Gynecol Surg (2014) 11:179–184
DOI 10.1007/s10397-014-0848-2

ORIGINAL ARTICLE

A randomised trial of Medgyn Endosampler® vs Endocurette® in an outpatient hysteroscopy clinic setting

A. S. Khalid · C. Burke

Received: 16 October 2013 / Accepted: 13 May 2014 / Published online: 1 June 2014

Abstract Outpatient hysteroscopy and endometrial biopsy are increasingly being used in the investigation of abnormal uterine bleeding. In our unit, both Endocurette® and Endosampler® endometrial biopsy devices are available in the outpatient hysteroscopy clinic. Literature comparing these devices is lacking. This was a prospective, randomised trial involving women attending the outpatient hysteroscopy clinic at Cork University Maternity Hospital. Women were randomised to endometrial sampling with either Endosampler® or Endocurette® devices. A number of device insertions, pain scores, ease of handling and histological reporting of sample adequacy and tissue histology were recorded. One hundred and six women were recruited comprising 55 pre-menopausal and 51 post-menopausal women. A substantially higher rate of multiple device insertions to obtain a visually adequate sample was recorded using Endocurette® compared with Endosampler®. In the Endosampler® group, 10.7 and 12.5 % of women in pre- and post-menopausal categories had ≥2 device insertions compared to 88.8 and 58.3 %, respectively, with Endocurette® (p=0.002 and p=0.0001). There was no difference in the rate of histologically inadequate samples or difficulty with device handling between matched groups. Mean pain scores in the pre- and post-menopausal groups were 5.83 and 4.58 for Endosampler®, and 4.69 and 4.88 for Endocurette® (p=0.02). The rate of histologically inadequate samples was higher in post-menopausal compared to pre-menopausal women (27.4 vs 3.7 %, p=0.0025). A significantly lower rate of multiple device insertions for adequate histological sample was recorded with Endosampler®. No significant differences in operational difficulties, patient acceptability and sample adequacy were shown. Higher overall pain scores were reported with Endosampler® with no difference in the rate of severe pain between groups' satisfaction with the procedure or willingness to undergo the procedure again.

Keywords Endometrial · Biopsy · Outpatient hysteroscopy · Post-menopausal bleeding · Menorrhagia

A. S. Khalid · C. Burke (✉)
Cork University Maternity Hospital, Wilton, Cork, Republic of Ireland
e-mail: Cathy.burke@hse.ie

Introduction

Outpatient hysteroscopy and endometrial sampling are increasingly being favoured in the investigation of abnormal uterine bleeding. Whilst hysteroscopy, D&C requires general anaesthesia, endometrial sampling can be done without any anaesthetic, or with local anaesthetic. Fine-calibre rigid hysteroscopes and flexible fibre-optic hysteroscopes now allow hysteroscopy without general anaesthetic. This method is increasingly replacing hysteroscopy D&C due to its benefits of avoiding hospital admission and general anaesthetic complications, thus being cost-effective to the hospital [1].

A range of endometrial sampling devices has been developed over the years. The most commonly used endometrial sampling device is the Pipelle de Cornier® device which has shown comparable sensitivity to D&C, supporting its use in an outpatient setting [2]. An inadequate sample rate of 13–20 % with a mean pain score of 1–5 has also been reported [3–7]. Pipelle® has been compared to Vacurette®, Novak®, Vabra®, Accurette® and Explora® in different studies [8–11], which have shown comparable tissue yields, better if not comparable pain scores and shorter procedure time with Pipelle®.

At Cork University Maternity Hospital, women attending the outpatient hysteroscopy clinic are routinely investigated with transvaginal ultrasound followed by saline hysteroscopy and endometrial sampling. The sampling devices available in this setting are Endosampler® and Endocurette®. To date, no

studies comparing these two devices have been reported in the literature. The aim of this study was to compare the Endosampler® and Endocurette® devices in terms of number of device insertions to achieve a visually adequate endometrial sample, pain scores using a visual analogue scale, patient acceptability and user acceptability.

Method

This was a prospective, randomised trial planned to involve around 100 women attending the outpatient hysteroscopy clinic at Cork University Maternity Hospital. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Women were given an information leaflet regarding the study prior to the procedure. Informed written consent was obtained from all women included in the study. Women were categorised into pre- and post-menopausal categories and were then randomised to Endosampler® or Endocurette® device use at the time endometrial biopsy. Stratified randomisation was used to ensure an approximately equal number of women in each group whilst minimising bias over time. Sealed opaque envelopes containing device allocation were randomly prepared in blocks of 10. Randomisation of device allocation was achieved using a random generator. Upon enrolment, an envelope was taken from the front of the relevant pack according to menopausal status. When 5 envelopes remained in a pack, an additional 10 envelopes were supplemented to the packs randomly. This method achieved blinded allocation at the point of enrolment, whist minimising bias over time.

All women had routine transvaginal ultrasound and saline hysteroscopy followed by endometrial sampling using the allocated device. Hysteroscopes used were diagnostic and not designed for directed biopsy, hence the need for blind endometrial sampling. Endocurette® is a straw-like structure with three radially arranged apertures at the tip of the device and an integrated piston which, when withdrawn, generates negative pressure within the cannula allowing endometrium to be drawn into the device as it is withdrawn from the uterus. Its appearance and mechanism of use are similar to the Pipelle® device. It measures 3.6 mm in diameter at the tip and 3.1 mm at the shaft. Endosampler® has a similar straw-like structure, slightly curved at the tip which contains a single aperture. The curette and shaft measure 3.0 mm and are attached to a 10 ml syringe prior to biopsy. The full withdrawn syringe becomes locked into position via a small stainless steel mechanism, generating a relatively strong vacuum effect. Radial curettage of the endometrium can thus be performed. The syringe can be removed from the cannula to expel residual saline from the uterine cavity following saline hysteroscopy, without the need to reinsert the cannula. Two operators were involved in performing sampling. Women and pathologists were blinded to the sampling device used. Clinicians were obviously not blinded, but the devices were used according to manufacturers' instructions to minimise bias. Figures 1 and 2 show the design of both endometrial sampling devices.

Women were asked to rate discomfort during both the hysteroscopy and biopsy procedures separately using a visual analogue scale (VAS), and were asked to verbally rate the worst pain experienced during both procedures where the number 0 represented no pain and the number 10 represented the worst imaginable pain. A post-procedure questionnaire was completed by each participant. To assess the acceptability of outpatient hysteroscopy and endometrial biopsy, women were asked whether they would opt for outpatient hysteroscopy again in the future if required, and whether they would recommend others to undergo this procedure.

A datasheet was completed by clinicians on which information was gathered on the use of local anaesthetic, number of passes of the biopsy device, ease of handling and adequacy of the sample obtained. Ease of device handling was assessed in terms of insertion and operational function. Clinicians were asked to assess using a scale of 1–3 (1 unacceptable, 2 acceptable, 3 excellent) in order to make an objective assessment. Clinicians made a subjective assessment of sample adequacy after biopsy was complete using a scale of 1–3 (1 unacceptable, 2 acceptable, 3 excellent).

Histology reports were followed up post-procedure and were analysed in terms of percentage of adequate samples retrieved and sample volume, as well as the report on histological features. Data was stored in a password-protected file in the hospital computer and patient record number only will be used to identify patients, to ensure patient confidentiality and data protection. Statistical analysis was done using the SPSS statistical package 18 and GraphPad Prism statistical software. Fisher's exact test was used to test for statistical significance between groups.

Results

A total of 112 women consented to the study, of which data on 106 women was obtained, comprising 55 pre-menopausal and

Fig. 1 Medgyn Endosampler®

Fig. 2 Endocurette®

51 post-menopausal women. Six women were excluded from analysis due to intolerance of the outpatient hysteroscopy procedure. There were 54 and 52 women in the Endosampler® and Endocurette® groups, respectively. No differences in age or parity were observed between patients in the two groups. Figure 3 summarises the allocation of women in this study.

In terms of ease of device handling, no significant difference was observed between groups with regard to ease of insertion. Excellent insertion was recorded in 97 and 91 % with Endosampler® and Endocurette®, respectively (p=0.61). There were two occurrences of insertion difficulties which were both in the pre-menopausal group, one in the Endosampler® group and the other in the Endocurette® group. These were both associated with fibroid uteri. In terms of operational difficulties, there was no report of any difficulties in either groups and no significant difference was observed in both groups. Excellence in operational function was recorded in 90 and 85 % in the Endosampler® and Endocurette® groups, respectively (p=0.43).

The rate of repeated (≥2) device insertions was eight times higher in the Endocurette® than the Endosampler® group in pre-menopausal women (p=0.0001), illustrated in Fig. 4. The percentage of patients requiring >2 device insertions to achieve a visually adequate biopsy sample with Endocurette® was 89 % and 58 % in the pre- and post-menopausal groups, compared with 11 and 12 % in respective groups where Endosampler® was used. (p=0.002 and p=0.0001). The overall inadequate sample rate according to the clinician performing the procedure was 17 % in the Endosampler® group and 14 % in the Endocurette® group. There was no significant difference in the rate of visually inadequate samples between groups. More inadequate samples were reported in post-menopausal women (27.4 % of post-menopausal women compared to 3.6 % of pre-menopausal women, p= 0.0025) due to the high level of endometrial atrophy in this group.

Mean pain scores of 5.8 and 4.6 were reported in the pre- and post-menopausal groups with Endosampler® use, compared with 4.7 and 4.9 in the Endocurette® group. The distribution of pain scores amongst all women is illustrated in Fig. 5. Whilst significantly more pre-menopausal women in the Endosampler® group reported pain scores ≥5 compared to the Endocurette® group (p=0.02), no significant difference was observed in post-menopausal women. When pain scores of ≥8 (severe pain) were analysed, no significant difference was observed between groups. Oral analgesics are routinely recommended prior to outpatient hysteroscopy, and were taken by 97 % of women in this study. Local anaesthetic was administered to 44 % (n=47) of women, 37 of which were post-menopausal and 10 pre-menopausal. Lignospan Special® (lignocaine hydrochloride 2 % and epinephrine 1:80,000) was the local anaesthetic used in all cases, two

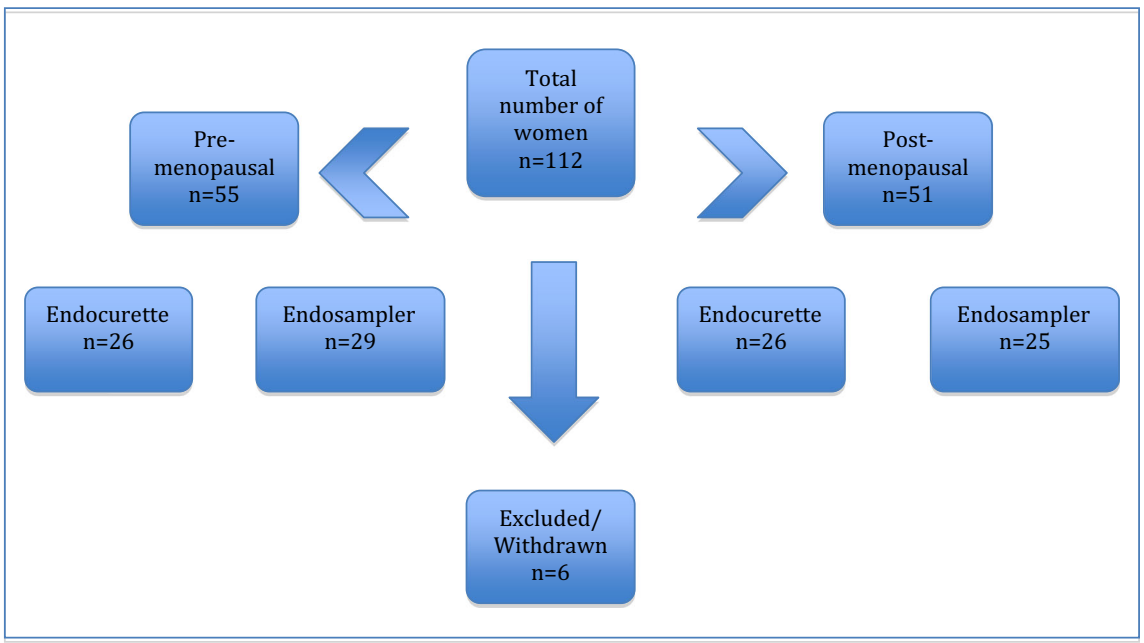

Fig. 3 Distribution of women who participated in our study

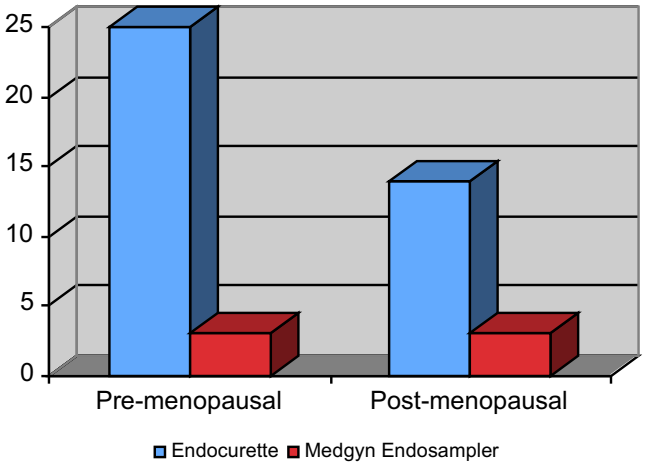

Fig. 4 Women with multiple (≥2) device insertions according to groups

ampoules of which were injected into four quadrants of the cervix prior to hysteroscopy. In cases where local anaesthetic was not used, mean pain scores were 3.39 and 2.30 in the Endosampler® and Endocurette® groups compared with scores of 5.0 and 4.3 in women given local anaesthetic. Significantly more women had pain scores ≥5 in the Endosampler® group (p=0.05). Side effects of local anaesthetic were not recorded in this study. Pain scores reported for hysteroscopy alone were recorded separately and found to be not significantly different between the two groups. In the Endosampler group, the mean was 3.17 (range 0–9), whereas in the Endocurette group, the mean pain score for hysteroscopy was 3.77 (range 0–8).

Histology reports commented on endometrial histology and tissue aggregate size. The aggregate size was subdivided into 'very scanty', 0.1–1.0 cm, 1.1–2.0 cm and >2.0 cm (Table 1). 'Very scanty' biopsy size was reported in 4 % in the Endosampler®, compared with 6 % in the Endocurette® group, all being in post-menopausal women. The difference in the yield of tissue of >2.0 and >1.0 cm in aggregate between devices was not statistically significant (p=0.43 and p=0.50), nor was the difference in 'very scanty' aggregates (0.67). In the Endosampler® group, one case of grade 2 endometrial cancer and two cases of endometrial hyperplasia were reported. In the Endocurette® group, one

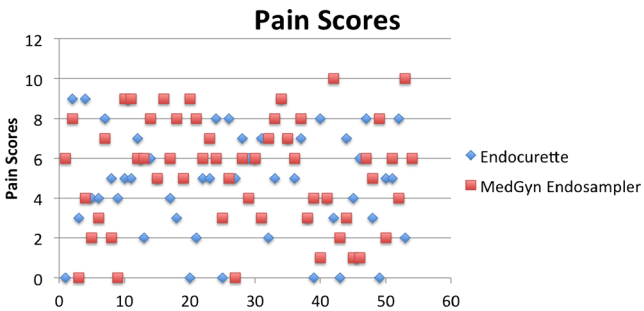

Fig. 5 Scatter plot of pain scores reported by women in all groups; x-axis representing the study number of participants

Table 1 Histology sample sizes reported in aggregates

	Endosampler® (%)	Endocurette® (%)
Very scanty	3.7	5.7
0.1–1.0 cm	70.3	73.0
1.1–2.0 cm	18.5	15.4
>2.0 cm	9.3	3.8

case of grade 1 endometrial cancer was detected. In the post-menopausal group as a whole, 78.4 % were found to have atrophic or inactive endometrium on histology, 3.9 % (n=2) were found to have endometrial cancer, with the remaining 17.6 % having other benign pathology such as endometrial or cervical polyps (Table 2).

There was no difference between groups in terms of patient either willingness to undergo the same procedure in the future or recommendation of the procedure to an acquaintance. Only 4.7 % (n=5) of women reported they would not have the procedure again, 3 of whom were in the Endosampler® group, and 2 in the Endocurette® group with variable pain scores ranging from 1 to 9. Only 3.8 % (n=4) of women, 2 from each group, would not recommend the procedure to others, with pain scores ranging from 5 to 10. Fifteen women (14.1 %) found the procedure more uncomfortable than expected, with pain scores ranging from 0 to 10, of which 9 were in the Endosampler® group and 6 in the Endocurette® group. Sixty-five women (61.3 %) found it less uncomfortable than expected, again with non-correlating pain scores ranging from 0 to 9.

Discussion

Mean biopsy-related pain scores were higher in the Endosampler® group by a factor of around 1 unit. Significantly more women in the pre-menopausal Endosampler® group had pain scores ≥5. Interestingly, pain scores in post-menopausal women were not higher in the Endosampler group. This may be because of the high rate of local anaesthetic use in this group (72.5 %), or the need for fewer device insertions. There was a significantly lower rate of multiple device insertions with Endosampler® compared to Endocurette® in this study, with a consequently shorter procedural time. There was no difference in operational

Table 2 Endometrial pathology in post-menopausal women

Histological findings	Post-menopausal women (%)
Atrophic endometrium	78.4
Benign pathology (endometrial polyps, simple hyperplasia)	17.6
Endometrial cancer	3.9

difficulties between the two devices. No difference in the number of inadequate samples was observed. There was no difference in the number of women consenting to a repeat procedure if required, or recommendation to others. The majority of women found the procedure to be less uncomfortable than expected, but this assertion did not correlate with low pain scores.

Pain scores were reported for the hysteroscopy and endometrial biopsy procedures separately using a visual analogue scale. As these were subsequent procedures, pain scores for both devices could have been affected. However, no significant differences between pain scores for hysteroscopy in both groups were seen. Significantly more women in the Endosampler® group had pain scores of ≥5. This could be explained by the degree of negative pressure generated within the uterine cavity with Endosampler® compared with Endocurette®, together with the technique of 'gentle radial curettage' similar to that done during a D&C. However no significant difference was found between devices when pain scores of ≥8 (severe pain) were examined. This could be limited by the sample size in this study, as only 22 women had pain scores of ≥8; 14 in the Endosampler® group and 8 in the Endocurette® group. The total number of insertions required to obtain a visually adequate endometrial sample was significantly higher in the Endocurette® group. This can be attributed to differences in the design of the two devices. Multiple device insertions theoretically pose a risk of subsequent post-procedural endometritis; however, this complication was not studied. There was no significant difference between the two devices in terms of ease of handling.

We believe that this study has good methodological strength. Women were randomised to either sampling devices in a manner allocating approximately equal numbers in each group according to menopausal status. Effort was also made to minimise potential bias in this study. Women and pathologists were blinded to the device used, allowing objective assessment of pain scores and histology samples. Only two operators were involved in performing sampling to ensure consistency in the technique used. The devices were used according to manufacturers' instructions. Although women and pathologists were blinded to the device used, it was impossible for the operator to be blinded due to the difference in the design and technique used for each device. A limitation of this study is that whilst repeated device insertions could potentially increase the risk of procedure-related endometritis, post-procedure complications were not recorded in the context of this study. Furthermore, the study was not designed to evaluate this risk, which would require a larger sample size, as the incidence of post-procedural endometritis is low. Time taken to obtain a visually adequate sample is likely to have been less in the Endosampler group, but this was not evaluated in our study.

Many studies have compared different endometrial sampling devices in recent decades; however, this is the first study which compares Endosampler® and Endocurette®. The adequacy of sample volume was assessed both subjectively by the clinician and objectively by the pathologist. The inadequate sample rate with both devices was comparable to that of Pipelle® in the published literature, and no significant difference was shown between the two devices in this respect [12]. The rate of diagnosis of endometrial malignancy was comparable to results of previous research [15]. The inadequate sample rate was much higher in post-menopausal women, which is to be expected given the high rate of endometrial atrophy in this group. Whilst some studies suggest further investigation [13–16], in the presence of a normal hysteroscopy, the need for further sampling is questionable. In terms of pain scores, similar visual analogue scoring systems were used in prior studies. Mean pain scores reported for the Pipelle vary between 1 and 6 [10, 11, 14], [17]. Studies comparing various sampling devices reported mean pain scores ranging from 1 to 6.9, comparable to our study [10, 11, 14, 17].

Comparison of different sampling devices is important in light of the increasing availability of outpatient hysteroscopy for the investigation of abnormal uterine bleeding. This study amongst others provides a comparison of two endometrial sampling devices used in an outpatient hysteroscopy setting. Whilst no significant difference in the handling of the devices and number of inadequate samples was observed, there was a significantly lower rate of multiple insertions recorded with Endosampler®, albeit at the expense of a higher mean pain score. In an outpatient hysteroscopy clinic setting where saline is used as the distension medium and a considerable amount of fluid may be present in the uterine cavity, it is particularly useful to use a device which minimises the number of device insertions. The higher pain scores experienced by patients in the Endosampler group, interestingly, did not translate into unwillingness to have the procedure again, or to recommend the procedure to others.

Future studies should seek to evaluate the performance of other available endometrial sampling devices in similar settings. Studies involving larger numbers should also be supported to compare and document the incidence of post-procedural endometritis.

Conclusion

No significant differences in operational difficulties, sample adequacy or acceptability to patients were shown between groups. Higher overall pain scores at endometrial biopsy were reported when Endosampler® was used, although not in the severe pain category and not translating into a reluctance to undergo a similar procedure in the future, or recommend the procedure to others. Significantly fewer device insertions were

required with Endosampler® to obtain a visually satisfactory biopsy sample. The design of Endosampler® allows removal of the distension medium during saline outpatient hysteroscopy without the need for removal and reinsertion of the device catheter. On this basis, we conclude that Endosampler® may be superior to Endocurette® in an outpatient hysteroscopy clinic setting.

Acknowledgments Special thanks to nursing, midwifery and secretarial staff involved in the Outpatient Hysteroscopy Clinic, CUMH as well as all women who kindly volunteered to participate in the study.

Conflict of interest ASK is the primary author who designed the study, collected data, did the statistical analysis and wrote the first draft of the manuscript. CB supervised the project, performed the endometrial sampling procedures and is the guarantor. On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals.

Reference

1. Ghaly S, de Abreu Lourenco R, Abbott JA (2008) Audit of endometrial biopsy at outpatient hysteroscopy. Aust NZ J Obstet Gynaecol 48(2):202–206
2. Russell JB (1988) History and development of hysteroscopy. Obstet Gynecol Clin N Am 15:1–11
3. Huang GS, Gebb JS, Einstein MH et al (2007) Accuracy of preoperative endometrial sampling for the detection of high-grade endometrial tumors. Am J Obstet Gynecol 196(243):e1–e5
4. Madari S, Al-Shabibi N, Papalampros P, Papadimitriou A, Magos A (2009) A randomised trial comparing the H Pipelle with the standard Pipelle for endometrial sampling at 'no touch' (vaginoscopic) hysteroscopy. BJOG 116:32–37
5. Agostini A, Shojai R, Cravello L et al (2001) Endometrial biopsy during outpatient hysteroscopy: evaluation and comparison of two devices. Eur J Obstet Gynecol Reprod Med 97:220–222
6. Tanriverdi HA, Barut A, Gün BD, Kaya E (2004) Is pipelle biopsy really adequate for diagnosing endometrial disease? Med Sci Monit 10:CR271–CR274
7. Machado F, Moreno J, Carazo M, León J, Fiol G, Serna R (2003) Accuracy of endometrial biopsy with the Cornier pipelle for diagnosis of endometrial cancer and atypical hyperplasia. Eur J Gynaecol Oncol 24(3–4):279–281
8. Teale GR, Dunster GD (1998) The Pipelle endometrial suction curette: how useful is it in clinical practice? J Obstet Gynaecol 18:53–55
9. Stovall TG, Ling FW, Morgan PL (1991) A prospective, randomized comparison of the Pipelle endometrial sampling device with the Novak curette. Am J Obstet Gynecol 165:1287–1290
10. Naim NM, Mahdy ZA, Ahmad S, Razi ZR (2007) The Vabra aspirator versus the Pipelle device for outpatient endometrial sampling. Aust N Z J Obstet Gynaecol 47:132–136
11. Lipscomb GH, Lopatine SM, Stovall TG, Ling FW (1994) A randomized comparison of the Pipelle, accurette, and explora endometrial sampling devices. Am J Obstet Gynecol 170:591–594
12. Renaud MC, Le T, Le T et al (2013) Epidemiology and investigations for suspected endometrial cancer. J Obstet Gynaecol Can 35:380–383
13. Farrell T, Jones N, Owen P, Baird A (1999) The significance of an 'insufficient' Pipelle sample in the investigation of post-menopausal bleeding. Acta Obstet Gynecol Scand 78: 810–812
14. Gordon SJ, Westgate J (1999) The incidence and management of failed Pipelle sampling in a general outpatient clinic. Aust N Z J Obstet Gynaecol 39:115–118
15. Renaud MC, Le T, Le T, et al (2013) Epidemiology and investigations for suspected endometrial cancer. J Obstet Gynaeco Can 35: 380–3
16. Gordon SJ, Westgate J (1999) The incidence and management of failed Pipelle sampling in a general outpatient clinic. Aust N Z J Obstet Gynaecol 39:115–8
17. Leclair CM, Zia JK, Doom CM, Morgan TK, Edelman AB (2011) Pain experienced using two different methods of endometrial biopsy: a randomized controlled trial. Obstet Gynecol 117: 636–641