allow generic pumps.
Version 5.0	21/Dec/2011	Version 6.0	27/Sep/2013	1) Follow up duration amended to 30(±5) days to give more flexibility 2) Clarification that cumulative dynamic pain scores are performed preoperatively (at 30 mins, 180 mins and following the initial femoral nerve block) 3) Changed to state that daily calorific

				intake and bowels (frequency and type) are not collected at pre-op 4) Assessment of nausea and vomiting clarified to ensure it matches the actual data collected and scoring system used in the CRF 5) Other typographical changes and changes to timelines. 6) Clarification of duration of catheter insertion and use of Oramorph which is standard practice on wards.

Protocol was changed to allow oral morphine for breakthrough pain instead of IV morphine and also to clarify length of time for catheters to remain in situ. Initially protocol said third post-operative day, this was clarified to 48 hours post op.

Protocol Deviations

Protocol deviations are listed in appendix 9. Most of these are related to timing issues regarding signing of consent forms within required time periods.

There were several protocol deviation regarding signing of verbal consent forms. The protocol stated that verbal consent would be performed by two members of the research team and this was always the case in practice. However for several participants the verbal consent form was only signed by one of the researchers present. This was discussed with R+D and reported to the MHRA and Research ethics committee.

Protocol deviations 002,010,011,018,019,028 related to catheter dislodgements. Catheters were pulled out either by patients themselves of by nursing staff. This represents one of the common complications of nerve catheters and something that would be encountered in clinical practice. The decision regarding these cases was to adopt a pragmatic approach that if catheters were removed within the first 24 hours they would be resited, otherwise they would be left. This reflects clinical practice at Queen's medical centre. In reality there is a balance between leaving

catheters in place and allowing sensation to recover to permit more rapid mobilisation. In clinical practice catheters are removed between 24-48 hours post operatively, usually in the morning. This number of dislocations was not considered to be excessive.

Patient Information & Consent

To facilitate rapid analgesia patients were consented as a two stage procedure. Patients were provided with the patient information sheet (appendix 5) and the study was discussed. Initial verbal consent was obtained in the ED by the attending anaesthetist. This was witnessed by a member of the research team and documented (see verbal consent form in appendix 12). This approach was taken to try to allow patients time to read the patient information sheet and understand the study but not to delay administration of initial nerve block or IV morphine in patients who would be in pain with their injuries.

Full written consent (informed consent form; appendix 3) was obtained 48 hours after verbal consent or as close to this as possible, this would usually be the first post-operative day when the first set of observations were taken. Written consent was usually taken by the anaesthetist responsible for inserting the catheter or another medical member of the research team.

Patients who developed confusion after study entry and were unable to give written consent had proxy consent sought (proxy consent form; appendix 4). Proxy consent was sought from listed next of kin or contact person in the first instance. If no primary contact person could be found the orthopaedic consultant in charge of the patients care was approached. Once patients had regained capacity formal written consent was sought as per usual study procedure.

All consent procedures were performed by the Investigators or study nursing staff.

Patients who gave initial consent but then became confused remained in the study until Proxy consent was provided. If consent was not provided then permission was sought to use the information obtained up to that point. Patients were reassessed daily and consented as soon as capacity was deemed to have returned. One patient was withdrawn following withdrawal of consent.

Randomisation

Randomisation was performed using web based computer generated tables using blocks of unequal size. This service was provided by Nottingham University Clinical Trials Unit. Random

allocation sequence and block sizes were created by NCTU and were not known to the research team.
Randomisation was performed in the ED after verbal consent was obtained either by the clinical research nurse or the research fellow.
There was no placebo arm for this trial. Sham block was considered unethical.
Due to the nature of the intervention blinding was not possible for this trial.
There was no data monitoring committee for this study.

Safety Reporting

Pain was assessed using ten point verbal assessment scale (0 = no pain, 10 = worst pain experienced). Pain on movement was assessed using the same verbal rating score after elevation of the affected limb to 15 degrees. If patients found elevation of the limb intolerable then it was abandoned and a score of ten was allocated.

A table SAEs is provided in Appendix 10.
There were six deaths in the trial. Four in the active group and two in the control group. This was not considered significant. Mortality in this group is approximately 10% at 30 days. Only one death occurred before a full set of primary outcome data could be obtained (SAE 4000-14, pt57) this participant was in the active group therefore she was not included in the primary analysis.

During a monitoring visit the sponsor noted that very few adverse events and serious adverse events had been reported and no adverse events were reported after February 2014. This was due to a change in reporting on initial events that were deemed to inevitably delay participants stay in hospital. Furthermore a number of SAE's were identified by the sponsor's monitor whilst reviewing the medical notes. It was identified at the time that AE and SAE data was being collected verbally during the follow up phone call from the participants of the trial and the medical notes were not being reviewed. As such the reporting of these events was reliant on the participants, who were often elderly and sometimes confused, to report these events. As such it is possible that AE's and SAE's have been under reported. Complications are common in this group and frequently result in a delay to discharge. Whilst this criticism was observed it is likely that AE/SAE events were distributed equally between the groups

There were no AEs or SAEs relating to study drugs. Ropivacaine is the hospital standard local anaesthetic agent for use in nerve catheters and is widely used outside of this study for similar purposes. It has a well-established safety record. The elastomeric pumps used for this study are only capable of administering at a fixed rate and therefore variation of dose was not possible or required.

Laboratory Evaluations.

Laboratory blood tests did not form part of the data collection for the trial.
Blood tests were done as part of the patient's routine care and if abnormalities were detected then these were reviewed to decide whether the abnormality constituted an adverse event or serious adverse event.

Statistical Analysis

Data was collected and inputted into an electronic database by the research team. Analysis was performed by Dr Rowlands and Dr Armstrong, using the latest version of IBM© SPSS© Statistics software (Copyright IBM Corporation 2012). There was no interim analysis.

No subgroup analysis was initially planned or subsequently undertaken.

Primary outcome data were cumulative dynamic pain score and cumulative ambulation score over three post-operative days. These were analysed using Mann-Whitney U tests.

Secondary outcome measures were:

- Pain scores pre operatively.
- Cumulative side effects (nausea and constipation)
- EUROQOL EQ-5D scores.
- Length of stay.
- Rehabilitation outcome (measured by New mobility score)

These were analysed using Mann-Whitney U tests or Chi squared tests as appropriate.

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One patient from each group was removed after information rendering them ineligible came to light after randomisation.

Sample size was estimated from the data for mean cumulative postoperative mobility, as measured by cumulative ambulation score(CAS), and dynamic pain scores from Foss et al 2005. A sample size of 37 participants per group would be required to detect a clinically relevant 2 point difference in mean CAS assuming a two-sided significance level of 0.05 and 80% power. For the cumulated dynamic pain score, a sample size of 67 participants per group would be required to detect a clinically relevant 2.5 point difference in mean scores between the two groups, using a 10 point pain scale. A sample size of 150 was therefore planned to allow for 10% attrition rate.

Recruitment was slow and only 141 patients were recruited in the study period. 12 patients from the active group and 11 from the control group were removed after randomisation as x-rays revealed there was no fracture. Full primary outcome data was collected on a total of 111 patients (55 active, 56 control).

Main Findings of the Study

There were no statistically significant differences in either cumulative dynamic pain scores or cumulative ambulation scores measured over the three postoperative days.

Table 1: Primary outcome measures.

Variable	Parameter	Treatment arm		P value
		Control	Active	
Total	N			
Cumulative ambulation score (CAS)	Median [IQR]	6 [5, 9]	7 [5, 10]	
	Minimum, maximum	0, 18	3, 15	0.76
Cumulative Dynamic pain score	Median [IQR]	20 [15.6-24.3]	19.5 [15.25-23.75]	0.505
	Minimum, maximum	7,30	5,30	

Variable	Parameter	Treatment arm		P value
		Control	Active	
Length of stay	Mean [SD] Median [IQR] Minimum, maximum	15.9 [10.67] 14 [9, 20] 3,57	16.2 [9.56] 13 [10, 18] 4,44	0.89
Pain on movement at 30 minutes	Median [IQR] Minimum, maximum	10 [10, 10] 2, 10	10 [8, 10] 2, 10	
Pain on movement at 60 minutes	Median [IQR] Minimum, maximum	10 [9, 10] 2, 10	10 [8, 10] 1, 10	
Pain on movement at 180 minutes	Median [IQR]	2 [1, 4]	1 [0, 3.25]	
Cumulative pain at rest score.	Median [IQR] Minimum, maximum	5 [0.5, 6.5] 0, 10	2 [0, 5] 0, 8	0.043
EuroQol EQ 5D at 30 days	Mean [SD] Median [IQR] Minimum, maximum	8.79 [2.20] 9 [7, 10] 5, 13	8.67 [2.10] 8 [7, 10] 5, 14	0.78
Constipation	Yes/No [%]	30/54 [55]	25/50 [50]	0.441
Nausea/Vomiting	Yes/No [%]	6/56 (10.7%)	5/51 (9.8%)	0.877
EuroQol EQ 5D at 3 days	Median [IQR] Minimum, maximum	10 [9, 11] 6, 14	10 [9, 10] 7, 13	0.73

Secondary outcome measures showed no statistical differences either.

Pain following hip fracture is usually severe and while early assessment and treatment of pain is recommended, nerve blocks are only suggested if regular paracetamol and opiates are failing to control pain. It is also recognised in national guidelines that use of nerve blocks should not prevent early surgical fixation.

Foss and colleagues demonstrated a significant reduction in a five-point pain scale with use of epidural analgesia which is more invasive and extensive cover than single femoral nerve block, but similarly to our study, without an overall benefit in terms of early mobilisation or hospital discharge and with an increase in nausea which we did not observe.

Several studies of various types of block for relief of pain have demonstrated efficacy but these studies have not looked at the longer term outcomes that we used.

Serious risks of nerve block are rare, and the techniques of nerve block especially with the use of ultrasound guidance are simple. Benefits to the patients with analgesia are balanced in favour of avoiding opiates in elderly frail patients who are more susceptible to the side effects of these types of drugs.

Placement of catheters which remain in place for days would be expected to increase infectious complications but none were observed in our population.

Group demographics are included in appendix 1. Groups were similar in term of age, gender, ASA status and residential status.

Information on randomisation is provided in appendix 8 In total 141 patients were randomised. After randomisation some patients were found not to have sustained PFF. These patients had initial data collected on them but were discontinued from the point of their x-ray. One patient from each group was discovered to have exclusion criteria after inclusion. In both cases it was use of long term opiates which was not discovered at trial outset. These participants were withdrawn from the study and their data was not used in the analysis. There was one death in the active group at day 2. This patient's data was not included as a full set of primary outcomes was not obtained.

Details of patients not included in the analysis are provided in appendix 2.

Conclusions

Local anaesthetic nerve blocks probably have a role to play in the multimodal management of pain in an elderly hip fracture population, certainly as an adjunct to strong opiates in the initial

management of pain in ED. Early surgery remains the mainstay of treatment both to enhance early rehabilitation and analgesia. Use of femoral nerve catheters cannot be either encouraged or discouraged based on these results.

Block of more than just the femoral nerve may be of benefit but catheter block of multiple nerves is technically difficult and requires careful attention to levels of local anaesthetic administered.

Future Research

This study is limited with regards to its blinding. Due to the nature of the intervention it was not possible to blind either the patients or the research staff to group allocation. Although other trials have done so, use of sham or placebo block was not considered ethical.
The study is under powered for the cumulative dynamic pain outcome but considering how similar the groups were statistically it is not though that even at full power there would have been a detectable difference.
Further research could look more closely at the morphine sparing nature of blocks. We did not collect data regarding opiate consumption between groups and it is possible that there were differences. That said there were no differences detected in commonly occurring side effects of strong opiate analgesics in terms of nausea or constipation.

Arrangements for Disseminating Findings

Details of study results will be published in appropriate journals if accepted. Local dissemination of results will occur through local meetings. Individual participants will not be informed of study results.

Appendices

Appendix 1: Table of Group Demographics

Appendix 2: Consort Flow Diagram

Appendix 3: Informed Consent Form

Appendix 4: Proxy Consent Form

Appendix 5: Participant Information Sheet

Appendix 6: Sample Case Report Form

Appendix 7: Audit Certificate

Appendix 8: Recruitment Study Log

Appendix 9: Details of Protocol Deviations

Appendix 10: Details of Serious Adverse Events

Appendix 11: Levobupivacaine Data Sheet

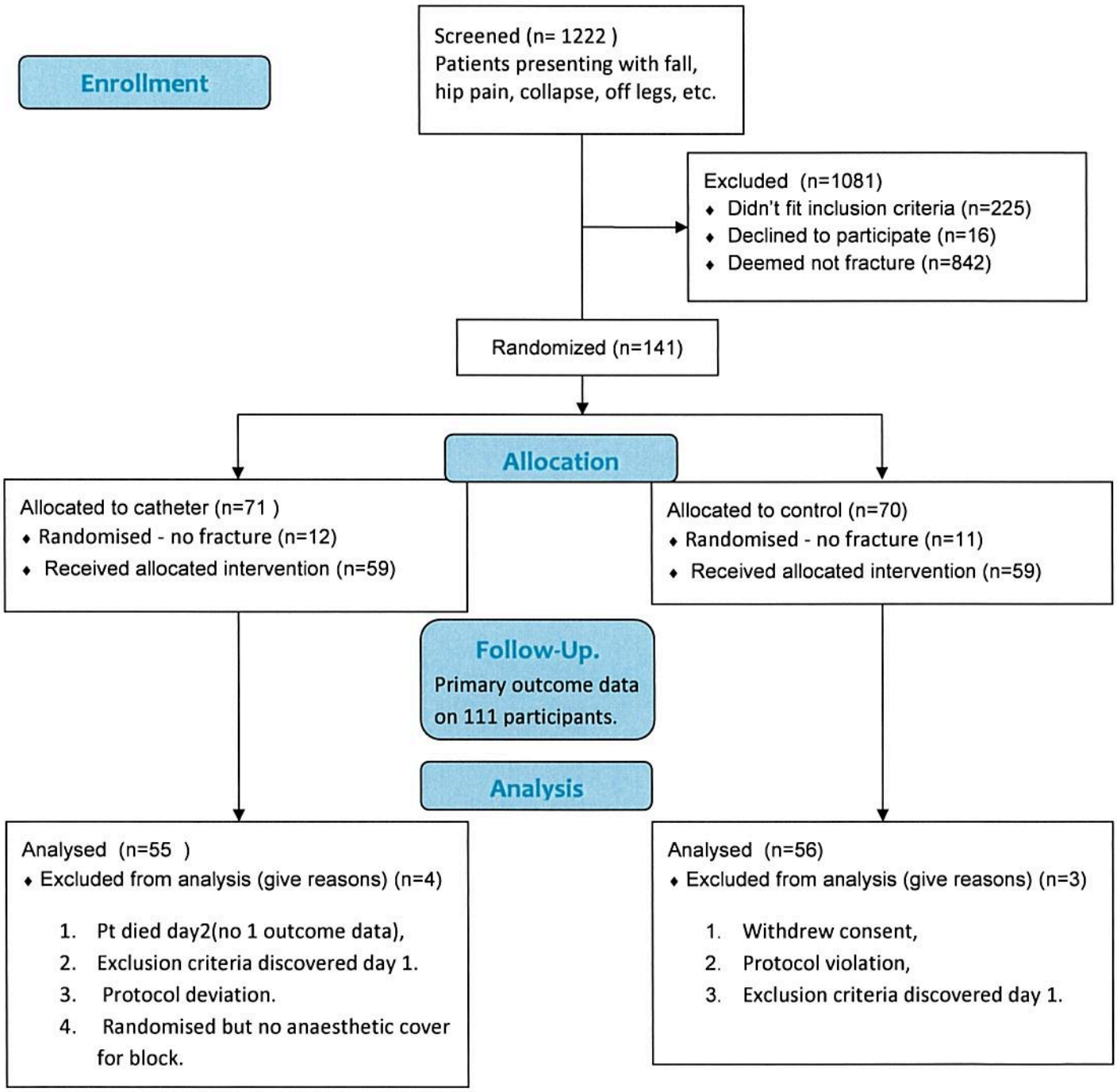
Appendix 12: Screening Document and Verbal Consent Form

Appendix 13: Figure of Catheter and Pump Insitu

Appendix 1- Table of group demographics.

Variable		Parameter	Treatment arm	
			Control	Active
Total		N		
Age at inclusion		Mean [SD]	83.9 [6.24]	83.0 [5.81]
		Median {IQR}	84 {79, 90}	83 {78, 88}
		Minimum, maximum	71, 97	73, 93
Gender	Female	N (%)	48 (76%)	54 (81%)
	Male		15 (24%)	13 (19%)
Body mass index (kg)		Mean [SD]	23.9 [3.98]	23.1 [5.96]
		Median {IQR}	24 {22, 26}	24 (20, 26.75}
		Minimum, maximum	16, 32	14, 35
Residential Status	Lives alone	N (%)	32(52.5%)	39 (58%)
	Lives with others		29 (47.5%)	28 (42%)
ASA grade	I	N (%)	3 (5%)	2 (3%)
	II		45 (71%)	40 (60%)
	III		6 (10%)	12 (18%)
	IV		0	2 (3%)
	V		0	0

Appendix 2: CONSORT Flow Diagram



FINOF (Femoral Nerve Block Intervention in Neck Of Femur Fracture) Study

PATIENT CONSENT FORM.

Patient Study number [ ]

Patient hospital sticker

NUH HOSPITAL NUMBER
DOB
ADDRESS

TELEPHONE NUMBER

Name of researcher _____

Initial box

1. I confirm that I have read and understand the information sheet dated 03/05/2011 (version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. [ ]

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. [ ]

3. I understand that relevant sections of my medical notes and data collected during the study will be looked at by members of the research team and by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records [ ]

4. I understand I may be asked to take part in a more detailed questionnaire about the study which will be recorded. [ ]

5. I agree to take part in the above study. [ ]

_____ _____

Name of participant Date Signature

_____ _____

Name of person taking consent Date Signature

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes.

Appendix 4: Proxy Consent Form

Queen's Medical Centre Campus
Health Care of Older People

FINOF (Femoral Nerve Block Intervention in Neck Of Femur Fracture) Study

PROXY CONSENT FORM.

Patient Study number ☐

Patient hospital sticker

NUH HOSPITAL NUMBER
DOB
ADDRESS

TELEPHONE NUMBER

Name of researcher _____

Initial box

1. I confirm that I have read and understand the information sheet dated 03/05/2011(version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that their participation is voluntary and that I am free to withdraw them any time without giving any reason, without their medical care or legal rights being affected. ☐

3. I understand that relevant sections of their medical notes and data collected during the study will be looked at by members of the research team and by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to the patient's records ☐

4. I agree on the patient's behalf for them to take part in the above study. ☐

_____ _____
Name of proxy Date Signature

_____ _____
Name of person taking consent Date Signature

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes.

FINOF Study

Nottingham University Hospitals NHS
NHS Trust

FINOF (Femoral Nerve Block Intervention in Neck Of Femur Fracture) Study

Investigators:

Prof Opinder Sahota	*Professor In Orthogeriatric Medicine & Consultant Physician*
Dr Iain Moppett	*Associate Professor / Consultant Anaesthetist*
Dr Nigel Bedforth	*Consultant Anaesthetist*
Dr Catherine Vass	*Lecturer School of Nursing*
Dr Nick Allcock	*Associate Professor School of Nursing*
Dr Sarah Armstrong	*Associate Professor in Medical Statistics*

PATIENT INFORMATION SHEET.

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Hip fracture is one of the most serious injuries that occur in older people. These fractures are very painful and usually require a powerful pain killing drug such as morphine, which has adverse side effects. Common side-effects include sickness, vomiting, constipation, and sometimes confusion. Patients then may feel too sick for treatment, including physiotherapy, and may remain in hospital for longer. This can lead to complications and a poor recovery which has an effect upon ability to walk and get around.

Another choice of pain relief is to numb the nerves around the hip during the repair of hip fracture in the operating theatre. This has none of the side effects mentioned above. No study has been done to find out whether numbing of the main nerve in the leg (femoral nerve) has a better result for overall pain control, and a better effect on rehabilitation and recovery compared to the standard pain relief.

Why is the study being done?

We want to carry out a well planned study to test whether pain relief by nerve block compared to usual pain relief will result in fewer drug side effects, earlier recovery, shorter length of stay in hospital and improved quality of life for patients after surgery for a hip fracture.

Why have I been chosen?
You are going to have an operation to repair your broken hip. We are undertaking a study of 150 patients who are going to have their fractured hip repaired by an operation.

Do I have to take part?
It is up to you to decide whether or not you take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw from the study at any time, without giving a reason, and your usual treatment will not be affected. If you do not wish to take part, it will not affect the standard of care you receive.

What will happen to me if I take part?
Sometimes we don't know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly). You and the surgeon doing the operation will know which method is being used. You will have an equal chance of being in either group.

The study will start in the Emergency department and continue through the operating theatre, and on the ward where you will recover.

If you consent, we will use a computer to tell us which treatment group you will join. You will either receive usual treatment or the nerve block treatment. Both groups of patients will receive the same standard of clinical care.

If you consent and the computer puts you in the nerve block group, you will firstly receive a nerve block in the Emergency Department. This consists of an injection around your femoral nerve (the nerve in the groin region at the top of your leg) using a needle smaller than a blood-taking needle. The injection is fairly painless. Soon after you are brought into the hospital from the Emergency department, we will place a small plastic tube (catheter) in the same place as the first injection. We can then continuously administer local anaesthetic slowly around your femoral nerve. This will continue for 48 hours after your operation.
We will also invite a small number of people in the nerve block group to talk to us in more detail about their experiences of the nerve block and their recovery during the first four days in hospital (10 out of 75 patients).

The interviews will be conducted in private by a member of the research team, last about one hour and be recorded. We may use direct quotes from the interviews in reports and publications but all the data will be anonymised and not identifiable.

What do I have to do?
There are no restrictions on what you do beyond the usual requirements for surgery.
We will visit you on the first, second and third day after your operation in the hospital ward , when we will ask you some questions about how you feel and how you are recovering. We will also telephone you at your place of residence on day 30 after your operation to ask some questions about your recovery. The study will then stop.

What are the drugs and procedure being tested?
We use local anaesthetic drugs (bupivacaine and ropivacaine) that are in common use around the world. Femoral nerve blocks are also well tested in patients having operations on their hip and leg, but we do not know how well it works in patients who are having operations following a hip fracture.

What are the side effects of the procedure received when taking part?
Nerve blocks are in general, very safe. You may notice that the leg feels a little heavy and tingly or numb. This is the normal effect of a nerve block.

Possible side effects of femoral nerve block (from the most common to the most rare) are as follows: bleeding and bruising, inadvertent injection into the blood stream causing collapse and cardiac arrest (this can occur in up to 1 in 1000 blocks performed), damage to the femoral nerve which can occur in about 1 in 5000 to 10 000 blocks, and infection (however this is very rare).

What are the possible advantages of taking part?
We cannot promise the study will help you, but the information we get from this study will help us to know if femoral nerve block pain relief is beneficial to patients recovering after hip fracture surgery compared to normal treatments, but we do not know this yet. Our hope is that patients having this treatment will suffer less pain during their hospital stay and recover more quickly.

What are the possible disadvantages and risks of taking part?
We do not anticipate any significant risk to you from taking part other than the risks of surgery and anaesthesia themselves.
The nerve block catheter will be inserted using local anaesthetic so there should be only very mild discomfort due to the local anaesthetic itself. It will be placed under ultrasound guidance to minimize any risk of damage to the surrounding area. The nerve block catheter will only be in place for a very short time, so complications such as infection and damage to the blood vessels are very unlikely.

When will the study stop?
Your participation in the study will end when we telephone you near to day 30 after your hip fracture operation.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

Complaints:
If you have a concern about any aspect of this study, you should contact the Professor Opinder Sahota (0115 9249924 x 66325), who will do his best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital Patient Advice and Liaison Service. Freephone QMC campus: 0800 183 0204.

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you will have your name and address removed and replaced with a study number so that the information we collect from records and questionnaires is anonymous and you cannot be recognised.

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from regulatory authorities or from the Nottingham University Hospitals NHS Trust. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty. Any reports or publications resulting from the study will contain information and outcomes from the study, but all the participants' names will be removed. Data files will be stored in a locked cupboard and on a hospital

computer with password access. If you withdraw from the study at any time, only the data we have collected so far will be used, anonymous and stored as detailed above.

What will happen to the results of the research study?
The results will be published in scientific journals and presented at meetings. These results will contain information and outcomes from the study, but all the participants' names will be removed. You will not be identified in any report or publication in anyway.

Who is organising the research?

The investigators are employees of the Nottingham University Hospitals NHS Trust and members of the University Department of Anaesthesia and School of Nursing.

The study is funded by the Department of Health under its Research for Patient Benefit programme.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by Nottingham Research Ethics Committee 2.

Thank you for considering taking part in this study.

Contact Details

You may contact: Professor Opinder Sahota or Dr Iain Moppett

By phone: 0115 924 9924 Ext. 66325 or 0115 924 9924 Ext. 61195

By email: opinder.sahota@nuh.nhs.uk or iain.moppett@nottingham.ac.uk

By post:

Health Care of the Older Person
Queens Medical Centre
Nottingham University Hospitals NHS Trust
Derby Road
Nottingham
NG7 2UH

University Dept. of Anaesthesia
C Floor, East Block
Queens Medical Centre
Derby Road
Nottingham
NG7 2UH

Nottingham University Hospitals NHS
NHS Trust

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture) Study

Ethics Ref:	**10/H0408/113**
R&D Reference:	**10HC005**
Eudract Number:	**2010-023871-25**
Funder:	**NIHR-RfPB**

STUDY NUMBER

Chief Investigators:	**Professor Opinder Sahota**
Investigators:	**Dr Iain Moppett, Dr Nigel Bedforth, Dr Nick Allcock, Dr Catherine Vass, Dr Sarah Armstrong**
Patient Representatives:	**Ms Angela Thornhill, Mr Mick Holmes**

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host NHS Trust (s), regulatory authorities, and members of the Research Ethics Committee.

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

ASSESSOR

CONFUSION ASSESSMENT SCORE (CAM)

DATE	ADMISSION SCORE

Comments

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

)EMOGRAPHICS ON ADMISSION

PATIENT STUDY NUMBER

	Dept.	Assessor	Date

Date of Birth **Age** **Gender** **Male / Female**

Lives alone or with husband / wife / partner / carer / friend / family

Accommodation / Bungalow / House / Flat / other

Comments:

Weight **Height** **BMI Score**

New Mobility Score

ASA Grading

Grade	Status
I	A normal healthy patient. The process for which the operation is being performed is localised and causes no systemic upset.
II	Mild systemic disease. All patients older than 80 years are put in this category.
III	Severe systemic disease. This from any cause that imposes a definite functional limitation on their activity e.g. chronic obstructive pulmonary disease.
IV	Incapacitating systemic disease which is a constant threat to life.
V	A moribund patient unlikely to survive 24 hours with or without surgery.

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

PAIN SCORE

Pain at rest and on movement (dynamic) will be assessed using the 10 point numerical pain rating scale with 0 indicating no pain and 10 the worst imaginable pain

Base line Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15° Flexion	0	1	2	3	4	5	6	7	8	9	10

COMMENTS

30 Minutes Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15° Flexion	0	1	2	3	4	5	6	7	8	9	10

COMMENTS

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

60 Minutes Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15° Flexion	0	1	2	3	4	5	6	7	8	9	10

COMMENTS

180 Minutes Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15° Flexion	0	1	2	3	4	5	6	7	8	9	10

COMMENTS

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture).

PATIENT STUDY NUMBER [ ] **DATE** **BASELINE** **ASSESSOR**

EUROQOL 5D QUESTIONNAIRE. By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

MOBILITY	TICK
I have no problems in walking about	
I have some problems in walking about	
I am confined to bed	
SELF-CARE	
I have no problems with self-care	
I have some problems washing or dressing myself	
I am unable to wash or dress myself	
USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure)*	
I have no problems performing my usual activities	
I have some problems performing my usual activities	
I am unable to perform my usual activities	
PAIN/DISCOMFORT	
I have no pain or discomfort	
I have moderate pain or discomfort	
I have extreme pain or discomfort	
ANXIETY/DEPRESSION	
I am not anxious or depressed	
I am moderately anxious or depressed	
I am extremely anxious or depressed	

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

NAUSEA/VOMITING SCORE

PATIENT STUDY NUMBER

	Date	Assessor

Baseline

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetics. Notify medical officer promptly

Circle which best describes the patient at the time

Nausea/Vomiting Score

Date Assessor

30 Minutes

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetics. Notify medical officer promptly

Circle which best describes the patient at the time

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

NAUSEA/VOMITING SCORE

Patient I.D Date Assessor

60 Minutes

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetics. Notify medical officer promptly

180 Minutes Date Assessor

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetics. Notify medical officer promptly

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

'ATIENT
STUDY NUMBER

Assessor

BLOCK ASSESSMENT

Sensory deficit to be defined as present if reduced sensation over the patella when sprayed with ethyl chloride as compare to unaffected limb.

Paraesthesia defined as the subjective feeling of pins and needles or numbness of the thigh or medial aspect of lower leg.

	30mins	60mins	180mins
Date			
Sensory deficit			
Paraesthesia			

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture)

PATIENT STUDY NUMBER | Date | Assessor

OPERATIVE DETAILS

Type of Operation

Grade of 1st Surgeon Cons SpR ST 5-7 Staff Grade Other

Grade of Anaesthetist Cons SpR ST 5-7 Staff Grade Other

Time of Operation o'clock

Duration of Operation

GA Spinal

Admission Time Exact

Admission Time to Randomisation mins

Time from admission to block mins OR IV morphine if given mins

Time from admission to catheter mins OR admission to ward mins

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

BLOOD INVESTIGATIONS

	Admission	Day 1 Post op	Day 2 Post op	Day 3 Post op
Date				
HB				
WCC				
Ur				
Cr				

Blood Transfused Units total admission until Day 3

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

Ward

PATIENT STUDY NUMBER

PAIN SCORE

Pain at rest and on movement (dynamic) will be assessed using the 10 point numerical pain rating scale with 0 indicating no pain and 10 the worst imaginable pain

Post op day 1 Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15°Flexion	0	1	2	3	4	5	6	7	8	9	10

Post op day 2 Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15°Flexion	0	1	2	3	4	5	6	7	8	9	10

Post op day 3 Date Assessor

	score										
Pain on rest	0	1	2	3	4	5	6	7	8	9	10
Pain on movement 15°Flexion	0	1	2	3	4	5	6	7	8	9	10

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

Ward

PATIENT STUDY NUMBER

BLOCK ASSESSMENT

Sensory deficit to be defined as present if reduced sensation over the patella when sprayed with ethyl chloride as compare to unaffected limb.

Motor deficit to be defined as

1 Normal
2 Reduced but able to fully extend knee when sitting on chair
3 Reduced and unable to fully extend knee when sitting upright in chair
4 Total motor weakness. No movement of quadriceps

Paraesthesia defined as the subjective feeling of pins and needles or numbness of the thigh or medial aspect of lower leg.

	Post op Day 1	Post Op Day 2	Post Op Day 3
Date			
Sensory deficit			
Motor deficit			
Paraesthesia			
Assessor			

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

Ward

CONFUSION ASSESSMENT SCORE (CAM)

	Post Op Day 1	Post Op Day 2	Post Op Day 3
Date			
Score			
Assessor Signature			

Comments

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture)

PATIENT STUDY NUMBER

Ward

CUMULATION AMBULATION SCORE.

POST OP DAY 1 Date Assessor

	Activity and Score		
Function	Transfer from supine-to-sitting-to-supine.	Transfer from sitting-to-standing-to-sitting	Walking (with appropriate walking aid)
Able to perform function independently **2**			
Only able to perform function with assistance from one or two people **1**			
Unable to perform function despite assistance from two people **0**			

POST OP DAY 2 Date Assessor

	Activity and Score		
Function	Transfer from supine-to-sitting-to-supine.	Transfer from sitting-to-standing-to-sitting	Walking (with appropriate walking aid)
Able to perform function independently **2**			
Only able to perform function with assistance from one or two people **1**			
Unable to perform function despite assistance from two people **0**			

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture)

PATIENT STUDY NUMBER

POST OP DAY 3* **Date** **Assessor**

	Activity and Score		
Function	Transfer from supine-to-sitting-to-supine.	Transfer from sitting-to-standing-to-sitting	Walking (with appropriate walking aid)
Able to perform function independently **2**			
Only able to perform function with assistance from one or two people **1**			
Unable to perform function despite assistance from two people **0**			

TOTAL SCORE FOR ALL 3 DAYS POST OP

*Day 3 only

The total score for 3 days to be added together.

Reasons why patient is unable to perform one of the above activities independently are/is due to;

PAIN	
MOTOR BLOCKADE	
NAUSEA/VOMITING	
DIZZINESS	
COGNITIVE DYSFUNCTION	
OTHER	

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

NAUSEA/VOMITING SCORE

PATIENT STUDY NUMBER

	Date	Assessor	Ward

Day 1 post op

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetics. Notify medical officer promptly

Circle which best describes the patient at the time

Nausea/Vomiting Score

Date Assessor

Day 2 post op

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetic. Notify medical officer promptly

Circle which best describes the patient at the time

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

NAUSEA/VOMITING SCORE

Date Assessor Ward

Day 3 post op

0 Nil nausea or vomiting

1 Mild nausea no treatment requested

2 Nausea only – give antiemetics as prescribed until resolved

3 Vomiting – give antiemetics as prescribed until resolved

4 Nausea/vomiting that doesn't respond to antiemetics. Notify medical officer promptly

Circle which best describes the patient at the time

PATIENT STUDY NUMBER

Ward

DAILY CALORIFIC INTAKE

	DATE	TOTAL CALORIFIC INTAKE	PROTEIN	COMMENTS	ASSESSSOR SIGNATURE
DAY 1					
DAY 2					
DAY 3					

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

PATIENT STUDY NUMBER

Ward

BOWEL FREQUENCY AND TYPE CHART (using Bristol Stool Chart)

	Post op Day 1	Post op Day 2	Post op Day3
Date			
Frequency			
Type			
Assessor			

EUROQOL 5D QUESTIONNAIRE

Patient Study No. ☐ **Date:**_____ **Assessor:**_____

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

MOBILITY	**TICK**
I have no problems in walking about	
I have some problems in walking about	
I am confined to bed	
SELF-CARE	
I have no problems with self-care	
I have some problems washing or dressing myself	
I am unable to wash or dress myself	
USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure)*	
I have no problems performing my usual activities	
I have some problems performing my usual activities	
I am unable to perform my usual activities	
PAIN/DISCOMFORT	
I have no pain or discomfort	
I have moderate pain or discomfort	
I have extreme pain or discomfort	
ANXIETY/DEPRESSION	
I am not anxious or depressed	
I am moderately anxious or depressed	
I am extremely anxious or depressed	

PATIENT
STUDY NUMBER [ ] Date Assessor

Day 30 Post op Phone call

NEW MOBILITY SCORE

	Ability and Score			
Mobility	No difficulty (3)	With an aid (2)	With help from another person (1)	Not at all (0)
Able to get about the house				
Able to get out of the house				
Able to go shopping				

Discharge Date and Time

Length of stay in hospital?

Location Discharged to?

Details of Phone call

Late Adverse events

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture).

PATIENT STUDY NUMBER | | **DATE** **ASSESSOR**

EUROQOL 5D QUESTIONNAIRE. By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

30 DAY FOLLOW UP

MOBILITY	**TICK**
I have no problems in walking about	
I have some problems in walking about	
I am confined to bed	
SELF-CARE	
I have no problems with self-care	
I have some problems washing or dressing myself	
I am unable to wash or dress myself	
USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure)*	
I have no problems performing my usual activities	
I have some problems performing my usual activities	
I am unable to perform my usual activities	
PAIN/DISCOMFORT	
I have no pain or discomfort	
I have moderate pain or discomfort	
I have extreme pain or discomfort	
ANXIETY/DEPRESSION	
I am not anxious or depressed	
I am moderately anxious or depressed	
I am extremely anxious or depressed	

Nottingham University Hospitals NHS
NHS Trust

Audit Certificate

Audit Type:	Pharmacovigilance Systems Audit
Audit Reference Number:	201408 - 10HC005 FINOF
Audit Scope:	To verify compliance of study pharmacovigilance systems - Serious Adverse Event (SAE) reporting and Safety Reporting systems
Auditee Details:	Professor Opinder Sahota - Chief Investigator
Audit Address:	FINOF Office, B Floor, South Block Healthcare of Older People
Date(s) Audit Conducted:	26th November and 5th December 2014
Auditor(s):	Melanie Boulter QA/GCP Auditor, Research and Innovation

This certificate verifies that the above audit has been performed by Nottingham University Hospitals NHS Trust Research and Innovation department and should be retained on file to serve as evidence an audit took place. This certificate is not a compliance statement.

Audit Certificate Issued by:	Melanie Boulter QA/GCP Auditor, Research and Innovation
Signature:	
Date:	26th January 2015

Original Audit Certificate Issued to:	Professor Opinder Sahota, Healthcare of Older People
Copy Audit Certificate Issued to:	Dr Sarah Skirrow Research and Innovation, NUH

ndix 8: Recruitment Log

tient ntifier	Sex	Group.	Date Recruited (Verbal Consent)	Day 1 Post-op	Day 2 Post-op	Day 3 Post-op	30-Day Follow-up	Notes	Deceased Date	Protocol Deviation identifier	SAE identifier
1	F	A	06-Jan-12	07-Jan-13	08-Jan-13	09-Jan-13	07-Feb-12				
2	M	C	20-Mar-12	22-Mar-12	23-Mar-12	24-Mar-12	19-Apr-12				
3	M	C	01-May-12	03-May-12	04-May-12	05-May-12	DECEASED		08-May-12		4000-01
4	F	C	16-May-12	18-May-12	19-May-12	20-May-12	DECEASED		31-May-12		4000-02
5	F	A	30-May-12	01-Jun-12	02-Jun-12	03-Jun-12	02-Jul-12				
6	M	A	11-Jul-12	14-Jul-12	15-Jul-12	16-Jul-12	13-Aug-12				
7	F	A	23-Jul-12	25-Jul-12	26-Jul-12	27-Jul-12	23-Aug-12				
8	F	A	24-Jul-12	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
9	F	C	31-Jul-12	01-Aug-12	02-Aug-12	03-Aug-12	03-Sep-12				4000-03
10	M	C	15-Aug-12	17-Aug-12	18-Aug-12	19-Aug-12	19-Sep-12				4000-04
11	F	C	04-Sep-12	06-Sep-12	07-Aug-12	08-Jul-12	05-Oct-12				
12	M	A	04-Sep-12	06-Sep-12	07-Aug-12	08-Jul-12	05-Oct-12				4000-05
13	F	A	05-Sep-12	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
14	M	C	05-Sep-12	07-Sep-12	08-Sep-12	09-Sep-12	05-Oct-12				4000-06 & 4000-17
15	F	C	11-Sep-12	13-Sep-12	14-Sep-12	15-Sep-12	12-Oct-12		18-Oct-12		
16	F	A	13-Sep-12	15-Sep-12	16-Sep-12	17-Sep-12	15-Oct-12				
17	M	A	13-Sep-12	14-Sep-12	15-Sep-12	16-Sep-12	15-Oct-12				
18	F	C	01-Oct-12	02-Oct-12	03-Oct-12	04-Oct-12	07-Nov-12			7	
19	F	C	01-Oct-12	03-Oct-12	04-Oct-12	05-Oct-12	05-Nov-12				
20	M	A	02-Oct-12	WITHDRAWN	-	-	-	Withdrawn: Pt was on pre fracture opiods.		6	
21	F	C	09-Oct-12	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
22	F	A	09-Oct-12	11-Oct-12	12-Oct-12	13-Oct-12	09-Nov-12				
23	F	A	09-Oct-12	11-Oct-12	12-Oct-12	13-Oct-12	09-Nov-12				
24	M	C	11-Oct-12	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
25	F	A	11-Oct-12	13-Oct-12	14-Oct-12	15-Oct-12	DECEASED		18-Oct-13		4000-07
26	F	C	22-Oct-12	24-Oct-12	25-Oct-12	26-Oct-12	22-Nov-12				
27	F	A	25-Oct-12	28-Oct-12	29-Oct-12	30-Oct-12	28-Nov-12				4000-08
28	F	C	29-Oct-12	31-Oct-12	01-Nov-12	02-Nov-12	30-Nov-12				
29	F	C	02-Nov-12	04-Nov-12	05-Nov-12	06-Nov-12	04-Dec-12				
30	F	A	05-Nov-12	07-Nov-12	08-Nov-12	09-Nov-12	11-Dec-12				
31	F	A	07-Nov-12	09-Nov-12	10-Nov-12	11-Nov-12	11-Dec-12				
32	F	C	16-Nov-12	18-Nov-12	19-Nov-12	20-Nov-12	20-Dec-12				
33	F	A	27-Nov-12	28-Nov-12	29-Nov-12	30-Nov-12	07-Jan-13			3	
34	F	C	05-Dec-12	07-Dec-12	08-Dec-12	09-Dec-12	07-Jan-13				
35	M	C	17-Dec-12	20-Dec-12	21-Dec-12	WITHDRAWN	-	Withdrawn: Became confused. Validity of result in question.		5	
36	M	C	07-Jan-13	08-Jan-13	09-Jan-13	10-Jan-13	08-Feb-13				4000-09
37	M	A	10-Jan-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
38	F	A	16-Jan-13	DISCONTINUED	-	-	-	Catheter disloged. Study team not made aware until too late.			
39	F	A	17-Jan-13	19-Jan-13	20-Jan-13	DECEASED	DECEASED		21-Jan-13		4000-10
40	F	C	23-Jan-13	25-Jan-13	26-Jan-13	27-Jan-13	DECEASED		19-Feb-13		4000-11
41	F	A	28-Jan-13	30-Jan-13	31-Jan-13	01-Feb-13	28-Feb-13				
42	F	A	04-Feb-13	06-Feb-13	07-Feb-13	08-Feb-13	06-Mar-13				

43	F	A	06-Feb-13	08-Feb-13	09-Feb-13	10-Feb-13	DECEASED		27-Feb-13		4000-12
44	F	A	13-Feb-13	15-Feb-13	16-Feb-13	17-Feb-13	14-Mar-13				
45	F	C	16-Feb-13	16-Feb-13	17-Feb-13	18-Feb-13	15-Mar-13				
46	M	C	22-Feb-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
47	F	A	28-Feb-13	02-Mar-13	03-Mar-13	04-Mar-13	01-Apr-13				
48	F	C	28-Feb-13	02-Mar-13	03-Mar-13	04-Mar-13	02-Apr-13				
49	F	C	06-Mar-13	08-Mar-13	09-Mar-13	10-Mar-13	09-Apr-13				
50	F	A	11-Mar-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
51	F	C	20-Mar-13	22-Mar-13	23-Mar-13	24-Mar-13	23-Apr-13				
52	F	C	27-Mar-13	29-Mar-13	30-Mar-13	31-Mar-13	01-May-13				
53	F	C	08-Apr-13	10-Apr-13	11-Apr-13	12-Apr-13	09-May-13				
54	F	A	08-Apr-13	10-Apr-13	11-Apr-13	12-Apr-13	DECEASED		26-Apr-13		4000-13 & 4000-15
55	F	A	09-Apr-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
56	F	A	11-Apr-13	12-Apr-13	13-Apr-13	14-Mar-13	14-May-13				
57	F	A	29-Apr-13	01-May-13	SUSPENDED	-	DECEASED		07-May-13	4	4000-14
58	F	C	30-Apr-13	02-May-13	03-May-13	04-May-13	WITHDRAWN			1	
59	F	A	01-May-13	03-May-13	04-May-13	05-May-13	04-Jun-13				
60	F	A	03-May-13	05-May-13	06-May-13	07-May-13	04-Jun-13				
61	F	A	20-May-13	22-May-13	23-May-13	24-May-13	24-Jun-13				
62	F	C	20-May-13	22-May-13	23-May-13	24-May-13	24-Jun-13				
63	M	C	03-Jun-13	05-Jun-13	06-Jun-13	07-Jun-13	08-Jul-13				4000-16
64	F	C	03-Jun-13	05-Jun-13	06-Jun-13	07-Jun-13	08-Jul-13				
65	F	C	10-Jun-13	WITHDRAWN	-	-	-	Withdrawn: Pt withdrew consent 11-Jun-13			
66	F	A	10-Jun-13	12-Jun-13	13-Jun-13	14-Jun-13	15-Jul-13				
67	F	C	17-Jun-13	19-Jun-13	20-Jun-13	21-Jun-13	21-Jul-13				
68	F	A	17-Jun-13	20-Jun-13	21-Jun-13	22-Jun-13	21-Jul-13			2	
69	F	A	27-Jun-13	29-Jun-13	30-Jun-13	01-Jul-13	30-Jul-13				
70	F	C	02-Jul-13	04-Jul-13	05-Jan-00	06-Jul-13	06-Aug-13				
71	F	A	17-Jul-13	20-Jul-13	21-Jul-13	22-Jul-13	19-Aug-13				
72	F	C	25-Jul-13	27-Jul-13	28-Jul-13	29-Jul-13	27-Aug-13				
73	M	C	29-Jul-13	31-Jul-13	01-Aug-13	02-Aug-13	UNK	Date missing for 30 day follow up but full data available			
74	F	A	30-Jul-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
75	M	C	05-Aug-13	07-Aug-13	WITHDRAWN	-	-	Patient received a nerve catheter despite being in the control group (decision of operative anaesthetist). Subsequently became confused and pulled catheter out. Removed from primary analysis as no full data set and not clearly in one group.		8	
76	M	A	06-Aug-13	08-Aug-13	09-Aug-13	10-Aug-13	10-Sep-13				
77	F	C	13-Aug-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
78	F	A	14-Aug-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
79	M	C	30-Aug-13	01-Sep-13	02-Sep-13	03-Sep-13	02-Oct-13			9	
80	F	A	10-Sep-13	12-Sep-13	13-Sep-13	14-Sep-13	09-Oct-13				
81	F	A	30-Oct-13	02-Oct-13	03-Oct-13	04-Oct-13	01-Nov-13			10	
82	F	C	10-Oct-13	12-Oct-13	13-Oct-13	14-Oct-13	13-Nov-13				
83	F	A	11-Oct-13	13-Oct-13	14-Oct-13	15-Oct-13	12-Nov-13			11	
84	F	C	18-Oct-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
85	F	C	21-Oct-13	23-Oct-13	24-Oct-13	25-Oct-13	22-Nov-13				
86	F	A	23-Oct-13	WITHDRAWN	-	-	-	Withdrawn: No anaesthetist available			

87	F	A	24-Oct-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
88	F	A	04-Nov-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
89	F	C	07-Nov-13	09-Nov-13	10-Nov-13	11-Nov-13	N/A	Lost to follow up			
90	F	C	11-Nov-13	13-Nov-13	14-Nov-13	15-Nov-13	10-Dec-13				
91	F	C	12-Nov-13	14-Nov-13	15-Nov-13	16-Nov-13	10-Dec-13				
92	F	A	19-Nov-13	21-Nov-13	22-Nov-13	23-Nov-13	17-Dec-13			12	
93	F	A	20-Nov-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
94	M	C	21-Nov-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
95	F	A	22-Nov-13	24-Nov-13	25-Nov-13	26-Nov-13	03-Jan-14			13,15	
96	M	C	02-Dec-13	04-Dec-13	05-Dec-13	06-Dec-13	03-Jan-14			14	
97	F	A	05-Dec-13	07-Dec-13	08-Dec-13	09-Dec-13	10-Oct-14				
98	F	C	09-Dec-13	11-Dec-13	12-Dec-13	13-Dec-13	03-Jan-14				
99	F	C	10-Dec-13	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
100	F	C	12-Dec-13	14-Dec-13	15-Dec-13	16-Dec-13	N/A	Lost to follow up			
101	M	A	16-Dec-13	18-Dec-13	19-Dec-13	20-Dec-13	DECEASED		18-Jan-14	30	4000-25
102	F	C	06-Jan-14	08-Jan-14	09-Jan-14	10-Jan-14	03-Feb-14				
103	F	C	20-Jan-14	22-Jan-14	23-Jan-14	24-Jan-14	17-Feb-14				4000-18, 4000-19 & 4000-20
104	F	C	03-Feb-14	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
105	F	C	03-Feb-14	05-Feb-14	06-Feb-14	07-Feb-14	05-Mar-14				
106	M	A	18-Feb-14	20-Feb-14	21-Feb-14	22-Feb-14	18-Mar-14				
107	F	A	19-Feb-14	21-Feb-14	22-Feb-14	23-Feb-14	21-Mar-14			17	
108	F	A	19-Feb-14	21-Feb-14	22-Feb-14	23-Feb-14	28-Mar-14			16,20	
109	F	A	26-Feb-14	28-Feb-14	01-Mar-13	02-Mar-14	28-Mar-14			18	
110	F	C	04-Mar-14	06-Mar-14	07-Mar-14	08-Mar-14	01-Apr-14				
111	F	C	04-Mar-14	06-Mar-14	07-Mar-14	08-Mar-14	01-Apr-14				4000-21
112	M	A	10-Mar-14	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
113	F	A	17-Mar-14	19-Mar-14	20-Mar-14	21-Mar-14	24-Apr-14			21	
114	M	A	24-Mar-14	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
115	F	C	25-Mar-14	28-Mar-14	29-Mar-14	30-Mar-14	25-Apr-14				4000-22
116	F	A	26-Mar-14	WITHDRAWN	-	-	-	Patient withdrawn due to protocol deviation.		19	
117	M	A	26-Mar-14	28-Mar-14	29-Mar-14	30-Mar-14	25-Apr-14				
118	F	C	03-Apr-14	06-Apr-14	07-Apr-14	08-Apr-14	N/A	Lost to follow up			
119	F	A	03-Apr-14	05-Apr-14	06-Apr-14	07-Apr-14	13-May-14			23	
120	F	C	29-Apr-14	01-May-14	02-May-14	03-May-14	28-May-14				
121	M	C	30-Apr-14	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
122	F	A	01-May-14	03-May-14	04-May-14	05-May-14	02-Jun-14			22	
123	M	A	20-May-14	22-May-14	23-May-14	24-May-14	-	Pt unreachable despite many attempts.			
124	M	C	20-May-14	23-May-14	24-May-14	25-May-14	23-Jun-14				
125	F	C	09-Jun-14	11-Jun-14	12-Jun-14	13-Jun-14	-	Withdrawn: No #NOF			
126	M	N/A	16-Jun-14	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
127	F	A	24-Jun-14	27-Jun-14	28-Jun-14	29-Jun-14	24-Jul-14				
128	F	C	07-Jul-14	11-Jul-14	12-Jul-14	13-Jul-14	11-Aug-14				
129	F	C	11-Jul-14	14-Jul-14	15-Jul-14	16-Jul-14	13-Aug-14				
130	F	A	29-Jul-14	31-Jul-14	01-Aug-14	02-Aug-14	27-Aug-14			24	
131	M	C	04-Aug-14	WITHDRAWN	-	-	-	Withdrawn: No #NOF			
132	M	A	08-Aug-14	10-Aug-14	11-Aug-14	12-Aug-14	15-Sep-14				
133	F	A	18-Aug-14	20-Aug-14	21-Aug-14	22-Aug-14	-	30day follow up not completed. No reason given.		33	
134	F	C	22.08.2014	24-Aug-14	25-Aug-14	26-Aug-14	23-Sep-14			32	
135	F	A	17-Sep-14	19-Sep-14	20-Sep-14	21-Sep-14	19-Oct-14			25	
136	M	C	08-Oct-14	10-Oct-14	11-Oct-14	12-Oct-14	09-Nov-14			26,35	4000-23 & 4000-27

137	F	C	13-Oct-14	15-Oct-14	16-Oct-14	17-Oct-14	19-Nov-14			31	
138	F	A	07-Nov-14	09-Nov-14	10-Nov-14	11-Nov-14	11-Dec-14			27	
139	F	A	12-Nov-14	14-Nov-14	15-Nov-14	16-Nov-14	11-Dec-14				
140	M	A	19-Nov-14	21-Nov-14	22-Nov-14	23-Nov-14	22-Dec-14			28,29,34	4000-24 & 4000-28
141	F	C	01-Dec-14	03-Dec-14	04-Dec-14	05-Dec-14	05-Jan-15			36	4000-26

Deviation Number	Date Deviation Identified	Participant Identifier	Brief Description of Deviation	Date Deviation Reported to Sponsor
001	01-May-2013	CS58	Patient was recruited into the FINOF trial but it transpired that the patient had already been recruited into another study.	11-Jun-2013
002	20-Jun-2013	VC68	Patient had femoral nerve catheter removed after only 24 hours instead of the required 48 hours.	01-Jul-2013
003	27-Jun-2013	SG33	30 day follow up was not performed within +/- 5 day window	20-Nov-2013
004	27-Jun-2013	KK57	Patient's day 2 and day 3 post op assessments could not be carried out as patient was unarousable. In addition research fellow signed proxy consent was proxy and person taking proxy consent, when the patients clinician should have been the proxy	20-Nov-2013
005	27-Jun-2013	FW35	Patient was withdrawn by research assistant due to confusion as such day 3 assessments were not performed, according to protocol day 30 follow up telephone call should have been performed regardless and it was not	20-Nov-2013
006	27-Jun-2013	SS20	Patient was taking pre-fracture opioids which the research team were not informed about (exclusion criterion), patient was randomised but later found to be ineligible.	20-Nov-2013
007	01-Aug-2013	DL18	30 day follow up was not performed within +/- 5 day window	19-Feb-2014
008	07-Aug-2013	HB75	Patient randomised to control group but received femoral nerve catheter as part of anaesthetic for hip surgery.	12-Aug-2013
009	03-Sep-2013	JP79	Patient entered into study on Friday 30/Aug/2013 and operation was on Saturday. Written consent due Sunday but no one available, patient seen on 03-Sep-2013 and was noted to be confused and unable to consent	25-Sep-2014
010	02-Oct-2013	PL81	Patient pulled out catheter during night due to confusion	02-Oct-2013
011	13-Oct-2013	JS83	Patient became confused and pulled out nerve catheter.	15-Oct-2013
012	19-Nov-2013	HL92	Research team has used new PIS and consent forms prior to their approval	09-Jan-2015
013	25-Nov-2013	AS95	Usual study staff not available over the weekend, pump required refill but no one could access FINOF drug cupboard, as such pump changed from study pump to hospital Ropivacaine 0.2% elastomeric pump.	02-Dec-2013
014	06-Dec-2013	BS96	Patient recruited to control group and should have received standard analgesia, instead patient had femoral nerve catheter as this was felt to be in the best interests of the patient	09-Dec-2013

015	03-Jan-2014	AS95	30 day follow up was not performed within +/- 5 day window	03-Jan-2013
016	20-Feb-2014	HC108	Elastomeric pump noted to be expired to nurses in theatre recovery	21-Feb-2014
017	20-Feb-2014	IH107	Elastomeric pump noted to be expired to nurses in theatre recovery	21-Feb-2014
018	28-Feb-2014	DP109	Elastomeric pump dislodged late in evening	04-Mar-2014
019	27-Mar-2014	AB116	Patient pulled out catheter.	31-Mar-2014
020	28-Mar-2014	HC108	30 day follow up was not performed within +/- 5 day window	31-Mar-2014
021	25-Apr-2014	AT113	30 day follow up was not performed within +/- 5 day window	29-Apr-2014
022	02-May-2014	DN122	Patient consent form not signed at time specified in the protocol due to patient confusion	17-Dec-2015
023	13-May-2014	JH119	30 day follow up was not performed within +/- 5 day window	14-May-2014
024	04-Aug-2014	LO130	Written consent was obtained on 04-Aug-2014 but the correct date should have been 31-Jul-2014, this occurred as nurse was not reminded that consent was due to be obtained on day 1 follow up	04-Aug-2014
025	18-Sep-2014	HJ135	Patient was identified and enrolled into FINOF trial, and randomised to active arm. On the evening of operation patient pulled out the catheter inserted as per protocol.	17-Oct-2014
026	10-Oct-2014	RB136	Patient consent form not signed at 24 hours post op due to patient confusion	14-Oct-2014
027	09-Nov-2014	BB138	Patient consent form not signed at time specified in protocol due to weekend recruitment	12-Nov-2014
028	21-Nov-2014	MO140	Patient pulled out femoral nerve catheter after only 1 day post op, protocol states that catheter should run for 48 hours post op	21-Nov-2014
029	26-Nov-2014	MO140	Proxy consent obtained over 48 hours post block, as relative not available earlier.	09-Jan-2015
030	26-Nov-2014	HT101	Patient deceased, SAE form not completed within 24 hours	26-Nov-2014
031	26-Nov-2014	EM137	Old version of written consent has been used by the researcher	09-Jan-2015
032	26-Nov-2014	OD134	Written consent has been obtained using proxy consent form.	07-Jan-2015
033	01-Oct-2014	DH133	Patient signed written consent over 48 hours after verbal consent.	09-Jan-2015

034	09-Jan-2015	MO140	SAE identified, not notified to monitor within 24 hours	09-Jan-2015
035	09-Jan-2015	RB136	30 day follow up phone call showed that patient had been readmitted to hospital, this was an SAE but was not reported until discovered at monitoring visit	09-Jan-2015
036	09-Jan-2015	AH141	SAE was identified on 05/JAN/2015 but was not reported to the sponsor until 09/JAN/2015 therefore breaching the 24 hour reporting timelines	18-Dec-2015
037	Various	Various	Patients written consent forms completed over 48 hours post op	25-Sep-2014
038*	Various	Various	Verbal consent forms signed by only one researcher, although verbal consent is always performed by 2 researchers.	07-Oct-2014

* Reported as a serious breach of GCP to the MHRA and REC on 22/Aug/2014

ppendix 10: Serious Adverse Events Log

Participant Identifier	Event Summary	Criteria	Date of Onset – Date Resolved	Relationship to IMP	Expected	Date Reported to Sponsor	Sponsor Reference	No Further Follow Up Required
EH03	Cardio respiratory arrest	Death	05/May/2012 - 05/May/2012	Not Related	☐ Yes ☐ No ☒ N/A	07/May/2012	4000-01	☒
AH04	Multi-organ failure	Death	29/May/2012 - 31/May/2012	Not Related	☐ Yes ☐ No ☒ N/A	01/Jun/2012	4000-02	☒
SB09	Pneumonia	Hospitalisation or Prolongation of Hospitalisation	31/Jul/2012 - 07/Aug/2012	Not Related	☐ Yes ☐ No ☒ N/A	02/Aug/2012	4000-03	☒
DC10	Aspiration Pneumonia	Life threatening	16/Aug/2012 - 18/Aug/2012	Not Related	☐ Yes ☐ No ☒ N/A	17/Aug/2012	4000-04	☒
BH12	Pneumonia, Jaundice	Hospitalisation or Prolongation of Hospitalisation	06/Sep/2012 - 16/Sep/2012	Not Related	☐ Yes ☐ No ☒ N/A	10/Sep/2012	4000-05	☒
RH14	Acute Kidney Injury	Hospitalisation or Prolongation of Hospitalisation	06/Sep/2012 - 22/Sep/2012	Not Related	☐ Yes ☐ No ☒ N/A	10/Sep/2012	4000-06	☒
DA25	Fat Embolism	Life threatening	12/Oct/2012 - 18/Oct/2012	Not Related	☐ Yes ☐ No ☒ N/A	15/Oct/2012	4000-07	☒
DS27	Atrial Fibrillation	Hospitalisation or Prolongation of Hospitalisation	29/Oct/2012 – 06/Nov/2012	Not Related	☐ Yes ☐ No ☒ N/A	31/Oct/2012	4000-08	☒

ppendix 10: Serious Adverse Events Log

EM36	Anaemia, Fainting	Hospitalisation or Prolongation of Hospitalisation	08/Jan/2013 – 15/Jan/2013	Not Related	☐ Yes ☐ No ☒ N/A	10/Jan/2013	4000-09	☒
KN39	Cardiac Arrest	Death	21/Jan/2013 - 21/Jan/2013	Not Related	☐ Yes ☐ No ☒ N/A	21/Jan/2013	4000-10	☒
FS40	Acute Kidney Failure	Hospitalisation or Prolongation of Hospitalisation	26/Jan/2013 - 07/Feb/2013	Not Related	☐ Yes ☐ No ☒ N/A	28/Jan/2013	4000-11	☒
EW43	Chest Infection	Hospitalisation or Prolongation of Hospitalisation	07/Feb/2013 - 11/Feb/2013	Not Related	☐ Yes ☐ No ☒ N/A	08/Feb/2013	4000-12	☒
ES54	Acute Kidney Injury	Hospitalisation or Prolongation of Hospitalisation	11/Apr/2013 – 23/Apr/2013	Not Related	☐ Yes ☐ No ☒ N/A	17/Apr/2013	4000-13	☒
KK57	Multiple Organ Failure secondary to Heart Failure	Death	01/May/2013 - 07/May/2013	Not Related	☐ Yes ☐ No ☒ N/A	08/May/2013	4000-14	☒
ES54	Pneumonia	Death	21/Apr/2013 - 26/Apr/2013	Not Related	☐ Yes ☐ No ☒ N/A	09/May/2013	4000-15	☒
63DL	Confusion	Hospitalisation or Prolongation of Hospitalisation	05/Jun/2013 – 10/Jun/2013	Not Related	☐ Yes ☐ No ☒ N/A	06/Jun/2013	4000-16	☒
14RH	Acute kidney injury/heart failure	Hospitalisation or Prolongation of	09/Sep/2012 – 17/Sep/2012	Not Related	☐ Yes ☐ No	18/Jun/2013	4000-17	☒

ppendix 10: Serious Adverse Events Log

		Hospitalisation			☒ N/A			
103LB	Drowsy and delirious following operation	Hospitalisation or Prolongation of Hospitalisation	21/Jan/2014 – 24/Jan/2014	Not Related	☐ Yes ☐ No ☒ N/A	19/Feb/2014	4000-18	☒
103LB	Hospital acquired infection	Hospitalisation or Prolongation of Hospitalisation	04/Feb/2014 – 11/Feb/2014	Not Related	☐ Yes ☐ No ☒ N/A	18/Feb/2014	4000-19	☒
103LB	NSTEMI	Hospitalisation or Prolongation of Hospitalisation	10/Feb/2014 – 12/Oct/2014	Not Related	☐ Yes ☐ No ☒ N/A	19/Feb/2014	4000-20	☒
111MS	Hypotensive	Hospitalisation or Prolongation of Hospitalisation	05/Mar/2014 – 07/Mar/2014	Not Related	☐ Yes ☐ No ☒ N/A	11/Jun/2014	4000-21	☒
115BT	Hypotension	Hospitalisation or Prolongation of Hospitalisation	27/Mar/2014 – 04/Apr/2014	Not Related	☐ Yes ☐ No ☒ N/A	02/Apr/2014	4000-22	☒
136RB	Confusion and drowsy	Hospitalisation or Prolongation of Hospitalisation	10/Oct/2014 – 14/Oct/2014	Not Related	☐ Yes ☐ No ☒ N/A	10/Oct/2014	4000-23	☒
140MO	Confusion and choreic	Hospitalisation or Prolongation of Hospitalisation	21/Nov/2014 – 01/Dec/2014	Not Related	☐ Yes ☐ No ☒ N/A	21/Nov/2014	4000-24	☒
101HT	Cause of death i) chest infection, ii) hip fracture, chronic renal impairment, obstructive nephropathy, emphysema, myelodysplasia	Death	18/Jan/2014 – 18/Jan/2014	Not Related	☐ Yes ☐ No ☒ N/A	26/Nov/2014	4000-25	☒

ıppendix 10: Serious Adverse Events Log

141AH	Stroke	Hospitalisation or Prolongation of Hospitalisation	01/Jan/2015 - Ongoing	Not Related	☐ Yes ☐ No ☒ N/A	09/Jan/2015	4000-26	☒
136RB	Chest infection	Hospitalisation or Prolongation of Hospitalisation	03/Nov/2014 – Ongoing	Not Related	☐ Yes ☐ No ☒ N/A	09/Jan/2015	4000-27	☒
140MO	Pneumonia	Hospitalisation or Prolongation of Hospitalisation	18/Dec/2014 – 25/Dec/2014	Not Related	☐ Yes ☐ No ☒ N/A	09/Jan/2015	4000-28	☒

COMPANY CORE DATA SHEET
Levobupivacaine injection

Levobupivacaine Injection

PRODUCT NAME

Levobupivacaine Injection

Trade Name

Chirocaine

DESCRIPTION

Levobupivacaine injection contains a single enantiomer of bupivacaine hydrochloride which is chemically described as (S)-1-butyl-2-piperidylformo-2', 6'-xylidide hydrochloride and it is related chemically and pharmacologically to the amino amide class of local anesthetics.

Levobupivacaine hydrochloride, the S-enantiomer of bupivacaine, is a white crystalline powder with a molecular formula of $C_{18}H_{28}N_2O$•HCl and a molecular weight of 324.9.

The solubility of levobupivacaine hydrochloride in water is about 100 mg per mL at 20°C, the partition coefficient (oleyl alcohol/water) is 1624 and the pKa is 8.09. The pKa of levobupivacaine hydrochloride is the same as that of bupivacaine hydrochloride and the partition coefficient is very similar to that of bupivacaine hydrochloride (1565).

Levobupivacaine is a sterile, non-pyrogenic, colorless solution (pH 4.0-6.5) containing levobupivacaine hydrochloride equivalent to 2.5 mg/mL, 5.0 mg/mL, and 7.5 mg/mL of levobupivacaine, sodium chloride for isotonicity, and water for injection. Sodium hydroxide and/or hydrochloric acid may have been added to adjust pH. Levobupivacaine is preservative free and is available in 10 mL single dose ampules.

INDICATIONS

Adults

Levobupivacaine is indicated in adults for:

Surgical Anesthesia

Major: Epidural (including for cesarean section), intrathecal, peripheral nerve block.

Minor: Local infiltration, peribulbar block in ophthalmic surgery.

Pain Management

Continuous epidural infusion, single or multiple bolus administration for postoperative, labor or chronic pain.

For continuous epidural analgesia, levobupivacaine may be administered in combination with epidural fentanyl, morphine or clonidine.

Children

Levobupivacaine is indicated in children for infiltration analgesia (ilioinguinal/iliohypogastric blocks).

DOSAGE AND ADMINISTRATION

The rapid injection of a large volume of local anesthetic solution should be avoided and fractional (incremental) doses should always be used. The smallest dose and concentration required to produce the desired result should be administered. The dose of any local anesthetic differs with the anesthetic procedure, the area to be anesthetized, the vascularity of the tissues, the number of neuronal segments to be blocked, the intensity of the block, the degree of muscle relaxation required, the duration of the anesthesia desired, individual tolerance, and the physical condition of the patient. Patients in poor general condition due to aging or other compromising factors, such as impaired cardiovascular function, advanced liver disease, or severe renal dysfunction, require special attention.

To reduce the risk of potentially serious adverse reactions, attempts should be made to optimize the patient's condition before major blocks are performed, and the dosage should be adjusted accordingly. Use an adequate test dose (3 to 5 mL) of a short-acting local anesthetic solution containing epinephrine prior to induction of complete nerve block. This test dose should be repeated if the patient is moved in such a fashion as to have displaced the epidural catheter. It is recommended that adequate time be allowed for the onset of anesthesia following administration of each test dose.

Disinfecting agents containing heavy metals, which cause release of ions (mercury, zinc, copper, etc.) should not be used for skin or mucous membrane disinfection since they have been related to incidents of swelling and edema.

When chemical disinfection of the container surface is desired, either isopropyl alcohol (91%) or ethyl alcohol (70%) is recommended. It is recommended that chemical disinfection be accomplished by wiping the ampule thoroughly with cotton or gauze that has been moistened with the recommended alcohol prior to use.

These products are intended for single use and do not contain preservatives; any solution remaining from an open container should be discarded.

For specific techniques and procedures, refer to standard contemporary textbooks.

Levobupivacaine Compatibility and Admixtures

Levobupivacaine may not be compatible with alkaline solutions having a pH greater than 8.5. Studies have shown that levobupivacaine is compatible with 0.9% Sodium Chloride Injection USP and with saline solutions containing morphine, fentanyl, and clonidine. Compatibility studies with other parenteral products have not been studied.

Dilution Stability

Levobupivacaine diluted to 0.625 to 2.5 mg levobupivacaine per mL in 0.9% Sodium Chloride Injection is physically and chemically stable when stored in PVC (polyvinyl chloride) bags at ambient room temperature for up to 24 hours. Aseptic technique should be used to prepare the diluted products. Admixtures of levobupivacaine should be prepared for single patient use only and used within 24 hours of preparation. The unused portion of diluted levobupivacaine should be discarded after each use.

Note: Parenteral products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Solutions that are not clear and colorless should not be used.

Shelf Life

Shelf life after first opening: The product should be used immediately.

Shelf life after dilution: Chemical and physical in-use stability has been demonstrated for seven days at 20 to 22°C. Chemical and physical in-use stability with clonidine, morphine or fentanyl has been demonstrated for 40 hours at 20 to 22°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Dosage Recommendations				
	Concentration %	**Dose (mL)**	**Dose (mg)**	**Motor Block**
Surgical Anesthesia				
Epidural for Surgery	0.5 - 0.75	10 - 20	50 -150	Moderate to Complete
Epidural for Cesarean Section	0.5	15 - 30	75 - 150	Moderate to Complete
Peripheral Nerve	0.25 - 0.5	1 - 40	maximum 150	Moderate to Complete
Intrathecal	0.5	3	15	Moderate to complete
Ophthalmic	0.75	5 - 15	37.5 - 112.5	Moderate to Complete
Local Infiltration - Adults	0.25	1 - 60	maximum 150	Not applicable
Local Infiltration - Children < 12 yrs	0.25	0.50 mL/kg/side	1.25 mg/kg/side	Not applicable
	0.5	0.25 mL/kg/side	1.25 mg/kg/side	Not applicable
Pain Management [a,b]				
Labor Analgesia (epidural bolus)	0.25	10 - 20	25 - 50	Minimal to Moderate
Labor Analgesia (epidural infusion)	0.125[c]	4 - 10 mL/h	5 - 12.5 mg/h	Minimal to Moderate

Post-Operative Pain (epidural infusion)	0.125[c]	10 - 15 mL/h	12.5 - 18.75 mg/h	Minimal to Moderate
	0.25	5 - 7.5 mL/h	12.5 - 18.75 mg/h	Minimal to Moderate

[a] In pain management levobupivacaine can be used epidurally with fentanyl, morphine or clonidine.

[b] In cases where levobupivacaine is combined with other agents e.g. opioids in pain management, the levobupivacaine dose should be reduced as use of a lower concentration (e.g. 1.25 mg/mL) is preferable.

[c] Dilutions of levobupivacaine standard solutions should be made with preservative free 0.9% saline according to standard hospital procedures for sterility.

The doses in the table are those considered to be necessary to produce a successful block and should be regarded as guidelines for use. Individual variations in onset and duration occur.

Epidural doses of up to 375 mg have been administered incrementally to patients during a surgical procedure.

The maximum dose in 24 hours for intraoperative block and post-operative pain management was 695 mg.

The maximum dose administered as a post-operative epidural infusion over 24 hours was 570 mg.

The maximum dose administered to patients as a single fractionated injection was 300 mg for brachial plexus block.

For cesarean section, the maximum recommended dose is 150 mg.

In children, the maximum recommended dose for infiltration analgesia (ilioinguinal-iliohypogastric block) is 1.25 mg/kg/side.

CONTRAINDICATIONS

General contraindications related to regional anesthesia should be taken into account with the use of any regional anesthetic agent, including levobupivacaine. Levobupivacaine solutions are contraindicated in those with a known sensitivity to local anesthetic amide agents.

Levobupivacaine is contraindicated in patients with severe hypotension such as cardiogenic or hypovolemic shock (see **WARNINGS AND PRECAUTIONS**).

Levobupivacaine also should not be used for intravenous regional anesthesia (e.g. Bier block). Additionally, levobupivacaine 7.5 mg/mL solution should not be employed for obstetric procedures, nor should it be used in paracervical blocks in obstetrics. Contraindications for use in Bier block, paracervical block, and 0.75% levobupivacaine use in obstetric procedures are based upon documented experiences with bupivacaine. Levobupivacaine has not been tested in such instances.

WARNINGS AND PRECAUTIONS

In performing levobupivacaine blocks, unintended intravenous injection is possible and may result in cardiac arrest (some cases fatal). Despite rapid detection and appropriate treatment, prolonged resuscitation may be required. The resuscitability relative to bupivacaine is unknown at this point in time as it has not been studied. As with all local anesthetics of the amide type, levobupivacaine should be administered in incremental doses.

Cases of severe bradycardia, hypotension and respiratory compromise with cardiac arrest (some of them fatal), have been reported in conjunction with local anesthetics, including levobupivacaine. Since levobupivacaine should not be injected rapidly in large doses, it is not recommended for emergency situations, where a fast onset of surgical anesthesia is necessary.

Historically, pregnant patients were reported to have a high risk for cardiac arrhythmias, cardiac/circulatory arrest and death when bupivacaine was inadvertently rapidly injected intravenously. For cesarean section, the 5 mg/mL (0.5%) levobupivacaine solution in doses up to 150 mg is recommended.

Local anesthetics should only be administered by clinicians who are well versed in the diagnosis and management of drug-related toxicity and other acute emergencies which might arise from the block being administered. The immediate availability of oxygen, other resuscitative drugs, cardiopulmonary resuscitative equipment, and the personnel resources needed for proper management of toxic reactions and related emergencies must be ensured (see also **ADVERSE REACTIONS**). Delay in proper management of drug-related toxicity, underventilation from any cause, and/or altered sensitivity may lead to the development of acidosis, cardiac arrest, and possibly death.

It is essential that aspiration for blood or cerebrospinal fluid (where applicable) be done prior to injecting any local anesthetic, both before the original dose and all subsequent doses, to avoid intravascular or intrathecal injection. However, a negative aspiration does not ensure against intravascular or intrathecal injection. Levobupivacaine should be used with caution in patients receiving other local anesthetics or agents structurally related to amide-type local anesthetics, since the toxic effects of these drugs are additive.

When contemplating a peripheral nerve block, where large volumes of local anesthetic are needed, caution should be exercised when using the higher mg/mL concentrations of levobupivacaine. Animal studies demonstrate CNS and cardiac toxicity that is dose related, thus, equal volumes of higher concentration will be more likely to produce cardiac toxicity.

The safe and effective use of local anesthetics depends on proper dosage, correct technique, adequate precautions, and readiness for emergencies.

Resuscitative equipment, oxygen, and resuscitative drugs should be available for immediate use (see **ADVERSE REACTIONS**). The lowest dosage that results in effective anesthesia should be used to avoid high plasma or dermatomal levels and serious adverse effects. Injections should be made slowly and incrementally, with frequent aspirations before and during the injection to avoid intravascular injection. When a continuous catheter technique is used, syringe aspirations should also be performed before and during each supplemental injection. During the administration of epidural anesthesia, it is recommended that a test dose of a local anesthetic with a fast onset be administered initially and that the patient be monitored for central nervous system and cardiovascular toxicity, as well as for signs of unintended intrathecal administration before proceeding. When clinical conditions permit, consideration should be given to employing local anesthetic solutions that contain epinephrine for the test dose because circulatory changes compatible with epinephrine may also serve as a warning sign of unintended intravascular injection. An intravascular injection is still possible even if aspirations for blood are negative.

Systemic adverse reactions following overdose or accidental intravascular injection reported with long acting local anesthetic agents involve both CNS and cardiovascular effects.

Levobupivacaine should be used with caution in conditions associated with impaired cardiovascular function (see **CONTRAINDICATIONS**).

Injection of repeated doses of local anesthetics may cause significant increases in plasma levels with each repeated dose due to slow accumulation of the drug or its metabolites or to slow metabolic degradation. Tolerance to elevated blood levels varies with the physical condition of the patient. Local anesthetics should also be used with caution in patients with hypotension, hypovolemia, or impaired cardiovascular function, especially heart block.

Careful and constant monitoring of cardiovascular and respiratory vital signs (adequacy of ventilation) and the patient's state of consciousness should be performed after each local anesthetic injection. The clinician must be aware that restlessness, anxiety, incoherent speech, lightheadedness, numbness and tingling of the mouth and lips, metallic taste, tinnitus, dizziness, blurred vision, tremors, twitching, depression, or drowsiness may be early signs of central nervous system toxicity.

Amide-type local anesthetics, such as levobupivacaine, are metabolized by the liver, therefore, these drugs, especially repeat doses, should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at a greater risk for developing toxic plasma concentrations. Local anesthetics should also be used with caution in patients with impaired cardiovascular function as they may be less able to compensate for functional changes associated with prolonged A-V conduction caused by these drugs.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for malignant hyperthermia. Amide-type local anesthetics are not known to trigger this reaction.

Epidural Anesthesia

During epidural anesthesia, levobupivacaine should be administered in incremental volumes of three to five milliliters (3 to 5 mL), with sufficient time between doses to detect toxic manifestations of unintentional intravascular or intrathecal injection. Syringe aspirations should also be performed before and during each supplemental injection in continuous catheter techniques. An intravascular injection is still possible even if aspirations are negative. During the administration of epidural anesthesia, it is recommended that a test dose is administered initially and the effects monitored before the full dose is given. A test dose of a short-acting amide anesthetic, such as three milliliters (3 mL) of lidocaine, is recommended to detect unintentional intrathecal administration. This will be manifested within a few minutes by signs of a subarachnoid block (e.g. decreased sensation of the buttocks, paresis of the legs or, in the sedated patient, absent knee jerk). Unintentional intrathecal injection of local anesthetics can lead to very high spinal anesthesia, possibly apnea, severe hypotension and loss of consciousness. An intravascular or intrathecal injection is still possible, even if the results of the test dose are negative. The test dose itself may produce a systemic toxic reaction, extensive subarachnoid block, or cardiovascular effects.

Use in Head and Neck Area

Small doses of local anesthetics injected into the head and neck area may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. The injection procedures require the utmost care. Confusion, convulsions, respiratory depression, and/or respiratory arrest and cardiovascular stimulation or depression have been reported. These reactions may be due to intraarterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their respirations and circulation monitored and be constantly observed. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded (see **DOSAGE AND ADMINISTRATION**).

Information for the Patient

When appropriate, patients should be informed in advance that they may experience temporary loss of sensation and motor activity in the anesthetized part of the body following correct administration of the regional anesthesia. Also, when appropriate, the physician should discuss other information including adverse reactions in the levobupivacaine package insert.

Geriatrics

Of the total number of subjects in clinical studies of levobupivacaine, 16% were 65 years and over, while 8% were 75 years and over. No overall differences in safety and effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

DRUG INTERACTIONS

Levobupivacaine should be used with caution in patients receiving other local anesthetics or agents structurally related to amide-type local anesthetics since the toxic effects of these drugs could be additive. In vitro studies indicate CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. Thus, agents likely to be concomitantly administered with levobupivacaine that are metabolized by this isoenzyme family may potentially interact with levobupivacaine. Although no clinical studies have been conducted, it is likely that the metabolism of levobupivacaine may be affected by the known CYP3A4 inducers (such as phenytoin, phenobarbital, rifampin), CYP3A4 inhibitors (azole antimycotics, e.g. ketoconazole; certain protease inhibitors, e.g. ritonavir; macrolide antibiotics, e.g. erythromycin; and calcium channel antagonists, e.g. verapamil), CYP1A2 inducers (omeprazole) and CYP1A2 inhibitors (furafylline and clarithromycin). Dosage adjustments may be warranted when levobupivacaine is concurrently administered with CYP3A4 inhibitors and CYP1A2 inhibitors, as systemic levobupivacaine levels may rise resulting in toxicity.

Levobupivacaine should be used with caution in patients receiving antiarrhythmic agents with local anesthetic activity, e.g. mexiletine, or class III antiarrhythmic agents since their use may be additive.

PREGNANCY AND LACTATION

Preg and Lact - Pregnancy

Teratogenicity studies in rats (180 mg/m^2/day) and rabbits (220 mg/m^2/day) did not show evidence of any adverse effects on organogenesis or early fetal development. The doses used were approximately one-half the maximum recommended human dose (570 mg/person or 352 mg/m^2) based on body surface area. There were no treatment-related effects on late fetal development, parturition, lactation, neonatal viability, or growth of the offspring in a perinatal and postnatal study in rats at dose levels up to approximately one-half the maximum recommended human dose based on body surface area. There were no adequate and well-controlled studies in pregnant women of the effects of levobupivacaine on the developing fetus. Levobupivacaine should only be used during pregnancy if the benefits outweigh the risks.

Labor and Delivery

Local anesthetics, including levobupivacaine, rapidly cross the placenta, and, when used for epidural block, can cause varying degrees of maternal, fetal, and neonatal toxicity. The incidence and degree of toxicity depend upon the procedure performed, the type and amount of drug used, and the technique of drug administration. Adverse reactions in the parturient, fetus, and neonate involve alterations of the central nervous system, peripheral vascular tone, and cardiac function. Maternal hypotension, fetal bradycardia and fetal decelerations have resulted from regional anesthesia with levobupivacaine for obstetrical pain relief. Local anesthetics produce vasodilation by blocking sympathetic nerves. Administration of intravenous fluids, elevation of the patient's legs and left uterine displacement will help prevent decreases in blood pressure. The fetal heart rate should also be monitored continuously and electronic fetal monitoring is highly advisable.

The 7.5 mg/mL solution is not recommended for obstetric use due to an enhanced risk for cardiotoxic events based on experience with bupivacaine. There is no experience of levobupivacaine 7.5 mg/mL in obstetric surgery.

Preg and Lact - Lactation

Some local anesthetic drugs are excreted in breast milk and caution should be exercised when levobupivacaine is administered to a nursing woman. The excretion of levobupivacaine or its metabolites in human milk has not been studied. Studies in rats demonstrated that small amounts of levobupivacaine can be detected in the pups after administration of levobupivacaine to the nursing mothers (see **WARNINGS AND PRECAUTIONS**).

ADVERSE REACTIONS

Reactions to levobupivacaine are characteristic of those associated with other amide-type anesthetics. A major cause of the adverse reactions to this group of drugs is associated with excessive plasma levels, or high dermatomal levels, which may be due to overdose, unintentional intravascular injection, or slow metabolic degradation. The reported adverse events are derived from studies conducted in the United States and Europe. The reference drug was primarily bupivacaine. The studies were conducted using a variety of premedications,

sedatives, and surgical procedures of varying lengths. A total of 1,220 were exposed to levobupivacaine. Each patient was counted once for each type of adverse event.

In Phase II/III studies, 78% of patients who received levobupivacaine reported at least one adverse event. Of those patients who received the 0.75% levobupivacaine concentration, 85% reported at least one adverse event.

Adverse Events That Occurred In > 5% Of All Levobupivacaine-Treated Patients In Phase II/III Studies (n=1,141)	
Hypotension (31%)	Pruritus (9%)
Nausea (21%)	Pain (8%)
Post-operative pain (18%)	Headache (7%)
Fever (17%)	Constipation (7%)
Vomiting (14%)	Dizziness (6%)
Anemia (12%)	Fetal distress (5%)

Adverse Events Reported With An Incidence of ≥1% In The Phase II/III Bupivacaine-Controlled Studies				
Event	Levobupivacaine n=509		Bupivacaine n=453	
Hypotension	100	(19.6)	93	(20.5)
Nausea	59	(11.6)	66	(14.6)
Anemia	49	(9.6)	37	(8.2)
Post-Operative Pain	37	(7.3)	37	(8.2)
Vomiting	42	(8.3)	30	(6.6)
Back Pain	29	(5.7)	19	(4.2)
Fever	33	(6.5)	35	(7.7)
Dizziness	26	(5.1)	22	(4.9)
Fetal Distress	49	(9.6)	41	(9.1)
Headache	23	(4.5)	18	(4.0)
Delayed Delivery	32	(6.3)	31	(6.8)
Pruritus	19	(3.7)	26	(5.7)
Pain	18	(3.5)	17	(3.8)
ECG Abnormal	16	(3.1)	17	(3.8)
Abdomen Enlarged	15	(2.9)	12	(2.6)
Albuminemia	15	(2.9)	6	(1.3)
Rigors	15	(2.9)	12	(2.6)
Constipation	14	(2.8)	20	(4.4)
Diplopia	13	(2.6)	14	(3.1)
Hypoesthesia	13	(2.6)	15	(3.3)
Flatulence	12	(2.4)	11	(2.4)
Abdominal Pain	11	(2.2)	6	(1.3)
Hypothermia	11	(2.2)	6	(1.3)
Bradycardia	11	(2.2)	10	(2.2)
Dyspepsia	10	(2.0)	11	(2.4)
Hematuria	10	(2.0)	5	(1.1)
Hemorrhage in Pregnancy	9	(1.8)	12	(2.6)

Adverse Events Reported With An Incidence of ≥1% In The Phase II/III Bupivacaine-Controlled Studies				
Event	Levobupivacaine n=509		Bupivacaine n=453	
Paresthesia	9	(1.8)	2	(0.4)
Tachycardia	9	(1.8)	7	(1.5)
Urine Abnormal	9	(1.8)	6	(1.3)
Purpura	7	(1.4)	4	(0.9)
Wound Drainage Increased	7	(1.4)	13	(2.9)
Coughing	6	(1.2)	3	(0.7)
Leukocytosis	6	(1.2)	3	(0.7)
Somnolence	6	(1.2)	4	(0.9)
Urinary Incontinence	6	(1.2)	1	(0.2)
Anesthesia Local	5	(1.0)	5	(1.1)
Anxiety	5	(1.0)	6	(1.3)
Breast Pain (Female)	5	(1.0)	4	(0.9)
Hypertension	5	(1.0)	8	(1.8)
Urine Flow Decreased	5	(1.0)	3	(0.7)
Urinary Tract Infection	5	(1.0)	3	(0.7)
Diarrhea	5	(1.0)	6	(1.3)

The following adverse events were reported during the levobupivacaine clinical program in more than one patient and occurred at an overall incidence of <1%, and were considered clinically relevant.

Body as a Whole	Asthenia, edema
Cardiovascular Disorders, General	Postural hypotension
Central and Peripheral Nervous System Disorders	Hypokinesia, involuntary muscle contraction, spasm (generalized), tremor, syncope
Heart Rate and Rhythm Disorders	Arrhythmia, extrasystoles, fibrillation (atrial), cardiac arrest
Gastrointestinal System Disorders	Ileus
Liver and Biliary System Disorders	Elevated bilirubin
Psychiatric Disorders	Confusion
Respiratory System Disorders	Apnea, bronchospasm, dyspnea, pulmonary edema, respiratory insufficiency
Skin and Appendage Disorders	Increased sweating, skin discoloration

Reactions to levobupivacaine are characteristic of those associated with other amide-type local anesthetics. Systems involved may include the central nervous system, the cardiovascular system, and the respiratory system (see **WARNINGS AND PRECAUTIONS** and **OVERDOSAGE**).

The incidences of adverse neurological reactions associated with the use of local anesthetics may be related to the total dose of anesthetic administered and are also dependent upon the particular drug used, the route of administration, and the physical status of the patient. Many of these effects may be related to local anesthetic techniques, with or without contribution from the drug.

Allergic-type reactions are rare and may occur as a result of sensitivity to the local anesthetic. These reactions are characterized by signs such as urticaria, pruritus, erythema, angioneurotic edema (including laryngeal

edema), tachycardia, sneezing, nausea, vomiting, dizziness, syncope, excessive sweating, elevated temperature, and, possibly, anaphylactoid-like symptomatology (including severe hypotension). Cross sensitivity among members of the amide-type local anesthetic group have been reported.

ADR – Post Marketing Experience

Anaphylaxis has been reported. Very rare reports of convulsions have occurred following accidental intravenous administration.

There have been reports of prolonged weakness or sensory disturbance, some of which may have been permanent, in association with levobupivacaine therapy. It is difficult to determine whether the long-term effects were the result of medication toxicity or unrecognized trauma during surgery or other mechanical factors, such as catheter insertion and manipulation.

Rare reports have been received of cauda equina syndrome or signs and symptoms of potential injury to the base of the spinal cord or spinal nerve roots (including lower extremity weakness or paralysis, loss of bowel control and/or bladder control and priapism) associated with bupivacaine or levobupivacaine therapy. However, it cannot be determined whether these events are due to an effect of levobupivacaine, mechanical trauma to the spinal cord or spinal nerve roots, or blood collection at the base of the spine.

There have also been rare reports of transient Horner's syndrome (ptosis, miosis, enophthalmus, unilateral sweating and/or flushing) in association with use of regional anesthetics, including levobupivacaine. This event resolves with discontinuation of therapy.

OVERDOSAGE

Acute emergencies from local anesthetics are generally related to high plasma levels or high dermatomal levels ("high spinal") encountered during therapeutic use of local anesthetics or to unintended intrathecal or intravascular injection of local anesthetic solution (see **ADVERSE REACTIONS** and **WARNINGS AND PRECAUTIONS**). There was one case of suspected unintentional intravascular injection which occurred during the clinical trial program. That patient received 19 mL of 0.75% levobupivacaine (142.5 mg) and experienced CNS excitation which was treated with thiopental. No abnormal cardiac changes were observed and the patient recovered without sequelae.

Management of Local Anesthetic Emergencies

The first consideration is prevention, best accomplished by incremental injection of levobupivacaine, careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic injection and during continuous infusion. At the first sign of change, oxygen should be administered, and further measures as warranted.

PHARMACOLOGIC PROPERTIES

Levobupivacaine is a member of the amino amide class of local anesthetics. Local anesthetics block the generation and the conduction of nerve impulses by increasing the threshold for electrical excitation in the nerve, by slowing propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In

general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: 1) pain; 2) temperature; 3) touch; 4) proprioception; and 5) skeletal muscle tone.

Pharmacodynamic Properties

Levobupivacaine can be expected to share the pharmacodynamic properties of other local anesthetics. Systemic absorption of local anesthetics can produce effects on the central nervous system and cardiovascular systems. At blood concentrations achieved with therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance have been reported. Toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrioventricular block, ventricular arrhythmias, and cardiac arrest, sometimes resulting in death. In addition, myocardial contractility is depressed and peripheral vasodilation occurs, leading to decreased cardiac output and arterial blood pressure.

Following systemic absorption, local anesthetics can produce central nervous system stimulation, depression, or both. Apparent central nervous system stimulation is usually manifested as restlessness, tremors, and shivering, progressing to convulsions. Ultimately central nervous system depression may progress to coma and cardio-respiratory arrest. However, the local anesthetics have a primary depressant effect on the medulla and on higher centers. The depressed stage may occur without a prior excited stage.

In nonclinical pharmacology studies comparing levobupivacaine and bupivacaine in animal species, both the central nervous system (CNS) and the cardiac toxicity of levobupivacaine were less than that of bupivacaine. Arrhythmogenic effects were seen in animal at higher doses of levobupivacaine than bupivacaine. Central nervous system toxicity occurred with both drugs at lower doses and at lower plasma concentrations than those doses and plasma concentrations associated with cardiotoxicity.

In two intravenous infusion studies in conscious sheep, the convulsive doses of levobupivacaine were found to be significantly higher than for bupivacaine. Following repeated intravenous bolus administration mean (±SD) convulsive doses for levobupivacaine and bupivacaine were 9.7 (7.9) mg/kg and 6.1 (3.4) mg/kg respectively. The associated median total serum concentrations were 3.2 mcg/mL and 1.6 mcg/mL. In a second study following a three-minute intravenous infusion, the mean convulsant dose (95% CI) for levobupivacaine was 101 mg (87 to 116 mg) and for bupivacaine 79 mg (72 to 87 mg).

A study in human volunteers was designed to assess the effects of levobupivacaine and bupivacaine on the electroencephalogram (EEG) following an intravenous dose (40 mg) that was predicted to be below the threshold to cause central nervous system (CNS) symptoms. In this study, levobupivacaine decreased high alpha power in parietal, temporal and occipital regions, but to a lesser extent than bupivacaine. Levobupivacaine had no effect on high alpha power in the frontal and central regions, nor did it produce the increase in theta power observed at some electrodes following bupivacaine.

In another study, 14 subjects received levobupivacaine or bupivacaine infusions intravenously until significant CNS symptoms occurred (occurrence of numbness of the tongue, light-headedness, tinnitus, dizziness, blurred vision, or muscle twitching). The mean dose at which CNS symptoms occurred was 56 mg (range 17.5 to 150 mg) for levobupivacaine and 48 mg (range 22.5 to 110 mg) for bupivacaine. The primary endpoints of the

study were cardiac contractility and standard electrocardiographic parameters. Both drugs produced transient increases in heart rate and systolic and diastolic pressure, but the change in diastolic pressure was significantly less with levobupivacaine than with bupivacaine. Cardiac function measured by transthoracic electrical bioimpedance showed significant differences in that levobupivacaine produced a lesser reduction in stroke index, the acceleration index, and the ejection fraction.

A double-blind, randomized, parallel group trial was conducted on 22 healthy male volunteers to compare the effects of levobupivacaine and bupivacaine on QT dispersion and signal averaged ECG. The objective of the trial was to determine the effect of levobupivacaine and bupivacaine on myocardial depolarization and repolarization as measured by the QRS duration of signal-averaged ECGs, QT dispersion, and other ECG variables. During double-blind dosing, subjects received either levobupivacaine or bupivacaine in tolerated doses ranging from 30 mg to 120 mg. The results showed that ten of eleven bupivacaine subjects experienced CNS systems compared with six of eleven levobupivacaine subjects. In those subjects who received more than 75 mg of randomized drug, the maximum changes from baseline QTc interval was statistically significantly lower for levobupivacaine (3 ± 11 msec) than bupivacaine (24 ± 17 msec, p=0.022). No other statistically significant changes were seen in cardiac parameters.

Clinical Trials

The clinical trial program included 1,220 patients and subjects who received levobupivacaine in 31 clinical trials. Levobupivacaine has been studied as a local anesthetic in adults administered as an epidural block for surgical cases, including cesarean section; in peripheral neural blockade; and for post-operative pain control. Clinical trials have demonstrated that levobupivacaine and bupivacaine exhibit similar anesthetic effects (see **PHARMACOLOGIC PROPERTIES**).

Central Administration

Epidural Administration in Cesarean Section

In one study, levobupivacaine and bupivacaine, 0.50% were evaluated as an epidural block in 62 patients undergoing cesarean section in a randomized, double-blind comparative trial. The mean (±SD) time to sensory block measured at T4 to T6 was 10 ± 8 minutes for levobupivacaine and 6 ± 4 minutes for bupivacaine. The mean duration of sensory block and motor block was 8 ± 1 and 4 ± 1 hour for levobupivacaine and 7 ± 1 and 4 ± 1 hour for bupivacaine, respectively. Ninety-four percent of patients receiving levobupivacaine and 100% of patients receiving bupivacaine achieved a block adequate for surgery. In a second bupivacaine-controlled cesarean section study involving 62 patients, the mean time to onset of T4 to T6 sensory block for levobupivacaine and bupivacaine was 10 ± 7 minutes and 9 ± 7 minutes, respectively, with 94% of levobupivacaine patients and 91% of bupivacaine patients achieving a bilateral block adequate for surgery. The mean time to complete regression of sensory block was 8 ± 2 hours for both treatments.

Epidural Administration During Labor and Delivery

Levobupivacaine 0.25% was evaluated as intermittent injections via an epidural catheter in 68 patients during labor in a randomized, double-blind comparative trial to bupivacaine 0.25%. The median duration of pain relief in the subset of patients receiving 0.25% levobupivacaine who had relief was 49 minutes; for

bupivacaine patients the median duration was 51 minutes. Following the first top-up injections, 91% of patients receiving levobupivacaine and 90% of patients receiving bupivacaine achieved pain relief.

Epidural Administration for Surgery

Levobupivacaine concentrations of 0.50% and 0.75% administered by epidural injection were evaluated in 85 patients undergoing lower limb or major abdominal surgery in randomized, double-blind comparisons to bupivacaine. Anesthesia sufficient for surgery was achieved in almost all patients on either treatment. In patients having abdominal surgery, the mean (±SD) time to onset of sensory block was 14 ± 6 minutes for levobupivacaine and 14 ± 10 minutes for bupivacaine. With respect to the duration of block, the time to complete regression was 551 ± 88 minutes for levobupivacaine and 506 ± 71 minutes for bupivacaine.

Postoperative Pain Management

Post-operative pain control was evaluated in 324 patients in four studies including one dose-ranging study and three studies assessing levobupivacaine in combination with epidural fentanyl, morphine or clonidine. The dose-ranging study evaluated levobupivacaine in concentrations of 0.0625%, 0.125%, and 0.25% in patients undergoing orthopedic surgery; the highest concentration was significantly more effective than were the other two concentrations. The levobupivacaine combination studies in post-operative pain management tested 0.125% levobupivacaine in combination with 4 mcg/mL fentanyl, 0.125% levobupivacaine in combination with clonidine 50 mcg/hour in orthopedic surgery, and 0.25% levobupivacaine and 0.005% morphine in abdominal surgery. In these studies, the efficacy variable was time to first request for rescue analgesia during the 24-hour epidural infusion period. In the studies, the combination treatment provided better pain control than clonidine, opioid or local anesthetic alone.

There is limited safety experience with levobupivacaine therapy for periods exceeding 24 hours. Therefore, use of levobupivacaine is not recommended for more than 24 hours.

Peripheral Nerve Administration

Levobupivacaine has been evaluated for its anesthetic efficacy when used as a peripheral nerve block. These clinical trials include brachial plexus (by supraclavicular approach) block study, infiltration anesthesia studies (for inguinal hernia repair), and peribulbar block studies.

Brachial Plexus Block

Levobupivacaine 0.25% and 0.50% were compared with 0.5% bupivacaine in 74 patients receiving brachial plexus (supraclavicular) block for elective surgery. In the levobupivacaine 0.25% treated group, 68% of patients achieved satisfactory block and in the levobupivacaine 0.50% treated group, 81% of patients achieved satisfactory block for surgery. In the bupivacaine 0.5% treated group, 74% of patients achieved satisfactory block for surgery.

Infiltration Anesthesia

Levobupivacaine 0.25% was evaluated in 68 patients in two randomized, double blind, bupivacaine controlled clinical trials for infiltration anesthesia during surgery and for post-operative pain management in patients undergoing inguinal hernia repair. No clear differences between treatments were seen.

Peribulbar Block Anesthesia

Two clinical trials were conducted to evaluate 0.75% levobupivacaine and bupivacaine in 110 patients for peribulbar block for anterior segment ophthalmic surgery, including cataract, glaucoma, and graft surgery, and for post-operative pain management. In one study, a ten mL (10 mL) injection of 0.75% levobupivacaine or bupivacaine produced a block adequate for surgery at a median time of ten minutes. In the second study, a five mL (5 mL) dose of 0.75% levobupivacaine or bupivacaine injected in a technique more closely resembling a retrobulbar block resulted in a median time to adequate block of two minutes for both treatments. Post-operative pain was reported in fewer than ten percent of patients overall.

Pharmacokinetic Properties

Table 1. Pharmacokinetic parameter values of levobupivacaine after administration of 40 mg levobupivacaine, and those of racemic bupivacaine, R(+)- and S(-)- enantiomers after the administration of 40 mg bupivacaine intravenously in healthy volunteers (mean ± SD).

Parameter	Levobupivacaine	Bupivacaine Racemate	R(+)-Bupivacaine	S(-)-Bupivacaine
C_{max}, mcg/mL	1.445 ± 0.237	1.421 ± 0.224	0.629 ± 0.100	0.794 ± 0.131
$AUC_{0-\infty}$, mcg hour/mL	1.153 ±0.447	1.166 ±0.400	0.478 ± 0.166	0.715 ± 0.261
$t_{1/2}$, hour	1.27 ± 0.37	1.15 ± 0.41	1.08 ± 0.17	1.34 ± 0.44
V_d, Liter	66.91 ± 18.23	59.97 ± 17.65	68.58 ± 21.02	56.73 ± 15.14
Cl, Liter/hour	39.06 ± 13.29	38.12 ± 12.64	46.72 ± 16.07	46.72 ± 16.07

After IV infusion of equivalent doses of levobupivacaine and bupivacaine, the mean clearance, volume of distribution, and terminal half-life values of levobupivacaine were similar. No detectable levels of R(+)-bupivacaine were found after the administration of levobupivacaine.

A comparison of the estimates for plasma AUC and C_{max} between levobupivacaine and bupivacaine in two Phase III clinical trials involving short duration administration of either agent found that neither total plasma exposure nor C_{max} differed between the two drugs when compared within studies. Between study values differed somewhat, likely due to differences in injection sites, volume, and total dose administered in each of the studies. These data suggest that levobupivacaine and bupivacaine have a similar pharmacokinetic profile. Pharmacokinetic data from the two Phase III studies are presented in Table 2.

Table 2. Pharmacokinetic parameter values of levobupivacaine and bupivacaine in patients administered the respective drugs epidurally and for brachial plexus block.

Route	Epidural			Brachial Plexus Block		
	Levobupivacaine		Bupivacaine	Levobupivacaine		Bupivacaine
Conc. (%)	0.50	0.75	0.50	0.25	0.50	0.50
Dose Received	75 mg	112.5 mg	75 mg	1 mg/kg	2 mg/kg	2 mg/kg
n	9	9	8	10	10	9
C_{max} (mcg/mL)	0.582	0.811	0.414	0.474	0.961	1.029
T_{max} (hour)	0.52	0.44	0.36	0.50	0.71	0.68
AUC(0 - t) (mcg.h/mL)	3.561	4.930	2.044	2.999	5.311	6.832

Between 0.5% and 0.75% levobupivacaine given epidurally at doses of 75 mg and 112.5 mg respectively, the mean C_{max} and AUC_{0-24} of levobupivacaine were approximately dose-proportional. Similarly, between 0.25% and 0.5% levobupivacaine used for brachial plexus block at doses of 1 mg/kg and 2 mg/kg respectively, the mean C_{max} and AUC_{0-24} of levobupivacaine were approximately dose-proportional.

The plasma concentration of levobupivacaine following therapeutic administration depends on dose and also on route of administration, because absorption from the site of administration is affected by the vascularity of the tissue. Peak levels in blood were reached approximately 30 minutes after epidural administration, and doses up to 150 mg resulted in mean C_{max} levels of up to 1.2 mcg/mL.

Plasma protein binding of levobupivacaine evaluated *in vitro* was found to be >97% at concentrations between 0.1 and 1 mcg/mL. The association of levobupivacaine with human blood cells was very low (0 to 2%) over the concentration range 0.01 to 1 mcg/mL and increased to 32% at 10 mcg/mL. The volume of distribution of levobupivacaine after intravenous administration was 67 liters.

Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine and feces. *In vitro* studies using [^{14}C] levobupivacaine showed that CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. *In vivo*, the 3-hydroxy levobupivacaine appears to undergo further transformation to glucuronide and sulfate conjugates. Metabolic inversion of levobupivacaine to R(+)-bupivacaine was not evident in both *in vitro* and *in vivo*.

Following intravenous administration, recovery of the radiolabelled dose of levobupivacaine was essentially quantitative with a mean total of about 95% being recovered in urine and feces in 48 hours. Of this 95%, about 71% was in urine while 24% was in feces. The mean elimination half-life of total radioactivity in plasma was 3.3 hours. The mean clearance and terminal half-life of levobupivacaine after intravenous infusion were 39 liters/hour and 1.3 hours, respectively.

Pharm - PK - Geriatric

The limited data available indicate that while there are some differences in T_{max}, C_{max}, and AUC with regards to age (between age groups of <65, 65 to 75, and >75 years), these differences are small and vary depending on the site of administration.

Gender

The small number of subjects in either of the male and female groups and the different routes of administration (data could not be pooled) in the different studies did not permit the assessment of gender differences in the pharmacokinetics of levobupivacaine.

Pharm - PK - Pediatric

No pharmacokinetic data of levobupivacaine are available in the pediatric population.

Maternal/Fetal Ratio

The ratio of umbilical venous and maternal concentration of levobupivacaine ranged from 0.252-0.303 after the epidural administration of levobupivacaine for cesarean section. These are within the range normally seen for bupivacaine.

Nursing Mothers

It is known that some local anesthetic drugs are excreted in human milk and caution should be exercised when they are administered to a nursing woman. The excretion of levobupivacaine or its metabolites in human milk has not been studied (see **PRECAUTIONS**).

Pharm - Renal Impairment

No special studies were conducted in renal failure patients. Unchanged levobupivacaine is not excreted in the urine. Although there is no evidence that levobupivacaine accumulates in patients with renal failure, some of its metabolites may accumulate because they are primarily excreted by the kidney.

Pharm - Hepatic Impairment

No special studies were conducted in hepatic failure patients. Levobupivacaine is eliminated primarily by hepatic metabolism and changes in hepatic function may have significant consequences. Levobupivacaine should be used with caution in patients with severe hepatic disease, and repeated doses may need to be reduced due to delayed elimination.

PRE-CLINICAL SAFETY DATA

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term studies in animals of most local anesthetics, including levobupivacaine, to evaluate the carcinogenic potential have not been conducted. Mutagenicity was not observed in bacterial mutation assay, mouse lymphoma cells mutation assay, chromosome aberrations in human blood lymphocytes, and micronuclei in the bone marrow of treated mice. Studies performed with levobupivacaine in rats at 30 mg/kg/day (180 mg/m^2/day) did not demonstrate an effect on fertility or general reproductive performance over two generations. This dose is approximately one-half the maximum recommended human dose (570 mg/person) based on body surface area (352 mg/m^2).

STORAGE

The storage statement should be established in accordance with relevant national/regional requirements.

HOW SUPPLIED

Chirocaine, 2.5 mg levobupivacaine in each mL.

Size
10 mL Single Use Plastic Ampules

Chirocaine, 5.0 mg levobupivacaine in each mL.

Size
10 mL Single Use Plastic Ampules

Chirocaine, 7.5 mg levobupivacaine in each mL.

Size
10 mL Single Use Plastic Ampules

verbal consent form

X-ray - Back.

Block In - Catheter | Analgesia.

Ward - Randomisation

ALLERGIES

Inclusion Criteria for FINOF

- Aged 70 years or over
- Resident in their own home or warden aided flat

MEDICAL CONDITIONS

- Inform about the study
- Cognitively intact (as defined by a score of 7 or more on the Abbreviated 10 point Mental Test Score) AMTS
- Have a prior fracture New Mobility Score of 3 or more (indicating independent indoor ambulation)
- Willing and able to give informed consent

Exclusion Criteria for FINOF

- Pre fracture hospitalisation
- Contraindications to femoral nerve block analgesia
- Alcohol or substance abuse or morphine intolerance?
- Post operative surgical restrictions for ambulation
- Any other disease or disorder which, in the opinion of the investigator, may either put the participants at risk because of participation in the study or may influence the result of the study or the participant's ability to participate in the study
- Participants participating in another research study
- Takes regular pre fracture opioid therapy:-

MEDICATION

  - Co-codamol QDS
  - MST
  - Tramadol QDS
  - Oxycodeine
- Takes regular pre fracture glucocorticoid therapy:-
  - Steroids
  - Prednisolone
  - Hydrocortisone

On Warfarin? * CHECK INR *

Also check alert bracelet if the patient has one

Nottingham University Hospitals NHS
NHS Trust

The FINOF (Femoral Nerve-Block Intervention in Neck of Femur Fracture) study

AMTS – ABBREVIATED MENTAL TEST SCORE

PATIENT STUDY NUMBER DATE ASSESSOR

1 How old are you? Must be correct.

2 What time is it? Without looking at a timepiece (To the nearest hour).

3 I want you to remember this address 42 West Street.

4 What year is it? Exact, except in Jan or Feb when last year is OK.

5 Name of place or type of place or town (in hospital is insufficient)/Home address, Residential institution.

6 Recognition of two people e.g. Doctor, Nurse, Home help (carer) etc.

7 What is your date of birth? Must be exact.

8 When did the First World War start? Must be exact 1914.

9 Can you name the present monarch?

10 Can you count down from 20 – 1?

Check the address

Total Score

Notes

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PATIENT STUDY NUMBER [ ] Date Assessor

BASELINE

NEW MOBILITY SCORE

	Ability and Score			
Mobility	No difficulty (3)	With an aid (2)	With help from another person (1)	Not at all (0)
Able to get about the house				
Able to get out of the house				
Able to go shopping				

NEED TO SCORE 3 AND ABOVE

Nottingham University Hospitals NHS
NHS Trust

The FINOF (Femoral Nerve-Block Intervention in Neck Of Femur Fracture)

VERBAL CONSENT

PATIENT STUDY NUMBER

Patient sticker

NUH Hospital Number
DOB
Address

Tel Number

Signature 1 _____ Date_____

Print _____

Signature 2 _____ Date_____

Print _____

Appendix 13: Figure of Catheter and Pump Insitu