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ORIGINAL ARTICLE

Analgesics for Pain Relief in Office Hysteroscopy: A Prospective Randomized Controlled Trial

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ABSTRACT

Background: A number of advancements have been implemented in recent years to reduce pain during office hysteroscopy and boost completion rates, for reduction of this pain, many drugs are offered as Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol. Paracetamol act centrally by inhibition of brain cyclooxgynase (Cox). This study aimed to assess the analgesic effect of paracetamol and ipubrofen tablets in pain perception during and after outpatient diagnostic hysteroscopy without anaesthesia. **Methods:** This was a Prospective, Randomized- Controlled clinical trial, conducted at the endoscopy unit of obstetrics and gynecology department at Zagazig university hospitals. Sixty patients included in our trial. The included women were divided into 3 groups; control group: did not receive any medication before the procedure. Group 2 (Paracetamol group): included 20 women received a 1000-mg oral paracetamol tablet, Group 3 (Ibuprofen group): included 20 women received a ibuprofen 600-mg tablet of the same appearance. The treatment was given one hour before the hysteroscopy. **Results:** The main indication for hysteroscopy was abnormal uterine bleeding in paracetamol group 12(60%), ibuprofen group 10(50%) and control group 7(35%). We found that uterine polyps were the major findings. In paracetamol group 8(40%), ibuprofen group 8(40%) and control group 5(25%). The pain scores, which comprised the VAS before hysteroscopy (p=0.976) and the VAS following hysteroscopy (p=0.832). **Conclusions:** The injection of ibuprofen and paracetamol one hour before to an office hysterscopy did not lessen pain during the procedure.
Keywords: Hysteroscopy; Paracetamol; Ibuprofen.

INTRODUCTION

Hysteroscopy is a safe and practical procedure that can be used to diagnose intrauterine pathology, such as irregular bleeding, infertility, and recurrent miscarriages. Furthermore, it has made a number of minimally invasive intrauterine therapeutic interventions either under anesthesia or not possible **[1].**

The gynecologist may find it difficult or impossible to do the outpatient hysteroscopy without anesthesia or sedation since it may cause pain, especially in more sensitive patients. Thus, the primary reason for the failure of outpatient hysteroscopy is patient discomfort and/or pain **[2].**

Less pain can be experienced during uterine cavity access when general or local anesthesia is used, however an operating room and an anesthesiologist are needed for their usage **[3].**

Hysteroscopy performed in an outpatient office is a well-tolerated technique that many women find acceptable. It is less expensive, requires less time in the hospital, heals more quickly, allows patients to return to work sooner, and avoids anesthesia-related side effects including nausea, vomiting, and vasovagal attacks than hysteroscopy performed under general anesthesia**[4].**

Furthermore, Para cervical anesthesia anesthetic blocking administered in the cervix can result in

cervical soreness and bleeding, which goes against the outpatient procedure's main idea **[5].**
Prostaglandins (PGs) in the uterus at high concentrations have been linked to pain during hysteroscopy. Prostaglandins released as a result of cervical manipulation and uterine distension may also induce further delayed pain **[6].**
NSADs (non-steroidal anti-inflammatory medications) decrease the release of prostaglandins. While various gynaecologic procedures can effectively reduce pain with their use **[7].**
As a well-known and efficient pain reliever, paracetamol works centrally by blocking the brain's cyclooxygenase (Cox) enzyme **[8]**.
The aim of this study was to assess the analgesic effects of ipubrofen and paracetamol tablets were evaluated for their ability to reduce pain during and after outpatient diagnostic hysteroscopy in the absence of anesthesia.

METHODS

This prospective-randomized controlled clinical trial study was conducted at the endoscopy unit of Obstetrics & Gynecology Department at Zagazig University Hospitals, Sharkia, Egypt in period from August 2023 to February 2024.
Inclusion Criteria were age between 18-50, women with recurrent pregnancy loss, women with abnormal uterine bleeding, women complaining of infertility. Exclusion criteria were women with a possible pregnancy or absent menses, patients with history of lower genital tract infection, morbid obesity BMI >30 kg/m2 as obesity interfere with using hysteroscopy, patients who had any contraindications for using NSAIDS, patients with compensated or decompensated liver cirrhosis because of precipitating hepatic encephalopathy and hepatorenal syndrome, any patients with known allergy to paracetamol and ibuprofen.

Ethics approval

The study was approved from the Institutional Ethics of the faculty of medicine. Zagazig University (ZU- IRB#10910-21-6-2023), Written informed consent was obtained from all the participants after explaining the details and benefits as well as risks to them. The study follows the Helsinki Declaration (1975), which is the World Medical Association's guideline of ethics for research involving human subjects.

Eighty women had been recruited to the study, Twenty patients were excluded (Fifteen patients did not meet our criteria and Five patients had refused to participate in the trial and Sixty patients were included in the trial. The included women were divided into 3 groups; Group 1(control group) it composed of 20 women who did not receive any medications 1 hour before the procedure. Group 2 (paracetamol group) it composed of 20 women who received a 1000mg oral paracetamol tablet 1 hour before the procedure. Group 3 (ibuprofen group) it composed of 20 women who received a 600mg oral ibuprofen tablet1 hour before the procedure.
All women were subjected to complete history-taking including Personal history (Name, age, education level, residence, smoking and history of medications). Menstrual history Including menstrual regularity and date of last menstrual period. Obstetric history including parity, gravida, previous abortions.

Pain assessment:

Before hysteroscopy, patients were informed about the visual analog pain rating scale is a numerical pain rating scale ranging from 0 to 10, with zero representing no pain and 10 being the worst agony possible.
Pain was evaluated during and 1 hour after procedure. Women included in this study were in the post menstrual or in bleeding free period. The patient was positioned in the dorsal lithotomy position. Hysteroscopy was operated by a well-experienced consultant as it was performed according to the usual technique. Karl Storz (Germany) manufactured the hesteroscope used in our investigation. This rigid continuous flow panoramic hysteroscopy has dimensions of 25 cm in length and 2.9 mm in diameter. It also has a 30° fibro-optic lens and an outer sheath of 3.2 mm. A metal halide automatic light source with a 150 Watt bulb from Circon Acmi G71/Germany was used for this experiment. The vaginoscopic method was used. Uterine distention by glycine solution at 1.5% was done using hystromate 3700 at pressure 50mmHg.
Vaginoscopy begins with inserting the hysteroscope into the vagina. The vagina is then dilated, and the cervix and external os can be found by gently moving the scope. The posterior fornix is typically clearly spotted. Once the external os is identified, the hysteroscope is carefully inserted and guided through the internal os into the uterine cavity.
Once inside the uterine cavity, a panoramic view was taken to rule out any uterine malformations. The fundus was examined first, and then the uterus's anterior, posterior, and lateral walls, and lastly, the uterotubal connections were seen. This methodical approach to the examination was used throughout. The shape, size, and location of any intrauterine pathology were evaluated. It took mental correction to determine the true size because of optical distortion. Measurements and

documentation were made of the endometrium's thickness, color, and vascularity. In order to look for any intracervical pathology and assess the internal os shuttering mechanism, the hysteroscope was carefully removed into the cervical canal at the end of the procedure. After the end of procedure, every patient was subjected to visual analogue scale to assess pain score and repeated after 1 hour.

Clinical finding:

Clinical finding was normal (Figure 1)
Bicornuate uterous (Figure 2)
Subseptate uteres (Figure 3)
Submucosal myoma (Figure 4)

STATISTICAL ANALYSIS

Data collected over time, with basic outcome measures tagged, entered, and analyzed using Microsoft Excel software. The data was then analyzed using the Statistical Package for the Social Sciences (SPSS version 20.0) program. While qualitative data was expressed as numbers and percentages, quantitative data was expressed as mean ± SD. The study employed the Chi square test (X2) to assess the correlations and differences among qualitative variables. Differences among multiple groups by ANOVA, paired by paired t. P value was set at <0.05 for significant results & <0.001 for high significant result.

RESULTS

Table 1; showed there was no statistically significant difference between all analyzed groups in terms of age (years), BMI (kg/m^2), marriage duration (years), or socioeconomic level.

Table 2; showed that there was no significant difference among 3 included groups and the main indication of hysteroscopy were AUB and Failure to conceive

Table 3; showed that there was no significant difference among groups regarding any past medical history as (DM, HTN, hepatic and thyroid disorders).

Table 4; showed that there was statistically insignificant difference between all studied groups regarding hysterscopic findings.

Table 5; showed that there was no significant difference among groups and the majority of included patient were less than 1 minute.

Table 6; showed that there was no statistically significant difference in pain scores across all tested groups, including VAS during hysteroscopy and VAS one hour following hysteroscopy.

Table 7; showed that there was no significant difference among groups

Table (1): Demographic characteristics of all study groups:

		Control Group	Paracetamol Group	Ibuprofen (brufen) Group	F	P
Age(Years)		31.3±6.40	33.4±6.53	34.3±10.01	0.761	0.472
Body mass index(BMI)(kg/m2)		25.06±3.66	24.97±2.6	25.79±3.58	1.922	0.195
Marital duration(Years)		9.72±2.85	10.26±3.85	12.96±4.29	2.741	0.078
Total	**N**	20	20	20		
	%	100.0%	100.0%	100.0%		

Data are mean ± SD or number (%) †. Unpaired t-test ‡. Fisher's exact test §. Chi-squared test for trend

Table (2): Indication of hysteroscopy (main complain) distribution among studied groups:

			Group		
			Control Group	Paracetamol Group	Ibuprofen Group
Indication of hysteroscopy (main complain)	**Primary and secondary infertility**	**N**	11	7	7
		%	55.0%	35.0%	35.0%
	Recurrent miscarriage	**N**	2	1	2
		%	10.0%	5.0%	10.0%
	Abnormal Uterine Bleeding	**N**	7	12	10
		%	35.0%	60.0%	50.0%
	Post-menopausal bleeding	**N**	0	0	1
		%	0.0%	0.0%	5.0%
Total		**N**	20	20	20
		%	100.0%	100.0%	100.0%

Data are number (%) †. Fisher's exact test NA = test not applicable

Table (3): Distribution of the studied groups as regard past medical history:

			Group		
			Control Group	Paracetamol Group	Ibuprofen Group
Medical history	Free	N	16	14	14
		%	80.0%	70.0%	70.0%
	Diabetes mellitus (DM)	N	1	1	4
		%	5.0%	5.0%	20.0%
	Hypertension (HTN)	N	0	2	1
		%	0.0%	10.0%	5.0%
	Hepatic disorders	N	2	1	0
		%	10.0%	5.0%	0.0%
	Fibromyalgia	N	1	0	0
		%	5.0%	0.0%	0.0%
	Thyroid disorders	N	0	2	1
		%	0.0%	10.0%	5.0%
Total		N	20	20	20
		%	100.0%	100.0%	100.0%

Data are number (%) †. Fisher's exact test

Table (4): Distribution of the studied group as regard hysteroscopic findings:

			Group		
			Control Group	Paracetamol Group	Ibuprofen Group
Finding	Normal finding	N	6	4	5
		%	30.0%	20.0%	25.0%
	Atrophic endometriumn	N	0	1	1
		%	00.0%	5.0%	5.0%
	Niche	N	4	3	4
		%	20.0%	15.0%	20.0%
	Polyp	N	5	8	8
		%	25.0%	40.0%	40.0%
	Myoma	N	1	1	0
		%	5.0%	5.0%	00.0%
	Anomaly	N	3	1	1
		%	15.0%	5.0%	5.0%
	Tubal obstruction	N	0	0	1
		%	0.0%	0.0%	5.0%
	Asherman	N	1	2	0
		%	5.0%	10.0%	0.0%
Total		N	20	20	20
		%	100.0%	100.0%	100.0%

Data are number (%) †. Fisher's exact test

Table (5): Distribution of the studied groups as regard duration of the procedure:

			Group			X^2	P
			Control Group	Paracetamol Group	Ibuprofen Group		
Duration	Less than 1 min	N	15	14	13	1.19	0.55
		%	75.0%	70.0%	65.0%		
	1:2 min	N	5	6	7		
		%	25.0%	30.0%	35.0%		
Total		N	20	20	20		
		%	100.0%	100.0%	100.0%		

Data are number (%) †. Fisher's exact test

Table (6): Pain score in all groups

	Control Group	Paracetamol Group	Ibuprofen Group	F	P
Visual analogue scale(VAS) during hysteroscopy	5.95±1.89	5.80±1.93	5.90±1.99	0.124	0.976
Visual analogue scale after hysteroscopy	2.20±0.85	2.30±0.78	2.10±0.69	0.271	0.832
P	0.00**	0.00**	0.00**		

Data are mean ± SD †. Unpaired t-test

Table (7): Distribution among studied groups according to satisfaction and recommendation to others

			Group			X2	P
			Control Group	Paracetamol Group	Ibuprofen Group		
Satisfaction	-VE	N	7	5	6		
		%	35.0%	25.0%	30.0%		
	+VE	N	13	15	14	2.13	0.34
		%	65.0%	75.0%	70.0%		
Recommend to others	-VE	N	7	8	9		
		%	35.0%	40.0%	45.0%		
	+VE	N	13	12	11	4.2	0.12
		%	65.0%	60.0%	55.0%		
Total		N	20	20	20		
		%	100.0%	100.0%	100.0%		

Data are number (%) †. Fisher's exact test

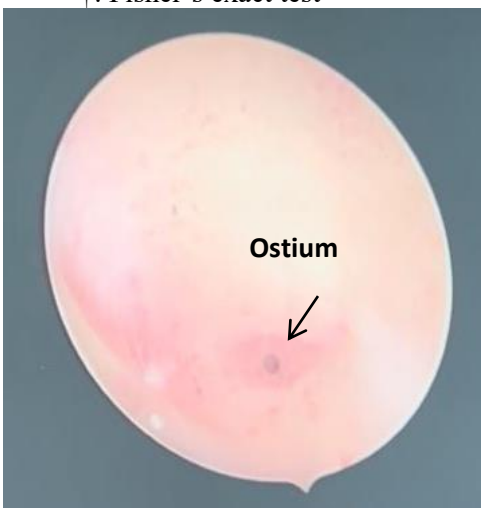

Figure (1): Normal hysteroscopic finding.

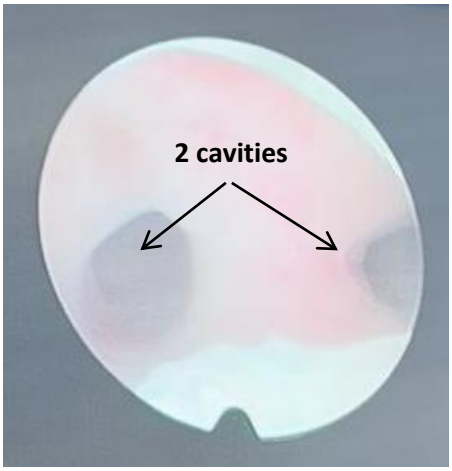

Figure (2): Bicornuate uterous.

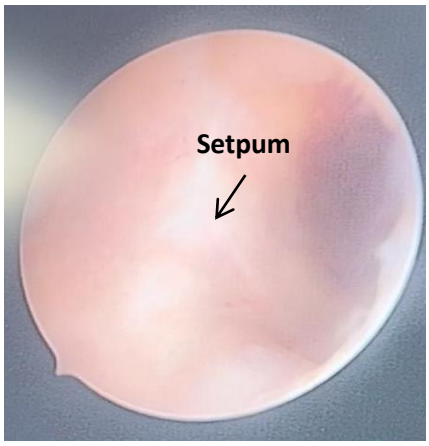

Figure (3): Subseptate uteres

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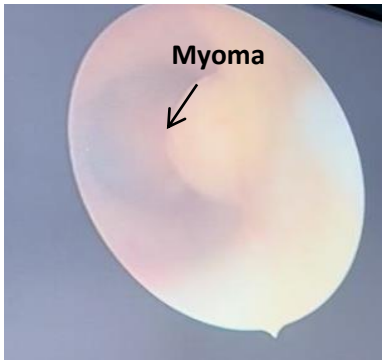

Figure (4): Submucosal myoma

DISCUSSION

In the current study we found that the three groups under study did not differ statistically significantly in terms of age, BMI, length of marriage, or socioeconomic status.

In agreement with us **Maria et al. [6]** revealed that there was no statistically significant age difference between the groups receiving medication and those not.

Maria and her group carried out a prospective, randomized trial with 200 patients split into 2 groups. The first group received oral medication one hour before hysteroscopy, consisting of 600 mg of ibuprofen and 1 g of paracetamol and the second group did not receive any medication before hysteroscopy).

In the present study regarding comorbidities, there was a statistically negligible difference between the three groups under study including Diabetes mellitus**,** thyroid disorders, hypertension, fibromylgia and hepatic disorders.

In the present study we found that regarding parity and prior abortions, there was a statistically

negligible difference between the three groups under investigation.

However **Maria et al. [6]** had stated demonstrated during the test, nulliparous women had felt noticeably higher pain than multiparous patients (5.06 - 2.74 vs. 4.14 - 2.90, respectively; p = 0.023).

Abbas et al. [9] declared that all groups participant characteristics were equivalent, including age, BMI, parity, residency, level of education, history of dysmenorrhea or persistent pelvic pain, number of vaginal births prior, CS, and miscarriages.

Abbas et al. [9] One hundred twenty-nine patients were sorted into one of three groups at random (n = 43 per group) and given a randomized double-blind placebo-controlled experiment. Group 1 received 50mg of diclofenac potassium, Group 2 was given hyoscine-N-butyl bromide (20 mg), while Group 3 was given tablets containing a placebo. Every tablet was given orally one hour before to the hysteroscopy.

In the present study we found that the three groups under investigation did not differ statistically regarding the main complain including abnormal uterine bleeding (AUB), failure to conceive and recurrent pregnancy loss.

In the present study we found that the main indication of our study was failure to conceive as in ibuprofen (Brufen) group: 35%, Paracetamol group 35%and control group55%

In agreement with our data**, Abbas et al. [9]** had reported stated in 69.7% of the study patients, primary or secondary infertility was the primary indication of office hysteroscopy (OH).

More ever, **El-Houssieny et al. [7]** had revealed that Infertility was the most frequent reason for an outpatient hysteroscopy, Menorrhagia and irregular uterine bleeding came next.

El-Houssieny et al. [7] studied seventy nulliparous women with primary infertility undergoing a diagnostic hysteroscopy in a double-blind, randomized, controlled research. One of two sets of subjects received either 5mL of 2% intrauterine lidocaine or 100mg of rectal diclofenac. A numerical rating system ranging from 0 to 10 was used to gauge the degree of pain. The intrauterine cavity was visualized, the hysteroscope was extruded, and pain was scored during each step of the procedure.

On the other hand, **Souza et al. [10]** had illustrated uterine polyps were the main finding of the hysteroscopy, and irregular uterine bleeding was the most significant indicator.

In the present study we found that polyp were the main finding as in ipubrofen group: 8 (40%) and paracetamol group: 8(40%) and 5 (25%) control group.

In agreement with us **Maria et al. [6]** reported that polyp were the major finding in both medicated and non-medicated groups: 52% and 59%respectivly.

Our data stated that the length of the process varied statistically not significantly among the three groups under study (p=0.55) as the majority of patients were less than 1 minute.

Furthermore, we found that the three groups under investigation had pain levels that were statistically not different from one another, including VAS during hysteroscopy (p=0.976) and VAS following hysteroscopy (p=0.832).

Maria et al. [6] The results, which support our own, demonstrated that the degree of pain experienced during the test and for five and thirty minutes after the procedure, as determined by the visual analog scale, found no statistically significant differences between the groups receiving medication and those not.

Furthermore**, Ahmad et al. [5]** meta-analysis did not show that NSAIDs had any appreciable analgesic impact before, during, or after outpatient hysteroscopy.

Hassan et al. [11] included three equal groups of Two hundred and ten women participated in a double-blind, randomized, placebo-controlled study that involved diagnostic outpatient hysteroscopy. Oral Tramadol 100 mg was given to group 1, 200 mg of Celecoxib was given to group 2, and an oral placebo was given to group 3. One hour prior to the operation, all medications were administered. Using a visual analogue scale (VAS), the patient's level of discomfort was measured during the surgery, right after, and 30 minutes later.

The application of small hysteroscopy is less invasive and more well accepted than traditional hysteroscopy, according to **Paulo et al. [12]** systematic study (5 mm scopes). But according to **Paulo et al.[13]** other meta-analysis, mini-hysteroscopy is still uncomfortable, and 30% of women may experience severe pain when using it. They advise further research into drugs and methods for managing discomfort during office hysterscopy.

CONCLUSIONS

Diagnostic hysteroscopy is an easy procedure espescially when performed by experienced surgeons so it is not important to use anesthesia or analgesia during the procedure. The use of paracetamol and ibuprofen administration 1 hour before office hysterscopy did not decrease the pain during hysteroscopic procedures.

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Author contributions
All the authors carried out this work. Taha Abd El Fatah Ahmed, Ahmed Mahmoud Abdou, designed and directed the study. Reham Abd El hamid Elsaid performed the investigations and analyzed the data.
All authors were involved in drafting the article and revising it for important intellectual content and all authors read and approved the final version to be published.
Availability of data
Data supporting the results of this article are included within article.

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