Research Article

Hysteroscopy and pain: what risk factors should we consider in office hysteroscopy? are there really any?

Antonio A. Paulo[1,2]*, Jose Damasceno-Costa[1], Antonio Pipa[1], Vera M. Afreixo[3]

[1]Department of Obstetrics and Gynecology, Hospital Centre Tondela-Viseu, Portugal
[2]Department of Health Sciences, University of Aveiro - Portugal
[3]Department of Mathematics and Institute of Biomedicine, University of Aveiro, Portugal

*Correspondence:
Dr. Antonio A. Paulo,
E-mail: antoniosantospaulo@sapo.pt

ABSTRACT

Background: Office hysteroscopy is the gold standard in abnormal uterine bleeding and an indispensable tool in modern gynecology. It is becoming increasingly popular leading to examinations and even operations without anesthesia as it is accurate, cheap and well tolerated. However, pain is still a limitation. The objective of the study was to determine if pain perception is linked to clinical predictors and how well they correlate with pain score.
Methods: Prospective observational trial enrolled one hundred and four women; four cases were excluded. One hundred cases were included and analyzed. Selection criteria: patients scheduled for Office Hysteroscopy who accepted to participate and had no contraindication for procedure.
Results: A ten centimeter visual analogue scale was used for pain evaluation. Presumed variables such as menopause, pelvic pain, previous cesarean section and cervical surgery, and body mass index were analyzed by ordered regression using standard statistical software tools.
Conclusions: Correlation between predictive factors and pain reporting showed no significance (p>0.05) except for body mass index which was found to significantly correlate to discomfort (p<0.05).

Keywords: Office hysteroscopy, Pain, Predictive factors

INTRODUCTION

In the past fifteen years gynecological care has shifted from hospital care to mostly outpatient interventions with added quality and reduced costs, making it affordable for generalized use. Hysteroscopy as a routine technique is recent, but it all started in 1967 when Fritz Menken used a pediatric cystoscope to examine the womb,[1] allowing direct visualization[2] and diagnosis.[3-6] It is now a day considered the gold standard in investigating uterine abnormal bleeding.[7-10]

Examinations and even operations are performed without anesthesia using Office Hysteroscopy (OH) and it is becoming increasingly popular; modern mini-hysteroscopes are slenderer (outer sheet between 3.1 and 3.6 mm) as opposed to "conventional" hysteroscopes (outer sheet of 5mm diameter) and therefor avoid cervical dilation. Slimmer scopes have been proven to associate to lower pain score at OH and there may be a cutoff around 3.5mm below which reduction in size does not further reduce pain.[11] Other improvements such as misoprostol administration prior to examination and the vaginoscopic no-touch approach seem to increase pain tolerance.[12-14]

De Angelis in 2003 wrote "The main purpose of our Gynecological Endoscopy Unit has always been to diminish the level of pelvic pain or discomfort felt by the

patient during office hysteroscopy in order to make this procedure acceptable and well tolerated; our aim was to make it `pain-free' and therefore widespread as against its presently limited application in Italy."[15] But, despite the enormous success of hysteroscopy, the procedure is not yet painless.[16]

Cicinelli[17] in 2007 published a paper where cesarean section, menopause and chronic pelvic pain were found to significantly influence pain perception (group A patients who reported no pain on a zero to five pain reporting score had lower incidence of these factors and group B where patients reported mild to severe pain). Fonseca in 2014[18] while evaluating predictors of unacceptable pain, found significance only with pain (dysmenorrhea) and hysteroscopist experience. Sessa[19] did not find association between cesarean section and pain. Raymundo[20] found body mass index (BMI) and history of previous curettage to lower pain perception, while menopause and dysmenorrhea would predict higher pain score; association as a determinant however was low. Fonseca in 2009[21] evaluated uterine retroversion as pain predictor and concluded there was no association with pain at hysteroscopy. Finally Mazzon[22] found a protective role in parity, while cervical synechiae and duration of procedure correlated with higher visual analogue score (VAS) for pain.

OH patients may have higher VAS scores with longer waiting time[23,24] and distractions such as music may be associated with lower pain and anxiety.[25] But the question remains, are there clinical predictors associated with pain perception at hysteroscopy? Could theses predictors help select women who would benefit from analgesia or anesthesia?

METHODS

From March to June 2015 patients one hundred and eighteen patients scheduled for OH at Centro Hospitalar Tondela-Viseu, Portugal were invited to enroll in this prospective observational study. Of theses one hundred and four accepted to participate but four cases had incomplete data and were excluded. One hundred cases were included and analyzed. The study was approved by the Institutional Review Board and conducted in compliance with the protocol, the Declaration of Helsinki, the Good Epidemiological Practice, and all applicable laws and regulations.

Inclusion criteria

All women with scheduled OH were considered candidates. Only those who accepted to participate, had no acute infection, were not pregnant and had sufficient understanding of the aim of this study were included. They were fully informed that whether they chose or not to participate, procedure would be the same. All others were excluded (Figure 1).
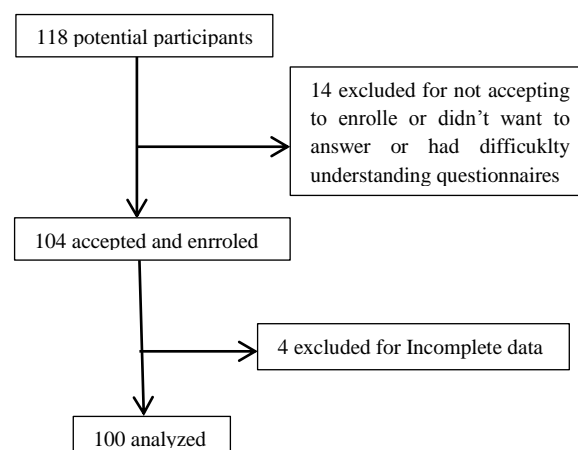

Figure 1: Flow diagram of selection of women.

Population characteristics are described on Table 1 and as shown, there's is a wide variation in age and body weight; fifty-five percent of women were menopausal.

Table 1: Population Characteristics.

	N=100	Minimum	Maximum	Mean	SE
Age		28	84	54.61	13.296
Gesta		0	9	2.19	1.376
Body weight		46	103	68.27	12.203
Height		145	179	159.13	6.447
C-section	21	0	3	.33	.697
Nuligest	9				
Parous	91				
Menopause*	55				
Fertile	45				

*last menses more than twelve months and woman not on hormone therapy

Women were referred to hysteroscopy to study common gynecological conditions: menorrhagia, post-menopausal bleeding, sonographic thickened endometrium and sterility (Table 2).

Table 2: Reason for hysteroscopy.

Frequency	
Menorrhagia	19
Post-menopausal bleeding	15
Thick endometrium	63
Sterility	3
Total	100

Hysteroscopy was performed using the vaginal no touch approach with a 3.5mm outer sheet device (2.9mm optics either from Fiegert Endotech® Tuttlingen, Germany or Karl Storz Hopkins® Tuttlingen, Germany) with a fore oblique 30° mini-hysteroscopy. An Ackermann® xenon

light source and a constant flow Richard Wolf ® hystero pump, using saline at eighty mm of mercury was standard in procedure. A 3CCD endocam® enable vision on a screen. Misoprostol had been prescribed to be applied intra-vaginal the previous night.

At the end of procedure a nurse would show the woman a ruler having on the side facing the patient a straight 10cm line with markings "no pain" at left end and "maximal pain" on the right. A sliding courser was freely placed by the patient over the line where she reported her pain experience. At the back the ruler was graded in millimeters allowing healthcare personnel (nurse) to read results of patient scoring. Authors chose to value centimeters and only whole numbers were taken into account (e.g. 0 to 9 mm score zero, 1 to 1.9 mm scored one and so forth).

Statistical analysis was performed with SPSS 22.0 IBM for windows and in a statistical hypothesis test with a p value <0.05 the effect was considered significant so confidence intervals are reported with 95% confidence level. We conducted multivariate ordered logistic regression analysis. We explored the effect of menopause, dysmenorrhea and history of menorrhagia, parity of women, previous cervical surgery and age in pain score. We tested the proportional odds assumption using a score test.

RESULTS

Hysteroscopy was complete in ninety three cases and failed in seven. Those failures were rescheduled for the same procedure two weeks later. Four cases were not successful at this second attempt and were then scheduled to hysteroscopy under anesthesia. All cases were analyzed irrespective of completion of procedure.

Hysteroscopy findings are as shown in table 3 and include normal cavity, polyp, endometrial hyperplasia, carcinoma, uterine septum and submucosal and intramural mioma.

Table 3: Hysteroscopy diagnosis.

		Frequency
	normal cavity	35
	polyp	45
	hyperplasia	1
Valid	carcinoma	4
	septum	1
	mioma	7
	incomplete visualization	7
	Total	100

Taking into account pain scoring is ordinal; we performed an ordered logistic regression which did not find significance in pain reporting with menopause, dysmenorrhea, and history of menorrhagia, parity of

women, previous cervical surgery or age. We did, however, find significance (p<0.05) in Body Mass Index (BMI) as seen on Table 4, although the effect size was small. We also tested the fitting of the model by performing a parallel lines test which showed a p value = 1.000. The goodness of the fit of the model can be evaluated taking into account the pseudo R squares (Table 5).

Table 4: Ordinal logistic regression.

Source	exp(B)	Wald Chi-Square	Sig.
Menopause	0.957	0.005	0.941
Dysmenorrhea	0.892	0.052	0.820
Menorrhagia	0.546	1.770	0.183
Parous	0.726	0.088	0.766
BMI	0.849	4.996	0.025
Cervical surgery	0.780	0.094	0.760
Age	1.023	1.054	0.305

Score test of the proportional odds assumption p=1.000

Table 5: Pseudo R-Square.

Pseudo R-Square	
Cox and Snell	.131
Nagelkerke	.132
McFadden	.031

Link function: Logit

E.g.: The Nagelkerke R Square indicates the model can account for 13.2% of the variance in tier of entry.
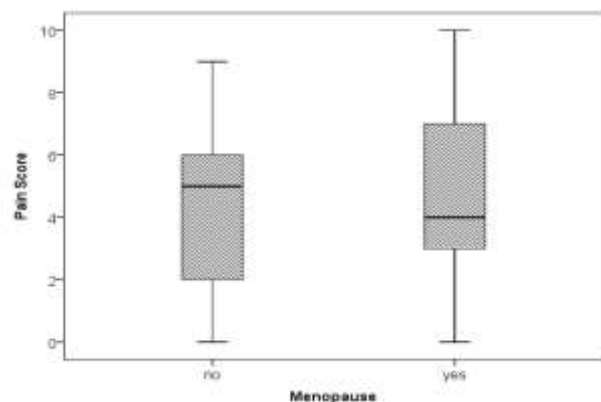

Figure 2: Boxplot pain score verses menopause.

Box plots comparing women before and after menopause, with or without history of dysmenorrhea and with and without cervical surgery, surprisingly showed a trend to lower pain reporting when each of these variables was "yes" (Figures 2, 3 and 4). We would expect menopause, painful menstruation and history of cervical surgery to associate with higher scores which doesn't seem to be the case. Regression results however had no statistical significance as shown on table 4.
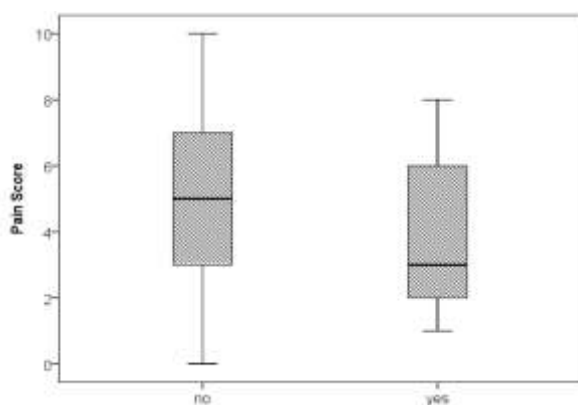
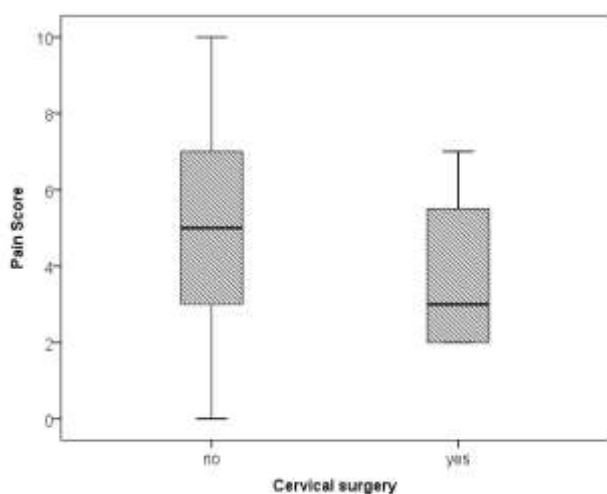**Figure 3: Boxplot pain score verses dysmenorrhea.**
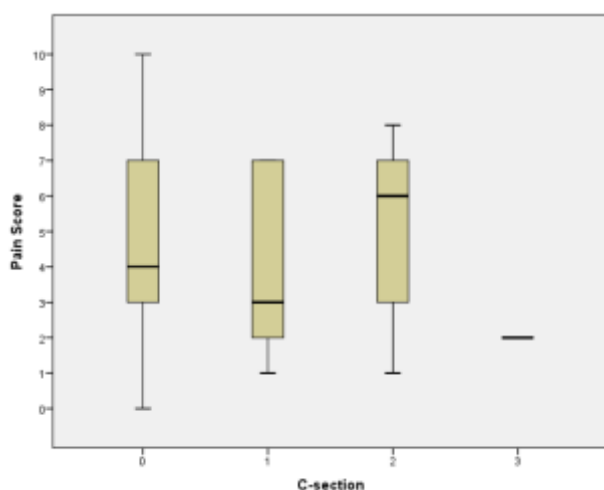

Figure 4: Cervical surgery.

Figure 5: Pain reporting and Cesarean-section.

Finally, cesarean section (C-section) was not included in our regression to avoid collinearity with parity. Boxplots comparing women without C-section and with one, two or three occurrences showed mix results but no clear increase in pain at hysteroscopy (Figure 5).

DISCUSSION

It is interesting to find BMI is associated with lower perceived pain at hysteroscopy and this finding goes in line with Raymundo's results.[20]

Increased levels of estradiol, a significant reduction of sex hormone binding-globulin (SHBG) and a rise in circulating androgens, all being mediated by obesity-related changes in insulin and having a direct relationship to augmented BMI have been well recognized.[26-28] Obesity also gives rise to an increased total body aromatization (in adipose tissue) and consequently moderately elevated estrogen serum levels in overweight postmenopausal women are, in theory, to be expected.

Insulin and SHBG have a 'gonadotropic' effect and insulin and Insulin-like growth factor one (IGF-I) activity may be of less significance before menopause than after its occurrence. In a fertile woman circulating sex-steroid hormones are under the tight control of hypothalamic and pituitary hormones: Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) and regulated by powerful feed-back mechanisms, which subsequently subside after menopause.

Decreased SHBG concentrations, characteristic of obesity, would lead to an increase in free testosterone.[26] Therefor there is an inverse correlation between SHBG with the calculated free levels of both testosterone and estrogens. Studies have suggested that the adipose tissue, with its 17b-hydoxysteroid dehydrogenase activity, may also be an important site of peripheral testosterone production and conversion to estrogens (namely estradiol or estrone).[26,29]

Gynecologists are well aware of obesity, diabetes and hypertension as risk factors for endometrial (and other female hormone dependent) cancers and poor response to aromatase inhibitor treatment in hormone dependent malignancies.[28]

Target tissues (vaginal, cervical and endometrial cell lining) response to these elevated hormones would expectedly counteract atrophy, contributing to eutrophic (hormone dependent) mucosal development and thus might help explain greater ease of the procedure and the lower pain perception in obese women.

CONCLUSIONS

From our results we conclude menopausal state, previous history of cervical surgery, dysmenorrhea, or abnormal uterine bleeding might not have a significant effect on pain.

On the other hand obesity is a reliable predictor of lower pain perception. It is most likely the single most important natural factor which might reduce pain in OH.

Strength's and limitations

This observational study gives us robust information regarding pain and menopausal state compared with pre-menopausal as 55% of women were menopausal upon examination. Elevated BMI has shown to be significant in reducing pain and theoretically this makes sense as, we know, there is a higher level of circulating hormones in these women.

Another putative factor which is parity, seems well represented in this series. It did not show to be associated with significant influence in pain scores. History of previous cervical surgery has few cases and might be less well represented so authors admit larger studies including more cases of women subjected to prior surgery, could help to better understand what role this factor might have in nociceptive experience following hysteroscopy.

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