A randomised controlled trial to investigate the effects of the use of preoperative GnRH analogue and intra-operative mechanical tourniquet for myomectomy on surgical blood loss.

Dr Salwa Abdullahi Idle[1], Miss Helen Cole[1], Dr Salma Ayis[2], Mr Nitesh Narvekar[1]

King's College Hospital, Women's Health

Introduction

Uterine leiomyomas are benign, smooth muscle tumours of the uterus with a prevalence of clinically significant fibroids estimated to be 50% among black women and 35% among white women. Women often present in the later part of their reproductive years with intractable vaginal bleeding (menorrhagia), an inability to conceive (sub-fertility), recurrent miscarriages and symptoms related to pressure effects on bowel, bladder and renal system. The exact aetiological basis for fibroids has not been established, however racial differences have been noted as they are up to 3 times more common in black women (Day Baird, Dunson et al. 2003) as compared to white or other ethnic populations. A large, population-based study using ultrasound examination in the United States found a cumulative incidence of over 60% for women approaching age 50 years (Day Baird, Dunson et al. 2003). Steroid hormones, particularly, oestrogen, are known to play a major role in the development of these tumours (Shaw 1998). The definitive treatment of fibroids is hysterectomy (removal of uterus), but, in women who wish to preserve their uterus and fertility, the mainstay of treatment is myomectomy (removal of the fibroids), a surgical treatment which was first described in 1844 (Mukhopadhaya, De Silva et al. 2008). Although endoscopic and vaginal approaches can be used in selected patient populations, most patients undergo myomectomy by a transverse or midline laparotomy incision (open myomectomy). The single biggest risk associated with myomectomy is severe intra-operative blood loss (LaMorte, Lalwani et al. 1993); approximately 6%-7% will require a blood transfusions (Hickman, 2016) and up to 2% of women may need a life-saving hysterectomy to control intractable uterine bleeding. Several mechanical and chemical interventions have been described to reduce intraoperative blood loss (Mukhopadhaya, De Silva et al. 2008; Kongnyuy and Wiysonge 2009). Most gynaecologists within the UK prefer pre-operative use of gonadotrophin releasing hormone (GnRH) analogues, intra-operative use of tourniquets or both combined(Taylor, Sharma et al. 2005) which is currently decided via clinician choice.

The aim of this trial was to compare the pre-operative use of GnRH analogues and/or intra-operative use of tourniquets to determine which intervention best reduces the intraoperative blood loss at open myomectomy.

Methods

Study design and participants

In this randomised controlled clinical trial comprising of three arms we compared the use of pre-operative GnRH analogue Prostap (Group A), intra-operative mechanical tourniquet (Group B) and a combination of preoperative GnRH analogue and intra-operative mechanical tourniquet (Group C). This was a single centre study at King's College Hospital, London. Women were eligible if they were

diagnosed with uterine fibroids on ultrasonography, opted for surgery and considered suitable for an open myomectomy by a consultant gynaecologist. Eligibility included women between ages 18-50 years, with a uterine size of over 14 weeks gestational equivalence and/or volume of over 600cm3. Protocol stipulated all participants must be willing to take adequate contraception for the duration of the trial. We excluded all women who had previously undergone a myomectomy, who would be suitable for a vaginal or laparoscopic myomectomy, and/or had any contraindications to Prostap. Each group was stratified into 2 sub-groups; sub-group 1 - patients with large uteri (14-20 weeks gestational equivalence and/or 500-1000 mls volume), and sub-group 2 – patients with extra-large uteri (greater than 20 weeks gestational equivalence and/or greater than 1000 ml volume). The trial was approved by Kings College Hospital, London Research Ethics Committee (REC), and the Medicines and Healthcare products Regulatory Agency (MHRA) for Clinical Trial Authorisation.

Randomisation and masking

Patients were randomly allocated a treatment group by a computer generated random sequence of numbers following a 1:1:1 ratio. The research team member gave the investigator (un-blinded) and the pharmacy department a copy of patient allocation for Prostap to be administered. Due to the nature of the intervention, patients could not be blinded to their treatment group. However, patients in groups A and C were not informed whether they were to receive a tourniquet or not. All patients in their consent form were asked not to disclose if they were given an injection to their surgeon or a member of their team. The allocations were stored in an envelope in patients notes to avoid the surgeon being un-blinded. Surgeons in Group A were un-blinded to patient allocation. Surgeons in groups B and C were blinded and unaware if the subject had pre-operative GnRH analogue.

Interventions

Patients allocated to use of pre-operative GnRH analogues (groups A and C) were prescribed Prostap (Leuprorelin acetate depot injection, Takeda, UK) as a single dose of 3.75 mg by intramuscular or subcutaneous injection every 28 days, 3 months prior to surgery; whereas patients allocated to the use of intra-operative mechanical tourniquet only (group B) had no injections. Patients from groups A and C were given 3 doses of GnRH analogue (visit 2) before proceeding to surgery using the intervention allocated to the group. These injections were given at the specified appointments and were documented clearly in the patient notes and data capture forms. All medicines were prescribed via the pharmacy at Kings College Hospital Foundation NHS Trust. Full accountability for dispensing and storage procedures was not completed and no trial specific labelling was required due to this being a type A trial with no higher risks than those of standard care. Prefilled syringes once used were not returned to pharmacy and were disposed of in accordance with the trust sharps disposal policy. Times of Prostap reconstitution and administration were recorded in the Case Report Form.

All subjects were added to the waiting list for an abdominal myomectomy at the screening visit. The Gynaecology admissions co-ordinator was contacted to check the time until surgery. All subjects had to wait between 6-9 months for the operation, which was stipulated in the Protocol and which subjects were informed of before consent was taken.

Follow Up

Participants were able to withdraw from the trial at either their own request or the discretion of the treating clinician. For the post-operative visits we allowed a period of one month as a window for follow up. Patients would also be followed up at 3, 12 and 18-months for assessment of ovarian reserve through blood tests Anti-Mullerian, Luteinising, and Follicular stimulating hormone levels. All follow up visits would also include a repeat ultrasound scan to asses uterine volume and quality of life questionnaires (SF-12) and a menstrual flow diary (PBAC).

Outcomes

The primary outcome measure was mean intraoperative blood loss. Swab weighing and blood collected in post-operative drains were used to compute the total blood loss.

Substantial amendments

Due to loss in follow up, secondary measures such as assessment of ovarian reserve, ultrasound, change in quality of life and menstrual diaries were abandoned part way through the trial. Follow up visits at 3-, 12- and 18months were discontinues due to low patient attendance. The research team performed standard assessments of safety reporting any adverse and serious adverse events according to governance protocol for a clinical trial.

Statistical analysis

Based on available data we assume a mean (standard deviation) blood loss of 100 (500) millilitres in group A, 600 (300) millilitres in Group B and 300 (150) millilitres in Group C. A total of 20 subjects were needed in each arm to detect these differences in mean blood loss with 90% power and a significance level of 0.05. To further stratify into sub-groups by uterine size we would needed 40 women to be recruited in each arm. Sample size estimation was performed using the statistical package 'Stata'(Statacorp LP Ltd).

All participants who were randomised to an intervention had their data analysed at the end of the trial using standard software (SPSS v25.0). Intergroup differences were assessed by the Kruskal-Wallis one-way analysis of variance (ANOVA) with Bonferroni correction. Post-Hoc analysis and Mann-Whitney U test, with two-Sample Kolmogorov-Smirnov Test to account for a smaller sample group, were applied. A subgroup analysis to test for blood loss versus uterine size was also performed.

Results

A total of 73 subjects were recruited in total between April 2012 and April 2019, with 43 participants into group A (n=14), B (n=12) and C(n=17) included in the analysis due to a high withdrawal rate.

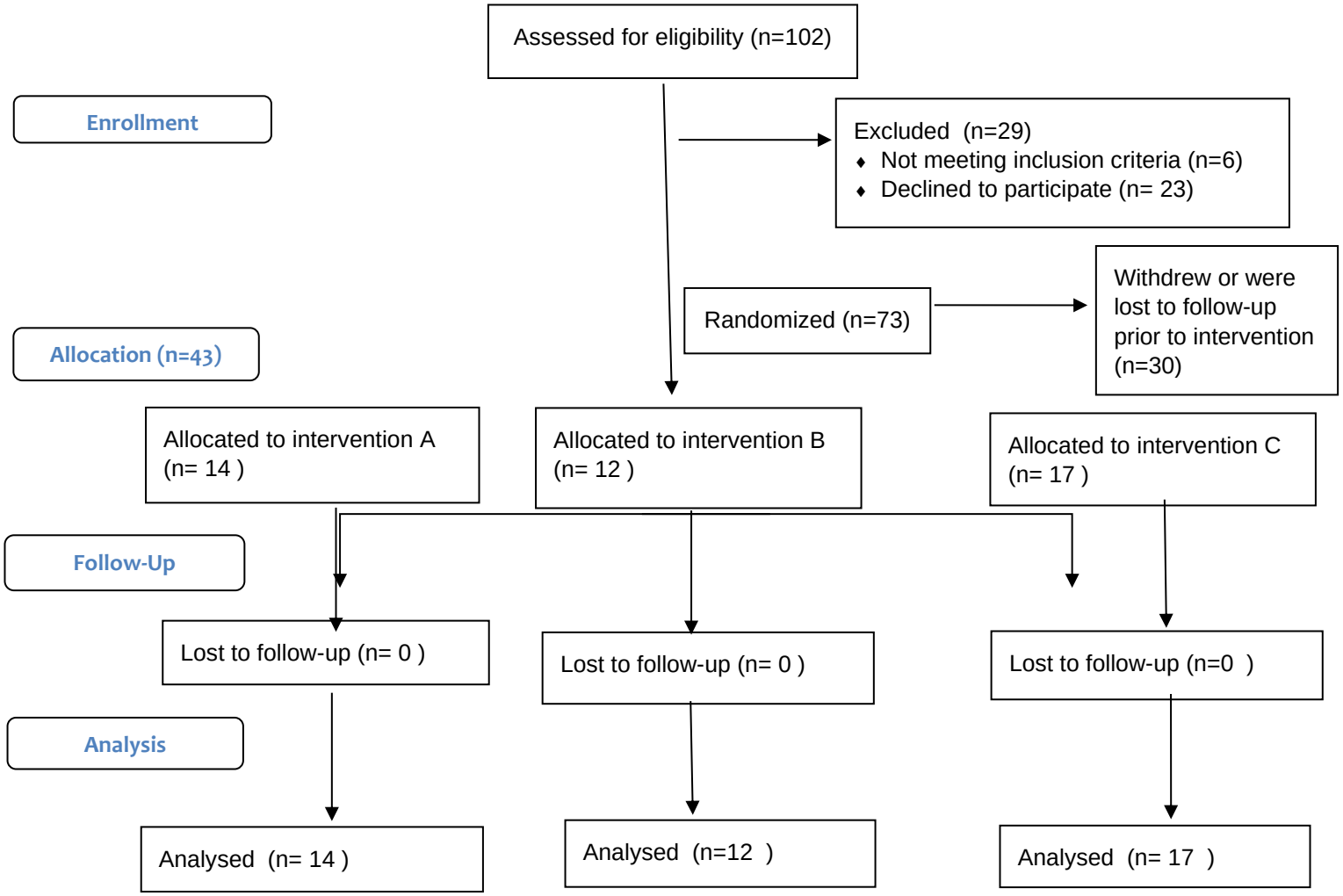

Figure 1 Trial Profile

Baseline characteristics seemed similar between the three groups.

Table 1 Maternal demographic and characteristics at randomisation

Number of subjects (n (%))		A(n=14) GnRH	B (n=12) Tourniquet	C (n=17) GnRH+Tourniquet
Age mean(SD)		40.8(4.7)	39.8(5.1)	41.1(4.6)
BMI mean(SD)		29.0(4.4)	30.9 (4)	29.8 (4.3)
Anaemia, Hb <12g/L n(%)		2(14%)	5(42%)	1(6%)
Ethnicity n(%)				
White		1 (2%)	0	1(6%)
Black		42 (96%)	12 (100%)	16 (94%)
Asian		1 (2%)	0	0
Parity n(%)	**No previous births**	11 (79%)	9 (75%)	14 (82%)
	≥ 1 birth	3 (21%)	3 (25%)	3 (18%)
Smoking status n(%)		1 (7%)	0	2 (12%)

Data are n (%) and mean (SD).

The proportion of women with a greater mean blood loss at surgery was higher in group A (GnRH) 1210mls (964) versus groups B (Tourniquet) 458mls (387) and C (GnRH+ Tourniquet) 406mls (285). It was noted that group A and B had a larger uterine size clinically (n=11/14, 79%) and (n=10/12, 84%) respectively as compared to group C (n=8/17, 47%). Similar numbers of fibroids were removed across groups and the mean number of uterine incisions at surgery across the three groups were balanced. The starting mean haemoglobin (Hb) was overall similar, with more anaemic patients (Hb <12g/L) (NICE guidelines) detected in group A (21%) and B (25%) as compared to C (18%). The Hb drop was largest in group A (27.1g/L) as compared to B (18.4g/L) and C (24.6g/L). Blood transfusion overall occurred in 29% of patients in group A, 25% in group B and 12% in group C.

Table 2 Primary outcome, secondary outcomes and uterine characteristics

		A(n=14) GnRH	B (n=12) Tourniquet	C (n=17) GnRH+Tourniquet
Blood loss (ml) mean (STD)		1210 (965)	458 (387)	406 (285)
Uterine size n (%)				
	14-20 week	3 (21%)	2 (16%)	9 (53%)
	>20 weeks	11 (79%)	10 (84%)	8 (47%)
Number of fibroids removed at surgery mean (STD)		15 (14)	12 (12)	13 (14)
Number of incisions (n)	1	1	3	3
	2 to 4	7	5	4
	≥ 5	6	4	10
	mean	4.7	4	5.7
	std	3.2	1	3.8

Starting Hb g/L* range (mean±STD)	85-145 (126.4±16.8)	99-144 (119.3±17.1)	93-139 (127.2±11.6)
Hb drop mean g/L mean (STD)**	27.1 (10.8)	18.4 (9.2)	24.6 (12.1)
Transfusion n (%)	4 (29)	3 (25)	2 (12)

Data are in mean (STD), n(%). * Missing starting Hb (B=1) **Missing Hb drop data; A(n=2), B(n=4) and C(n-6).

The Kruskall-Wallace shows that the distribution of blood loss was not the same across the three groups (p=0.02), and therefore the null hypothesis is rejected. There was a significant difference between groups A versus B and A versus C (p<0.05). There was no difference in mean blood loss between groups B and C (p=1).

Table 3 The Kruskall-Wallace test with Bonferroni correction.

Sample 1-Sam...	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj.Sig.
B-C	-.103	4.732	-.022	.983	1.000
B-A	14.464	4.937	2.930	.003	.010
C-A	14.361	4.529	3.171	.002	.005

Each row tests the null hypothesis that there is no difference in the primary outcome between the groups (p=0.05). Significance values have been adjusted by the Bonferroni correction for multiple tests.

To reduce the risk of type I error ANOVA was applied with Bonferroni correction (Table 4). This showed a significant difference between groups, with a mean difference in blood loss of A Vs B (752mls, p=0.01) and A Vs C (804mls, p=0.002). There was no significant mean difference in blood loss between groups B and C (52mls, p=1).

Table 4 Multiple comparisons; ANOVA with Bonferroni correction

		Mean Difference			95% Confidence Interval	
(I) Group	(J) Group	(I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
A	B	751.95*	241.332	**.010**	148.90	1355.01
	C	804.11*	221.398	**.002**	250.87	1357.35
B	A	-751.95*	241.332	**.010**	-1355.01	-148.90
	C	52.16	231.295	1.000	-525.82	630.13
C	A	-804.11*	221.398	**.002**	-1357.35	-250.87
	B	-52.16	231.295	1.000	-630.13	525.82

Multiple Comparisons

(I) Group assigned	(J) Group assigned	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
A	B	751.952*	241.332	**.009**	164.57	1339.33
	C	804.109*	221.398	**.002**	265.24	1342.98
B	A	-751.952*	241.332	.009	-1339.33	-164.57
	C	52.157	231.295	**.972**	-510.80	615.11
C	A	-804.109*	221.398	.002	-1342.98	-265.24
	B	-52.157	231.295	.972	-615.11	510.80

*. The mean difference is significant at the 0.05 level.

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The Post-hoc analysis reveals that between group A and B there is a statistically significant difference in blood loss (p=0.09), and this is also seen between group A and C (p=0.02). However, there was no significance in blood loss between groups B and C (p=0.97).

Table 5 Post-Hoc Analysis

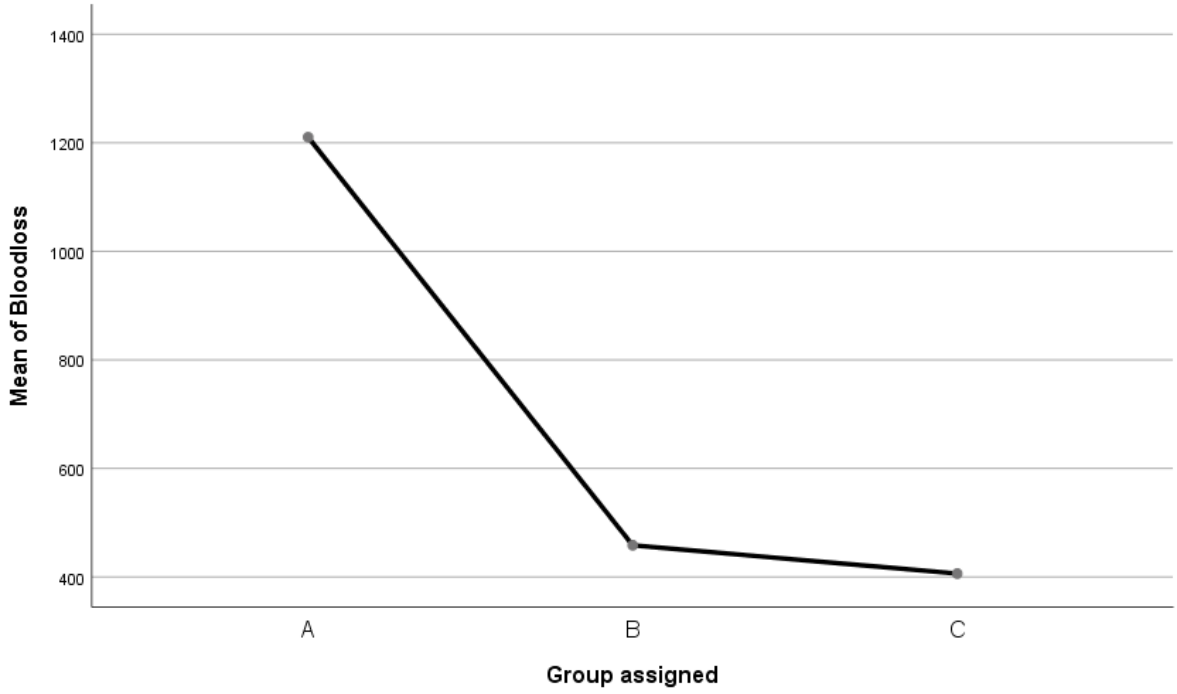

Figure 2 Mean blood loss versus group assigned.

Mann-Whitney U analysis showed the groups were not equal with a significant mean blood loss at surgery between group A and B (p=0.04); A and C (p=0.01) and A and BC (p=0.001). In order to account for the smaller sample size, the Two-Sample Kolmogorov-Smirnov (KS) test was applied and this showed a significant difference between groups A and B (p=0.012,) A and B (p=0.08) and A versus BC (p=0.02).

Table 6 Mann-Whitney U analysis with Kolmogorov-Smirnov

	A Vs B	A Vs C	A Vs BC
Mann-Whitney U	29.000	38.000	67.000
Wilcoxon W	107.000	191.000	502.000
Z	-2.831	-3.216	-3.527
P value	**.004**	**.001**	**.001**
Kolmogorov-Smirnov Z	**0.012**	**0.08**	**0.02**

A subgroup analysis was used for hypothesis generating purposes. Mann-Whitney U for the sub-analysis shows that there is no statistical significance (p=0.45) between mean blood loss at surgery and uterine size across the groups.

Table 7 Mann-Whitney Test- Blood loss Vs Uterine size

	UterineSize	N	Mean Rank	Sum of Ranks
Bloodloss	14-20 weeks	14	19.93	279.00
	>20 weeks	29	23.00	667.00
	Total	43		
Mann-Whitney U		174.000		
Wilcoxon W		279.000		
Z		-.752		
p-value		**.452**		

Adverse Events

System Organ Class	**Preferred term**	**Number of Subjects Experiencing the**	**Total Number of Occurrences of**	**Number of Subjects Experiencing the**	**Total Number of Occurrences of**	**Number of Subjects Experiencing the**	**Total Number of Occurrences of**

		AE in A Arm	the AE in A Arm	AE in B Arm	the AE in B Arm	AE in C Arm	the AE in C Arm
Infections and Infestations	Sepsis	1	1	1	1	0	0
Infections and Infestations	LRTI	0	0	0	0	1	1
Investigations	Haemoglobin decreased	0	0	0	0	1	1

Discussion

Main findings

In this randomised clinical trial in women undergoing open myomectomy, the application of a mechanical tourniquet with or without pre-surgical GnRH at the time of surgery significantly reduced the intraoperative blood loss. The mean blood loss in group A (GnRH) was significantly higher as compared to groups B (Tourniquet) and C (GnRH+Tourniquet). There was no significant difference in mean intraoperative blood loss between patient receiving a tourniquet alone or in combination with GnRHa. The patients who received pre-operative GnRHa had a greater Hb drop post-operatively and patients in this group received blood transfusion more frequently. The size of the uterus did not correlate significantly with the mean blood loss at surgery, but rather the treatment group did.

The strength of this study was that it was a randomised clinical trial with an objective analysis of the mean blood loss at open myomectomy comparing conventional methods known to gynaecologists. The trial was conducted to required standards, with a prespecified protocol requiring amendments only to secondary outcomes. The surgeons using a tourniquet at surgery were blinded as to whether a patient had GnRH prior to the operation, allowing for no bias in operative techniques. The trial was undertaken at a tertiary hospital with a wide demographic representation of women who present with fibroids. Thus, the findings from the trial are transferrable to other similar groups of patients and hospital settings.

The limitations of the trial include lower than required number of participants due to a prolonged trial time, changeover of research teams and significant follow up required over the years. Although there is an evident difference between treatment groups, the secondary outcomes could not be

assessed nor the impact on the quality of life for women who undergo an open myomectomy in this study.

Women with uterine fibroids who undergo open myomectomy as a treatment modality are at a significant risk of excessive intraoperative blood loss which may require blood transfusion and emergency hysterectomy. Effective measures at reducing blood loss at surgery have been reported previously in the literature and can be categorised as either pre-operative or intra-operative.

Pre-operative measures include Gonadotrophin releasing hormone (GnRH) analogues, progesterone receptor modulators and aromatase inhibitors. These measures are used to shrink the fibroid(s) pre-operatively and therefore potentially reduce intra-operative blood loss. Intra-operative measures at reducing blood loss include the use of medications to work on the coagulation pathway such as tranexamic acid or uterotonics e.g. oxytocin, vaginal misoprostol and intramyometrial vasopressin with varying degrees of effectiveness on blood vessels and blood loss. Mechanical intraoperative options include the use of a peri-cervical tourniquet or temporary occlusion of the uterine arteries through clamping, ligating or clipping (Bhagavath, 2019).

Despite the many varied interventions that have been described to reduce intraoperative blood loss, the effect size of these measures is unknown (Kongnyuy & Wiysonge, 2011). A recent survey of 68 Canadian gynaecologist (57% response rate) showed that GnRHa was used by 79% of clinicians and 66% used mechanical tourniquet (Nensi 2020), with no data showing how many used these methods simultaneously. There is a lack of data in the literature comparing different interventions used in myomectomies and therefore a need to identify the most effective procedures with minimal adverse effects to facilitate the gynaecology surgeon choice (Kongnyuy & Wiysonge, 2011).

Gonadotrophin releasing hormone analogues (GnRHa) bind to the GnRH receptor in the anterior pituitary and over a period desensitize the pituitary gland via negative feedback (Shaw 1998) leading to a pseudo-menopausal hypo-oestrogenic state. It is now well established that use of GnRHa results in a temporary reduction in fibroid size, reducing uterine volume by up to 2 weeks gestational size (Lethaby, Cochrane) with improvement in fibroid-related symptoms. Although, fibroids continue to shrink with long-term use, the major reduction in size is attained following 3 months of use (Shaw 1998) and hence most clinicians restrict the use of pre-operative GnRHa to this duration, thereby avoiding unpleasant side-effects and risks of long-term use.

Pre-operative GnRHa have also been shown to significantly reduce intra-operative blood loss during myomectomy as compared to placebo (Lethaby 2009 Cochrane, Vollenhoven et al. 2001). This has been reported as a benefit of around 100mls intraoperatively as compared to no treatment (Miliano et al 2017). In the past the blood loss has been correlated with uterine size with suggestions that the benefit of pre-operative GnRHa is greatest in uteri that are larger than 600 ml in volume (Shaw 1998). However, our subgroup analysis showed that there was no statistical significance ($p=0.45$) between mean blood loss at surgery and uterine size across the groups, but rather that the allocated treatment group influenced the blood loss.

The use of GnRHa is also known to help correct anaemia pre-operatively and can increase the Hb by as much as 13g/L (Lethaby, Cochrane review). A Cochrane review on the effect of GnRHa (Lethaby 2001) showed that its use provided a small improvement in post-operative haematological indices, however, there was no association with a reduced need for blood transfusion due to limited evidence. The starting Hb for 8/43 patients (19%) in our study classified them as anaemic by the NICE guideline's definition (Hb < 12g/L) at randomisation (NICE). A total of 20% of participants in our

study required a blood transfusion which is significantly higher than what has been reported in literature of 6-7% for an open myomectomy (Lethaby). The patients who received a tourniquet alone had a lower starting Hb (119.3 g/L (17.1)) at randomisation with 42% of them being anaemic at onset. Despite having the lowest mean intraoperative blood loss, their requirement for blood transfusion (25%) was comparative to those who received GnRH alone (29%), suggesting a suboptimal pre-surgical treatment of their anaemia.

In addition to a correction of anaemia and reduction of blood loss, GnRHa has also been shown to avoid a mid-line incision (Myers, Barber et al. 2002), and this may facilitate a quicker recovery and a reduced in-patient stay. A major disadvantage of pre-operative GnRHa often quoted, is an increased level of surgical complexity due to loss of surgical planes (Deligdisch, Hirschmann et al. 1997) and the high risk of recurrence of fibroids (Fedele, Vercellini et al. 1990). In a randomised trial investigating the loss of surgical planes following GnRHa administration surgeons reported that in up to 40%-58% of cases there was a loss of the cleavage plane between the fibroid and the surrounding healthy myometrium, rendering the operation more difficult to perform (De F 2009).

The use of tourniquets for open myomectomies has been documented since the 1950's (Rubin 1952; Rubin 1953) and they have been shown to be highly effective (Taylor, Sharma et al. 2005). Their efficacy appears to be independent of uterine size. The classic technique involves either placing a single clamp, tourniquet, or suture around the cervix or a triple tourniquet where the infundibulopelvic ligaments are also occluded (Al-Shabibi, 2010). However, there is a theoretical concern of inducing ischemic damage to ovarian (Fletcher, Frederick et al. 1996) and uterine tissue and their function, especially in patients with very large uteri who often require long duration of tourniquet use. They may also mask inadequate haemostasis, leading to excessive blood loss once the tourniquet is removed (Kongnyuy & Wiysonge, 2011).

In a small case-control study (Essone et al, 2019) tourniquet exposure times of <90minutes did not show an increase in plasma ischemic markers. Moreover, the study suggests that uterine ischemia is likely related to the surgical technique rather than the haemostatic method used for an open myomectomy. Therefore, there is limited evidence to suggest that ischemia is ensued by the use of tourniquet alone (Al-Shabibi 2010, Esoone 2010). However, because the potential for ischemic injury does exist, surgeons will monitor the time of tourniquet use with some opting for intermittent release, whilst keeping its overall use to a minimum.

A randomised single blinded parallel group study with 24 patients allocated to either the use of a tourniquet versus intramyometrial vasopressin showed a similar reduction as our study in mean intraoperative blood loss of 465mls ($p<0.001$) and a Hb drop by 16g/L ($p<0.001$) when using tourniquet alone (Saha et al, 2016). This study suggest that intramyometrial vasopressin eliminates the risk of any ischaemic damage to the uterus. However, vasopressin is a fast-acting vasoconstrictor with a half-life of 10-20min and therefore is time dependent. Furthermore, there have been cases of significant side effects such as severe bradycardia, cardiovascular collapse and even death with the use of intramyometrial vasopressin (Chilkoti, 2016).

A similar randomised trial to our study with allocation to two intervention groups, GnRHa versus triple tourniquet, of 40 patients showed the measured intra-operative blood loss was significantly higher in the GnRH analogue group (median 2482 ml, 95% CI 1744–3151) compared with the triple tourniquet group (mean 640 ml, 95% CI 418–881) (Al-Shabibi 2009). There was a higher blood loss in both groups than in our study and this was likely due to 2 outliers in their GnRHa group with a blood loss of over 5000mls and significant postoperative complications. Furthermore, a larger number of fibroids were removed in their triple tourniquet group as compared to our single use of tourniquet group (22 fibroids Vs 11 fibroids) which may again have accounted for the blood loss being higher

than in our cohort. Nevertheless, this study showed that GnRHa was not superior to the use of tourniquets for the reduction of intraoperative blood loss.

There is no consensus as to which haemostatic method is most effective at reducing intra-operative blood loss. A Cochrane systematic review was carried out in 2011 (Kongnyuy & Wiysonge) of 12 randomised control trials (RCT) with 674 participants undergoing minimal access (hysteroscopic, laparoscopic) or open myomectomy. This study found that several medical (including misoprostol and vasopressin) and mechanical methods (tourniquet) showed a significant reduction in blood loss of 69mls-545mls ($p<0.05$). Of interest the use of a tourniquet significantly reduced intra-operative blood loss (mean difference -289.44mls, 95% CI -406.55 to -172.32). As it was not a comparative study it did not answer the questions as to which the best method is.

In our study the additional comparison of the use of GnRHa with tourniquet shows that there is no added benefit to the use of GnRHa to reduce the intraoperative blood loss. The use of GnRHa as discussed will certainly reduce uterine volume, fibroid size, improve haematological indices and help avoid a midline laparotomy. But its effect on reducing intraoperative blood loss is not significant.

There is a wide variation in clinicians' choice when it comes to haemostatic measures taken at open myomectomy. This study has shown that clinicians can be more confident in the effect of intraoperative blood loss when performing open myomectomies where patients have not received prior GnRH. This is useful in avoiding delays for surgery in cases where there will be difficulty with patient compliance, significant side effects experienced from GnRH and/or dispensary issues with GP's. It will allow for a more individualised approach and patients will also benefit from having the choice to avoid GnRH if this is their preferred option.

Conclusion

The use of a mechanical tourniquet with or without pre-operative gonadotrophin releasing hormone analogues is significantly more effective at reducing intraoperative blood loss at open myomectomy than the use of pre-operative gonadotrophin releasing hormone analogues alone.