Clinical trial results:
Skin bacteria as a source of surgical infections: molecular epidemiology and prevention of wound contamination

Summary

EudraCT number	2009-016566-82
Trial protocol	GB
Global end of trial date	07 July 2014

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022

Trial information

Trial identification

Sponsor protocol code	05/SP/120

Additional study identifiers

ISRCTN number	ISRCTN73863246
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Belfast Health and Social Care Trust
Sponsor organisation address	Research Office, 2nd floor King Edward Building, Royal Hospital Site, Belfast, United Kingdom, BT12 6BA
Public contact	Alison Murphy, Research Office, Belfast Health and Social Care Trust , ResearchSponsor@belfasttrust.hscni.net
Scientific contact	Research Office, Belfast Health and Social Care Trust, ResearchSponsor@belfasttrust.hscni.net
Sponsor organisation name	Queen's University Belfast (QUB)
Sponsor organisation address	Research Governance, Ethics and Integrity, QUB, 63 University Road, Belfast, United Kingdom, BT7 1NN
Public contact	researchgovernance@qub.ac.uk, Research Governance, Ethics and Integrity, QUB , 028 90972572, researchgovernance@qub.ac.uk
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2014
Global end of trial reached?	Yes
Global end of trial date	07 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to determine whether the sequential application of povidone iodine-alcohol (PVI) followed by chlorhexidine gluconate-alcohol (CHG) would reduce surgical wound contamination to a greater extent than PVI applied twice in patients undergoing spinal surgery.

Protection of trial subjects:

The following exclusion criteria were applied:
Patients who had more than 7 days in hospital prior to surgery.
Patients who had been transferred from another hospital, i.e. patients who had been inpatients in another hospital and transferred for surgery.
Patients with overt spinal infections suspected pre-operatively, or where evidence of purulence in any part of the wound is observed
during surgery.
Patients who were sensitive or allergic to the skin antiseptics.
Patients on antibiotics prior to surgery as antibiotics can be excreted in sweat and could therefore affect the normal resident microbiota.
Patients aged less than 18 years.
Pregnant women.

A data monitoring committee was also convened for the trial.
As the intervention being investigated was part of a routine surgical procedure no other protections were required.

Background therapy:

Not applicable.

Evidence for comparator: -

Actual start date of recruitment	23 May 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 407
Worldwide total number of subjects	407
EEA total number of subjects	407

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	350
From 65 to 84 years	56
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients admitted for spinal surgery (Belfast Trust) were invited to participate in the study at pre-op assessment (4 to 6 months prior to their operation). Following admission 408 patients were recruited to the trial between 23/05/2010 and 07/07/2014.

Pre-assignment

Screening details:

All patients undergoing elective spinal surgery were screened and invited to participate in the study at a preoperative visit or by letter. 557 patients were approached and screened in accordance with the trial inclusion/exclusion criteria. 149 patients were deemed ineligible and were not recruited.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Investigator, Data analyst[2]

Blinding implementation details:

The randomisation schedule was generated before the start of the trial by a statistician not involved in the trial or assessing outcomes. The trial was open label to the patients and hospital staff as the antiseptics were different colours and formulations. The principal investigator and staff who analysed and recorded bacterial culture from samples were however blinded to the treatment group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1

Arm description:

Patient skin disinfected before surgery using PVI (10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, povidone iodine; Videne Alcoholic Tincture) twice.

Arm type	Active comparator
Investigational medicinal product name	PVI (povidone iodine; Videne Alcoholic Tincture)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution, Cutaneous solution + medicated sponge
Routes of administration	Cutaneous use

Dosage and administration details:

10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, applied neat, twice to skin surface before surgery.

Arm title	Arm 2

Arm description:

Patient skin was disinfected before surgery using PVI (10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, povidone iodine; Videne Alcoholic Tincture) once followed by CHG (2% [w/v] chlorhexidine gluconate in 70% [v/v] isopropyl alcohol; Chloraprep with tint).

Arm type	Experimental
Investigational medicinal product name	PVI (povidone iodine; Videne Alcoholic Tincture) CHG (chlorhexidine gluconate; Chloraprep with tint)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution, Cutaneous solution + medicated sponge
Routes of administration	Cutaneous use

Dosage and administration details:

10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, applied once neat to skin surface followed by 2% [w/v] chlorhexidine gluconate in 70% [v/v] isopropyl alcohol, applied once neat to skin surface before surgery.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: The trial was open label to the patients and hospital staff as the antiseptics were different colours and formulations. The principal investigator and staff who analysed and recorded bacterial culture from samples were however blinded to the treatment group.

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The trial was open label to the patients and hospital staff as the antiseptics were different colours and formulations. The principal investigator and staff who analysed and recorded bacterial culture from samples were however blinded to the treatment group.

Number of subjects in period 1	Arm 1	Arm 2
Started	204	203
Completed	204	203

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1
Reporting group description:	
Patient skin disinfected before surgery using PVI (10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, povidone iodine; Videne Alcoholic Tincture) twice.	
Reporting group title	Arm 2
Reporting group description:	
Patient skin was disinfected before surgery using PVI (10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, povidone iodine; Videne Alcoholic Tincture) once followed by CHG (2% [w/v] chlorhexidine gluconate in 70% [v/v] isopropyl alcohol; Chloraprep with tint).	

Reporting group values	Arm 1	Arm 2	Total
Number of subjects	204	203	407
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41	49	
full range (min-max)	19 to 84	18 to 87	-
Gender categorical Units: Subjects			
Female	100	112	212
Male	104	91	195
Surgeon Details Units: Subjects			
Surgeon 1	121	124	245
Surgeon 2	83	79	162
Surgical Site Units: Subjects			
Anterior Cervical	12	13	25
Anterior Thoracic	1	0	1
Posterior Cervical	5	6	11
Posterior Cervico-Thoracic Junction	1	0	1
Posterior Lumbar	179	180	359
Posterior Thoracic	3	2	5
Posterior Thoraco-Lumbar Junction	3	2	5
Surgical Site Shaved Units: Subjects			
Yes	50	47	97
No	154	156	310
Systemic antibiotics received Units: Subjects			
Yes	203	203	406
No	1	0	1
Ioban Drape			
Use of an Ioban drape (3M, Bracknell, United Kingdom)			

Units: Subjects			
Yes	30	31	61
No	174	172	346
Implanted metal work Units: Subjects			
Yes	36	40	76
No	168	163	331
Mean Incision Length Units: cm			
arithmetic mean	7.7	7.7	
standard deviation	± 5.1	± 4.0	-

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description:	
Patient skin disinfected before surgery using PVI (10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, povidone iodine; Videne Alcoholic Tincture) twice.	
Reporting group title	Arm 2
Reporting group description:	
Patient skin was disinfected before surgery using PVI (10% [w/w (1% w/w available iodine)] in 95% industrial denatured alcohol, povidone iodine; Videne Alcoholic Tincture) once followed by CHG (2% [w/v] chlorhexidine gluconate in 70% [v/v] isopropyl alcohol; Chloraprep with tint).	

Primary: Culture-positive

End point title	Culture-positive
End point description:	
Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions. These were then transported to the lab and processed (destructively) asap same day. Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week. After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.	
End point type	Primary
End point timeframe:	
After surgical incisions have been performed	

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	85	59		

Statistical analyses

Statistical analysis title	Culture-positive
Statistical analysis description:	
Proportion of patients with bacterial contamination of surgical site samples after skin disinfection	
Comparison groups	Arm 1 v Arm 2
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.574

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.866

Primary: Internal samples culture-positive

End point title	Internal samples culture-positive

End point description:

Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions.
These were then transported to the lab and processed (destructively) asap same day.
Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week.
After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.

End point type	Primary

End point timeframe:

After surgical incisions have been performed

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	62	39		

Statistical analyses

Statistical analysis title	Internal samples culture-positive

Statistical analysis description:

Proportion of patients with bacterial contamination of surgical site samples after skin disinfection

Comparison groups	Arm 2 v Arm 1
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.545
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.344
upper limit	0.862

Primary: Aerobic Culture-Positive

End point title	Aerobic Culture-Positive

End point description:

Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions.
These were then transported to the lab and processed (destructively) asap same day.
Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week.
After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.

End point type	Primary

End point timeframe:

After surgical incisions have been performed

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	45	20		

Statistical analyses

Statistical analysis title	Aerobic Culture-Positive

Statistical analysis description:

Proportion of patients with bacterial contamination of surgical site samples after skin disinfection

Comparison groups	Arm 1 v Arm 2
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.386
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.219
upper limit	0.681

Primary: Anaerobic Culture-Positive

End point title	Anaerobic Culture-Positive

End point description:

Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions.
These were then transported to the lab and processed (destructively) asap same day.
Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week.
After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.

End point type	Primary

End point timeframe:

After surgical incisions have been performed

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	79	59		

Statistical analyses

Statistical analysis title	Anaerobic Culture-Positive

Statistical analysis description:

Proportion of patients with bacterial contamination of surgical site samples after skin disinfection

Comparison groups	Arm 2 v Arm 1
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.648
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.429
upper limit	0.98

Primary: High total viable count

End point title	High total viable count

End point description:

Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions.
These were then transported to the lab and processed (destructively) asap same day.
Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week.
After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.

End point type	Primary

End point timeframe:

After surgical incisions have been performed

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	67	47		

Statistical analyses

Statistical analysis title	High total viable count

Statistical analysis description:

Proportion of patients with bacterial contamination of surgical site samples after skin disinfection

Comparison groups	Arm 1 v Arm 2
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.616
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.398
upper limit	0.955

Primary: High aerobic total viable count

End point title	High aerobic total viable count

End point description:

Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions.
These were then transported to the lab and processed (destructively) asap same day.
Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week.
After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.

End point type	Primary

End point timeframe:

After surgical incisions have been performed

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	23	10		

Statistical analyses

Statistical analysis title	High aerobic total viable count
Statistical analysis description:	
Proportion of patients with bacterial contamination of surgical site samples after skin disinfection	
Comparison groups	Arm 1 v Arm 2
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.408
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.189
upper limit	0.88

Primary: High anaerobic total viable count

End point title	High anaerobic total viable count
End point description:	
Several different samples were taken during first 20mins of surgery and immediately stored under anaerobic conditions. These were then transported to the lab and processed (destructively) asap same day. Aliquots of processed samples were grown on a range of agar media, under both anaerobic and aerobic conditions, for 1 week. After 1 week, cross-section of morphologically different isolates were removed from agar plates and subjected to molecular analysis.	
End point type	Primary
End point timeframe:	
After surgical incisions have been performed	

End point values	Arm 1	Arm 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	203		
Units: Positive Patients	65	47		

Statistical analyses

Statistical analysis title	High anaerobic total viable count
Statistical analysis description: Proportion of patients with bacterial contamination of surgical site samples after skin disinfection	
Comparison groups	Arm 1 v Arm 2
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	0.644
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.415
upper limit	1

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The timeframe for reporting of AE and SAEs was three months after the collection of the last sample of each patient.

Assessment type	Systematic

Dictionary used

Dictionary name	SNOMED CT
Dictionary version	2

Reporting groups

Reporting group title	Arm 2 PVI + CHG

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: There was one serious adverse event reported for the study and no non-serious adverse events reported.

Serious adverse events	Arm 2 PVI + CHG		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Nerve injury	Additional description: The SAE reported a nerve injury which is a recognised risk of all lumbar spine surgery and was not related to the study drug.		
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm 2 PVI + CHG		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2010	Protocol version 1.2: Protocol amendment
28 January 2010	Protocol version 1.3:Amendment to letter of invitation to participant
23 May 2011	Protocol version 1.5: Change to exclusion criteria in protocol: Number of days in hospital prior to surgery increased from no more than 2 to no more than 7 to increase recruitment rate.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28963158