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ARTICLE

Optimum uterine filling pressure for outpatient diagnostic hysteroscopy: a double-blind, randomized controlled trial

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Abstract This study designed a double-blind, randomized controlled trial to assess whether adequate visibility can be achieved with lower uterine filling pressures using normal saline for diagnostic outpatient hysteroscopy and whether patient discomfort can be reduced. A total of 234 patients were randomized to 40 mmHg (77 patients), 70 mmHg (78 patients) or 100 mmHg (79 patients) of uterine filling pressures. The primary outcome measure was the proportion of procedures where adequate visibility was achieved during diagnostic outpatient hysteroscopy. The secondary outcome was the level of pain experienced by the patient as assessed using a visual analogue scale. There was adequate visibility in 87.0% of cases in 40 mmHg group, 94.9% in 70 mmHg group and 97.5% in 100 mmHg group. Visibility was lower with 40 mmHg compared with 70 and 100 mmHg ($P < 0.05$). The mean pain score in each group was not significantly different. In conclusion, this study showed that there was a higher trend towards inadequate visibility with lower filling pressures. Pressures of 70 and 100 mmHg may be equivalent to each other but not to a pressure level of 40 mmHg. Pain scores do not differ significantly with the pressure options used.

KEYWORDS: office hysteroscopy, outpatient diagnostic hysteroscopy, outpatient hysteroscopy, pain score, uterine filling pressure, uterine distension

Introduction

Outpatient hysteroscopy is now widely available for the diagnostic assessment of uterine cavity and treatment of simple intrauterine pathology. With continuing improvements in technology and the introduction of mini-hysteroscopes, the acceptability and feasibility of office hysteroscopy has increased (Campo et al., 1999; RCOG, 2011). It is generally accepted vision that all gynaecology units should provide a dedicated outpatient

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hysteroscopy service to aid the management of women with abnormal uterine bleeding as such a service is associated with clinical and economic benefits (van Dongen et al., 2007).

For adequate visualization at hysteroscopy, an appropriate medium is required to distend the uterine cavity. Carbon dioxide, normal saline or lactated Ringer's solutions are the most commonly used distension media in the office setting. Carbon dioxide can be used for diagnostic procedures, but for see-and-treat procedures, liquid distension media are necessary and are usually administered under pressure using pressure bags/chambers or hysteroscopic pumps. In the outpatient, setting pressure bags are commonly used for practical reasons.

While high-pressure administration of distension media provide better visualization, such methods are unlikely to be tolerated by a conscious patient. Hence, the clinicians use a pressure level tolerated by the patient that also gives an adequate image. However, despite numerous publications in the literature on the topic of outpatient or office hysteroscopy, robust clinical evidence or consensus is lacking as to what constitutes the optimal uterine filling pressure to perform office diagnostic hysteroscopy. Therefore, this study carried out a double-blind, randomized clinical trial in an attempt to assess whether adequate visibility and reduced pain scores can be achieved with lower uterine filling pressures. The study was designed to evaluate if lower uterine filling pressures were at least as good as the commonly used pressure of 100 mmHg to perform outpatient diagnostic hysteroscopy and whether using lower pressure levels could be used to reduce patient discomfort.

Materials and methods

This equivalence trial was approved by the local Research Ethics Committee (reference no. 06/Q0502/69, approved 14 November 2006) and included three randomized groups comparing 100 mmHg to lower uterine filling pressures of 40 mmHg and 70 mmHg. The primary outcome measure was the proportion of procedures where adequate visibility was achieved during diagnostic outpatient hysteroscopy. The secondary outcome measure was the level of pain experienced by the patient during the procedure as assessed using a visual analogue scale. The design was a double-blind, randomized controlled trial where both investigator and the patient were unaware of the uterine filling pressure used.

Randomization was performed using computer-generated numbers and opaque, sealed envelopes. The sample size for the study was calculated based on the outcome of visualization using calculations described by Machin et al. (1997). One-sided significance was used as this was an equivalence trial. By using difference defining equivalence at 10% and response rate at 90–94%, sample size was calculated at 230 for a three-group study for this study to be adequately powered.

This study was conducted at the University College London Hospital. A total of 234 patients undergoing office hysteroscopy who consented for the study were recruited from March 2007 to May 2011. All signed a written informed consent form and and were given an information leaflet. Non-English speaking women and patients for whom cervical dilation was required were excluded.

The patients were randomized into three groups comprising three different uterine filling pressures used: 40, 70 and 100 mmHg. Visibility was described as adequate for diagnosis when it was possible to assess the entire uterine cavity to include the cornual areas from the level of isthmus satisfactorily. Pain experienced by the patient during the procedure was assessed immediately after completion of the diagnostic hysteroscopy using a visual analogue scale. The scale consisted of a 10-cm line ranging from ordinal number zero as no pain through to 10 as unbearable pain. Any necessary endometrial biopsy or treatment of pathology was carried out after the pain assessment. Successful outcome was considered in terms of adequate visibility to perform diagnostic hysteroscopy.

Data were statistically analysed using Statistical Package for Social Sciences for Windows version 19 (IBM SPSS, USA), and the statistical tests included the chi-squared test and one-way analysis of variance with multiple comparisons. To compare different uterine filling pressures with regards to visibility, the chi-squared test was used. Pain experienced by the patients in the three pressure groups was compared using mean and standard deviation by one-way analysis of variance test. P-values < 0.05 were considered significant.

Hysteroscopy was carried out using a 1.8-mm semi-rigid mini-hysteroscope with a 3.5-mm single-use outer sheath. The telescope had a 0° or forward-looking viewing angle and a 75° panoramic field of view (Gynecare Versascope, Ethicon, Johnson and Johnson). The sheath had a rotatable 10° distal curvature, and included inflow, outflow and expandable instrument channel. Normal saline was used as the distension medium at a pressure of 40, 70 or 100 mmHg. One-litre normal saline bags were housed in a pressure chamber which provided the pressure using an automated pressurizer utilizing CO_2 to maintain the same pressure evenly until the bag was empty (Laprasurge Hi-Flow Irrigation Pump and Bag Chamber, London, UK). The same infusion set (Infusomat Space Line, Braun, Melsungen, Germany), same camera, monitor and light source (Gimmi, Germany) were used for all procedures. A bivalved speculum was passed and the uterine cervix was visualized and cleansed with a disinfectant. No instrument was applied on the cervix to steady it. No local anaesthetic was used. The inflow and outflow channels were completely open during the procedure and the infusion set was primed with saline without pressure. The distal end of the hysteroscope was passed into the endocervical canal under direct visualization and the filling pressure was applied. The hysteroscope was then advanced into the uterine cavity, visualizing the tubal ostia, giving a panoramic view of the cavity, identifying any lesions and slowly removing the instrument as the endocervical canal was viewed (Gulumser et al., 2010). The authors themselves performed all procedures. The procedures were not performed in the presence of active uterine bleeding/menstruation, in which case they were rescheduled. Most women were given 500 mg mefenamic acid orally at least 1 h before the procedure unless contraindicated.

Results

A total of 264 patients were assessed for eligibility and 243 patients were recruited and randomized. Nine patients were excluded due to cervical dilatation requirements and the remaining 234 patients were included in the analysis. There were 77 patients in group 1 (40 mmHg), 78 in group 2 (70 mmHg) and 79 in group 3 (100 mmHg) respectively (Figure 1).

The three groups were comparable with regards to age, parity, indication for hysteroscopy and menopausal status (Table 1). It was possible to perform diagnostic hysteroscopy using all three uterine filling pressures, but higher pressures increased the proportion of adequate visibility. There was adequate visibility at hysteroscopy in 87.0% of cases in group 1, 94.9% in group 2 and 97.5% in group 3 (Figure 2).

The correlation between different uterine filling pressures and adequate visibility was statistically significant ($P = 0.01$). In the analysis of data by cross tabulation, the visibility appeared to be significantly higher with distension pressures of 70 and 100 mmHg compared with 40 mmHg (chi-squared 7.228, $P < 0.05$). The difference between the 70 and 100 mmHg groups was not significant.

The mean ± SD pain scores with the visual analogue scale were 3.84 ± 2.35, 4.56 ± 2.75 and 4.30 ± 2.51 for 40, 70 and 100 mmHg pressure groups, respectively. The differences between the groups were not significant (Figure 3).

Discussion

Over the last two decades, major advances in the field of hysteroscopy have increased the acceptability and feasibility of office diagnostic hysteroscopy (Cicinelli et al., 2003). The advent of micro-hysteroscopy has made it possible to perform this procedure in the outpatients department (De Angelis et al., 2003). This shift in emphasis has arisen partly as a result of advances in technology and also in conjunction with perceived benefits to patients (in terms of convenience and avoidance of general anaesthetic) as well as distinct benefits to the health service in terms of cost reduction (Marsh et al., 2004; Saridogan et al., 2010). This trend is unlikely to be reversed.

There have been several reports on intrauterine pressure at hysteroscopy in the literature (Baker and Adamson, 1996, 1998; Bajka et al., 2009) but no comparative or randomized controlled studies. Studies by Baker and Adamson (1996, 1998) measured the minimum intrauterine pressure required for distension of the uterine cavity during hysteroscopy using saline as the distending medium. In this study, intrauterine perfusion pressure was measured in seven women at the time of hysteroscopy and laparoscopy performed for infertility, pain or both. Distension of the uterine cavity was achieved when the intrauterine perfusion pressure reached a median of 40 mmHg (range 25—50 mmHg). They concluded that fluid with the same

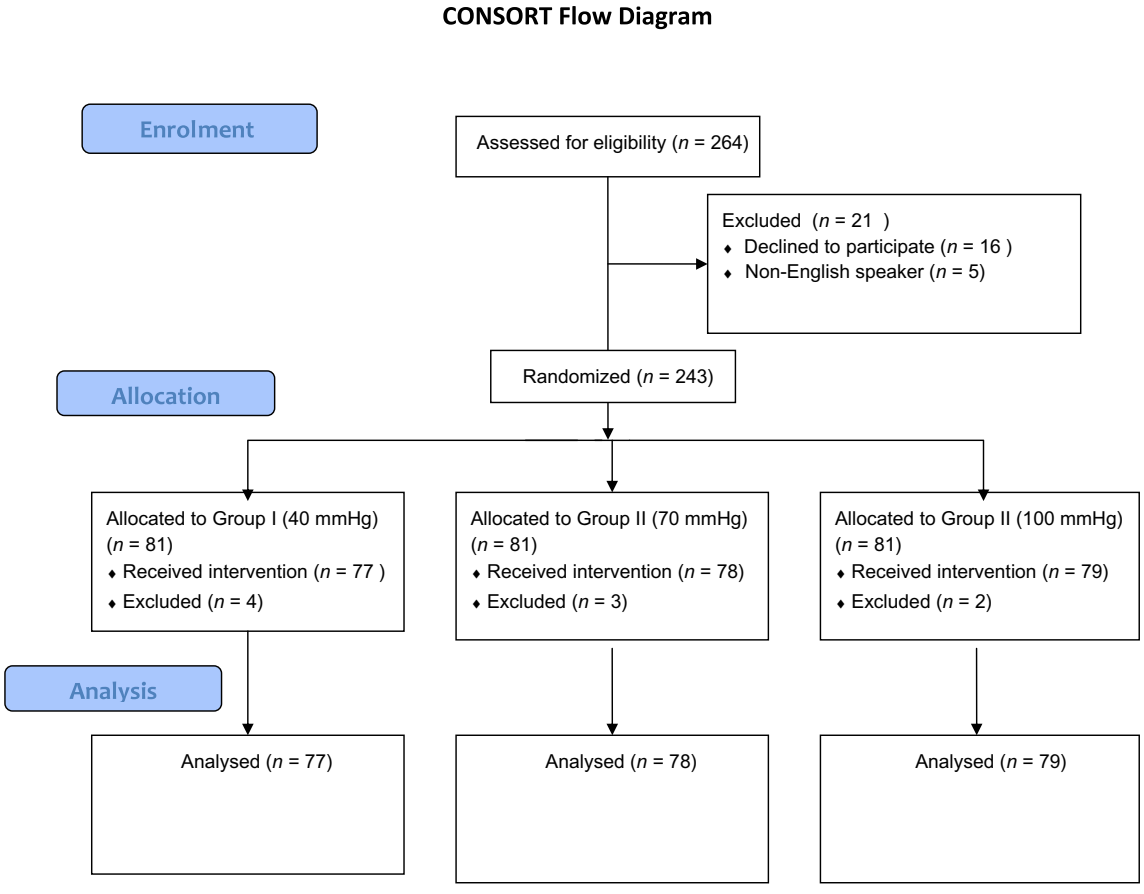

Figure 1 CONSORT flowchart showing recruitment of women into the study.

Table 1 Characteristics of patients included in the trial.

Characteristic	*40 mmHg group* (n = 77)	*70 mmHg group* (n = 78)	*100 mmHg group* (n = 79)
Age (years)	46 (23—81)	44 (24—85)	46 (24—73)
Parity	2 (0—5)	1.5 (0—5)	1.5 (0—5)
Menopause	22 (29)	17 (22)	20 (26)
Indications			
Menorrhagia	17	19	19
Post-menopausal bleeding	16	11	13
Intermenstrual bleeding	17	18	11
HSG/USG abnormalities	13	12	14
Familial cancers	10	15	16
Subfertility	4	3	6

Values are median (range), *n* (%) or *n*. There were no statistically significant differences between the groups.
HSG/USG = hysterosalpingogram/ultrasonogram.

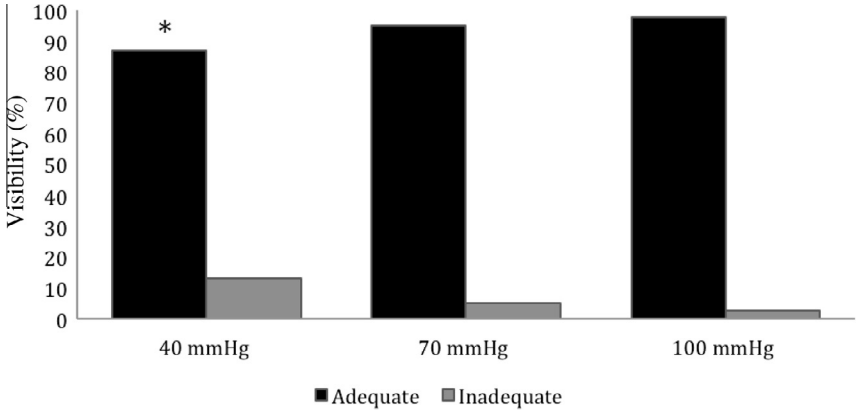

Figure 2 Number of adequate and inadequate visibility in 40, 70 and 100 mmHg uterine filling pressure groups ($^{*}P < 0.05$ compared with 70 and 100 mmHg groups).

viscosity as normal saline would distend the uterine cavity at a pressure of approximately 40 mmHg.

Another study investigated the relation between intrauterine pressures and volumes for virtual-reality-based surgical training in hysteroscopy using 10 freshly extirpated uteri that were insufflated by a commercial hysteroscopy pump using air and imaged by computed tomography. In this study, the hydrostatic pressures to distend the cavity ranged between 16—69 mmHg (Bajka et al., 2009).

In clinical practice, intrauterine pressures are rarely measured for practical reasons and adjustments are usually made on the external pressure applied on the distension medium via pressure bags or chambers. With this in mind, it is recommended that the uterine filling pressures with saline should start at 75—120 mmHg, giving an intrauterine pressure of 50 mmHg, and higher pressures of 150—250 mmHg can safely be used for short periods if required (Clark and Gupta, 2005). The current study did not measure intrauterine pressures for practical reasons and randomized the patients on the basis of external pressures using a simple pressurizer chamber applied on to the bag containing the distension medium. The randomization was based on the filling (or external) pressure applied on to the bag which contained the distension medium (or distension fluid).

Our clinical practice uses 100 mmHg routinely and extremely rarely exceeds this to obtain adequate views of the cavity. This pressure level was compared with lower pressures in this study to see if adequate visibility could still be achieved while reducing pain. A pressure level >100 mmHg was not investigated as it could potentially be more uncomfortable and may not be acceptable.

Discomfort or pain during outpatient hysteroscopy may result from a number of factors in addition to the distension pressure, such as the diameter of the telescope used, use of oral analgesics, local anaesthetics or sedation, parity and menopausal status and whether additional therapeutic procedures are carried out (Cicinelli, 2010). The visibility and pain scores were assessed at the end of the diagnostic procedure before any biopsy or treatment was carried out. The diameter and type (rigid, semirigid or flexible) of the

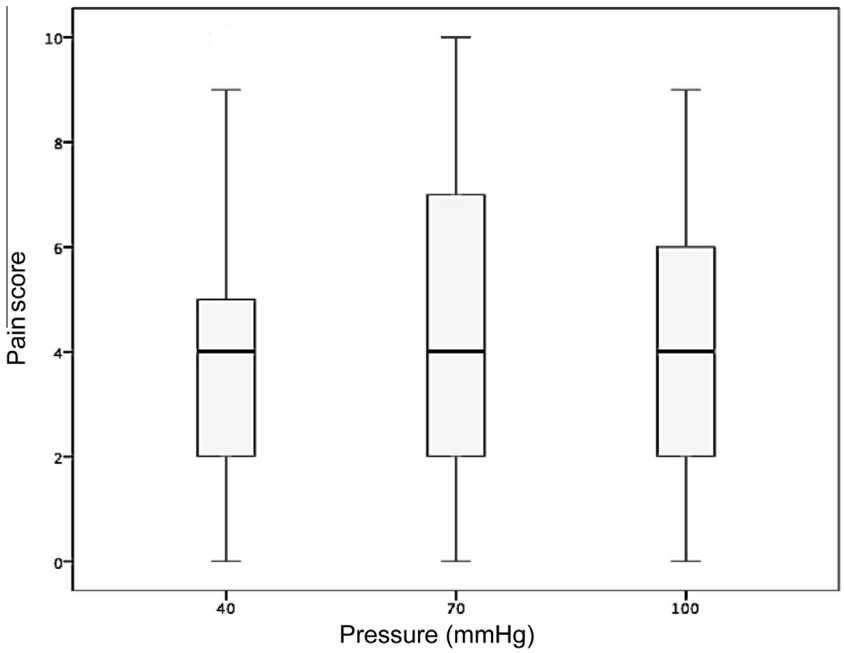

Figure 3 Pain scores in 40, 70 and 100 mmHg uterine filling pressure groups as determined by a visual analogue scale (zero as no pain through to 10 as unbearable pain). Horizontal lines indicate the median, base and top of the boxes indicate the 25th and 75th percentiles and the whiskers indicate the minimum and maximum values. There were no statistically significant differences between the groups.

hysteroscope and the type of distension medium may affect the pain level and visibility (RCOG, 2011). In this study, the hysteroscope, size of fluid bags, distension medium and tubing system were the same for all patients. The age, parity, indication for hysteroscopy and the menopausal status of the patients did not differ between the groups. Most of the patients were given 500 mg mefenamic acid orally approximately 1 h before the procedure. A recent Cochrane review shows that oral nonsteroidal anti-inflammatory drugs do not reduce pain/discomfort during hysteroscopy (Ahmad et al., 2010). This trial did not use local anaesthetic in any of the patients and excluded all who required cervical dilatation.

These results suggest that it is possible to perform office hysteroscopy procedures with external pressures as low as 40 mmHg in the majority of women. However, there was a trend towards increased inadequate visibility with lower pressures, with a significant difference noted in the 40 mmHg group compared with the 70 and 100 mmHg groups. This indicates that there is more likelihood of failure to reach the required intrauterine pressure to distend the cavity with external pressures lower than 70 mmHg. This finding is consistent with the aforementioned experimental studies which measured intrauterine pressures (Baker and Adamson, 1996, 1998; Bajka et al., 2009).

It is generally believed that using saline at low pressures is associated with low pain during outpatient hysteroscopy (Baker and Adamson, 1998). The current study did not find that to be the case, as pain scores in all the three pressure groups did not differ significantly. This supports the concept that the pain threshold is an important factor, or perhaps the most important factor, in determining the level of discomfort/pain experienced. This study does not exclude the possibility that higher filling pressures (i.e. $>$100 mmHg) are associated with higher pain score.

In conclusion, it appears that lower uterine filling pressures (i.e. $<$100 mmHg) can be used for performing office diagnostic hysteroscopy but are associated with a higher trend towards inadequate visibility. Pressure levels of 70 and 100 mmHg may be equivalent to each other but not to a pressure level of 40 mmHg. Pain scores do not differ significantly with the pressure options used.

Clinical Trial registration

ISRCTN 78400671.

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