International Journal of Clinical Trials
Kiridi EK et al. Int J Clin Trials. 2022 Nov;9(4):243-250
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: https://dx.doi.org/10.18203/2349-3259.ijct20222687

Original Research Article

Effect of addition of antispasmodic to local and systemic analgesics on pain perception during hysterosalpingography: a randomized controlled trial

Enefia Kelvin Kiridi[1,2], Peter Chibuzor Oriji[3]*, Akaninyene Eseme Ubom[4], Johnpatrick Uchenna Ugwoegbu[5], Addah Abednigo Ojanerohan[6], Isaac Joel Abasi[6], Bosrotsi Panebi[7], Adesina Adedotun Daniel[8,9]

[1]Department of Radiology, Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria
[2]Silhouette Radiodiagnostic Consultants, Yenagoa, Bayelsa State, Nigeria
[3]Department of Obstetrics and Gynaecology, Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria
[4]Department of Obstetrics, Gynaecology and Perinatology, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria
[5]Department of Radiology, Federal Medical Centre, Owerri, Imo State, Nigeria
[6]Department of Obstetrics and Gynaecology, Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria
[7]Department of Obstetrics and Gynaecology, Diete Koki Memorial Hospital, Yenagoa, Bayelsa State, Nigeria
[8]Department of Medical Services, Nigerian Law School, Yenagoa Campus, Yenagoa, Bayelsa State
[9]Oasis Public Health Consulting Ltd, Yenagoa, Bayelsa State

Received: 01 August 2022
Accepted: 01 October 2022

***Correspondence:**
Dr. Peter Chibuzor Oriji,
E-mail: chibuzor54@gmail.com

ABSTRACT

Background: Tubal factor is responsible for most of the causes of infertility, especially in our environment, and hysterosalpingography (HSG) is the investigation of choice for assessing tubal patency. Objective of current study was to evaluate the effect of the addition of intramuscular hyoscine-N-butyl bromide (HBB) to local and systemic analgesics on pain perception during hysterosalpingography.
Methods: This randomized controlled trial was conducted at the radiology departments and infertility clinics of four health institutions in Bayelsa State, Nigeria, from January 2020 to April 2022. One thousand and forty infertile women undergoing hysterosalpingography were randomized into four groups, and each group administered four different pain relief methods. Pain scores at different steps of the procedure were recorded. Data were analysed using the Statistical Product and Service Solutions for Windows®, version 25. Student's t-test was used to compare sample means, while the chi-square test was used to compare the proportion of women in the two study groups, who expressed pain during the procedure.
Results: The Paracervical block+HBB appeared to the most effective agent for pain relief in the study as women receiving this medication indicated the least pain intensity scores at all levels of the procedure except at the insertion of the speculum. The differences observed in the indicated pain intensity scores were also statistically significant ($p<0.05$).
Conclusions: Our study revealed that adding HBB, an antispasmodic agent, to diclofenac and paracervical block significantly reduces pain perception during HSG compared to using diclofenac and paracervical block alone.

Keywords: Hysterosalpingography, Infertility, Pain, Diclofenac, Paracervical block, Hyoscine-N-butyl bromide, Placebo

INTRODUCTION

Infertility is a major health condition that affects the reproductive age-group. It causes a lot of stress and anxiety for the couple involved.[1] About 17% of couples worldwide, are affected by infertility. It is defined as the inability to conceive after 12 months of adequate and regular unprotected, peno-vaginal, ejaculatory sexual intercourse.[2] Tubal factor is responsible for most of the causes of infertility, especially in our environment, and hysterosalpingography is the investigation of choice for assessing tubal patency.[3-6] Pain, especially at instillation of contrast media into the uterine cavity has been reported by most women as the most painful step during hysterosalpingography.[7-10] Many drugs have been used to provide pain relief in hysterosalpingography, including oral, intravenous, topical and intrauterine analgesics, with varying results.[11,12] The pain expressed during hysterosalpingography is associated with the uterine distension from the instillation of contrast media, which releases prostaglandins, that in turn cause uterine cramps. Antispasmodic drugs like hyoscine-N-butyl bromide have been used for relief of gastric, intestinal and urinary bladder cramps, by causing smooth muscle relaxation. Therefore, its addition to analgesics during hysterosalpingography may reduce the muscle spasms and cramps from uterine distension from instillation of contrast media, thereby reducing the overall pain perception during hysterosalpingography.

Hyoscine-N-butyl bromide acts by binding to muscarinic receptors on smooth muscle cells, blocking synaptic cholinergic transmission. Hyoscine-N-butyl bromide prevents neural impulse conduction in pelvic-abdominal parasympathetic ganglia, by binding to nicotinic receptors.[13,14] There is no consensus among clinicians on the effectiveness of hyoscine-N-butyl bromide, as varying results have been reported by various authors.[15-17] During hysterosalpingography, there may be transient muscular spasm of the cornual portion of the fallopian tube, which is encased by the smooth muscle of the uterus, and this may be mistaken for true pathological obstruction of the proximal fallopian tube.[18] Cornual spasm is reversible but may persist for over 15 minutes. If suspected, the hysterosalpingography study is paused for some minutes, to allow the spasm resolve. Alternatively, parenteral hyoscine-N-butyl bromide (Buscopan®) is administered to relax the muscle spasm.[2,19] The objective of this randomized controlled trial was to evaluate the effect of the addition of intramuscular hyoscine-N-butyl bromide to intramuscular diclofenac and paracervical block with 2% lignocaine on pain perception in infertile women undergoing hysterosalpingography.

METHODS

Study setting

This randomized controlled trial was conducted at the radiology departments and infertility clinics of the Federal Medical Centre, Yenagoa, Niger Delta University Teaching Hospital, Okolobiri, Diete Koki Memorial Hospital, Yenagoa, and Silhouette Radiodiagnostic Consultants, Yenagoa, all in Bayelsa State, Nigeria. It was conducted between January 2020 and April 2022. The first two study centres are tertiary health institutions that provide specialized gynaecological services to women in Bayelsa State, and serve as referral centres for other hospitals in Bayelsa State, and surrounding Rivers and Delta States, both in South-South Nigeria. The third study centre is a secondary health institution. The fourth study centre is the biggest radiodiagnostic Institution in Bayelsa State, Nigeria.

Sample size

The sample size for this study was calculated using the formula[20]

$$n = (Z\alpha + Z\beta)2\ x\ 2\ x\ p\ (1 - p)\ /\ d2$$

Where n=minimum sample size, Zα=95% confidence level=1.96, Zβ=20% β error (at 80% power)=0.84, p=proportion of women with infertility which was 18.2% (0.182) from a previous study in Bayelsa State, South-South Nigeria.[21] d=expected margin of error=10%=0.1, substituting the values into the sample size formula, sample size was calculated to be 233. Allowing for an attrition rate of 10% (23.3), n=256.3, rounded off to 260, thus the calculated sample size was therefore 260 per group, giving a total of 1,040 study participants.

Study randomization

One thousand and forty infertile women undergoing hysterosalpingography were enrolled in the study. Following adequate counselling, explaining the aim and possible benefits of the study, as well as the procedure, written informed consent was obtained from all the study participants. Their baseline sociodemographic, gynaecologic and infertility characteristics were obtained and recorded in the study proforma. The women were equally randomized (1:1:1:1 ratio) into four groups I, II, III and IV by means of a computer-generated list of random numbers (generated from www.randomization.com). The allocating team and the team performing the hysterosalpingography were different, to prevent selection bias. Women in Group I were administered intramuscular diclofenac (voltaren®, manufactured by GSK) 75 mg and placebo with 1 ml of water for injection manufactured by Medlab Pharmaceuticals, India. Women in Group II received paracervical block with 10 ml (200 mg) 2% lignocaine hydrochloride manufactured by Pfizer and placebo with 1 ml of water for injection. Women in Group III received intramuscular diclofenac and intramuscular hyoscine-N-butyl bromide (buscopan®, manufactured by Sanofi Consumer Healthcare) 20 mg (1 ml) stat. Women in Group IV received paracervical block with 10 ml (200

mg) 2% lignocaine hydrochloride and intramuscular hyoscine-N-butyl bromide 20 mg (1 ml) stat.

Inclusion and exclusion criteria

All infertile women undergoing hysterosalpingography, who consented to participate in the study, and completely filled the consent/questionnaire form, were included in the study. Exclusion criteria included abnormal uterine/vaginal bleeding, on-going menstruation, cervicovaginal discharge, cervical stenosis/cervical pathology, evidence of pelvic inflammatory disease, previous history of contrast hypersensitivity, history of allergy to lignocaine, hyoscine-N-butyl bromide and diclofenac, and all patients that declined consent or incompletely filled the consent form and questionnaire.

Procedure

Hysterosalpingography for the women was performed during the proliferative phase of the menstrual cycle (7th-10th day). Prior to the procedure, the medications were administered to the patients as outlined in the study randomization above. The procedure started after five minutes of administration of intramuscular diclofenac/ hyoscine-N-butyl bromide/placebo. Protective lead apron and eye shield were put on by the radiologists performing the hysterosalpingography. After passing urine to empty her urinary bladder, the woman was initially placed in the supine position on the x-ray table. A scout radiograph of the antero-posterior view of the pelvis was taken. She was then placed in the lithotomy position, and draped to ensure privacy. Wong-Baker FACES Pain Rating Scale[22] was used to document the level of pain expressed by the patients at different stages of the procedure, by an assistant who was blinded to the randomization (Figure 1).

Figure 1: Wong-Baker faces pain rating scale.[22]

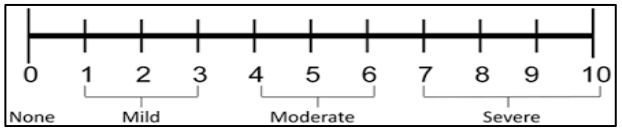

Figure 2: Numerical Rating Scale (NRS).[23]

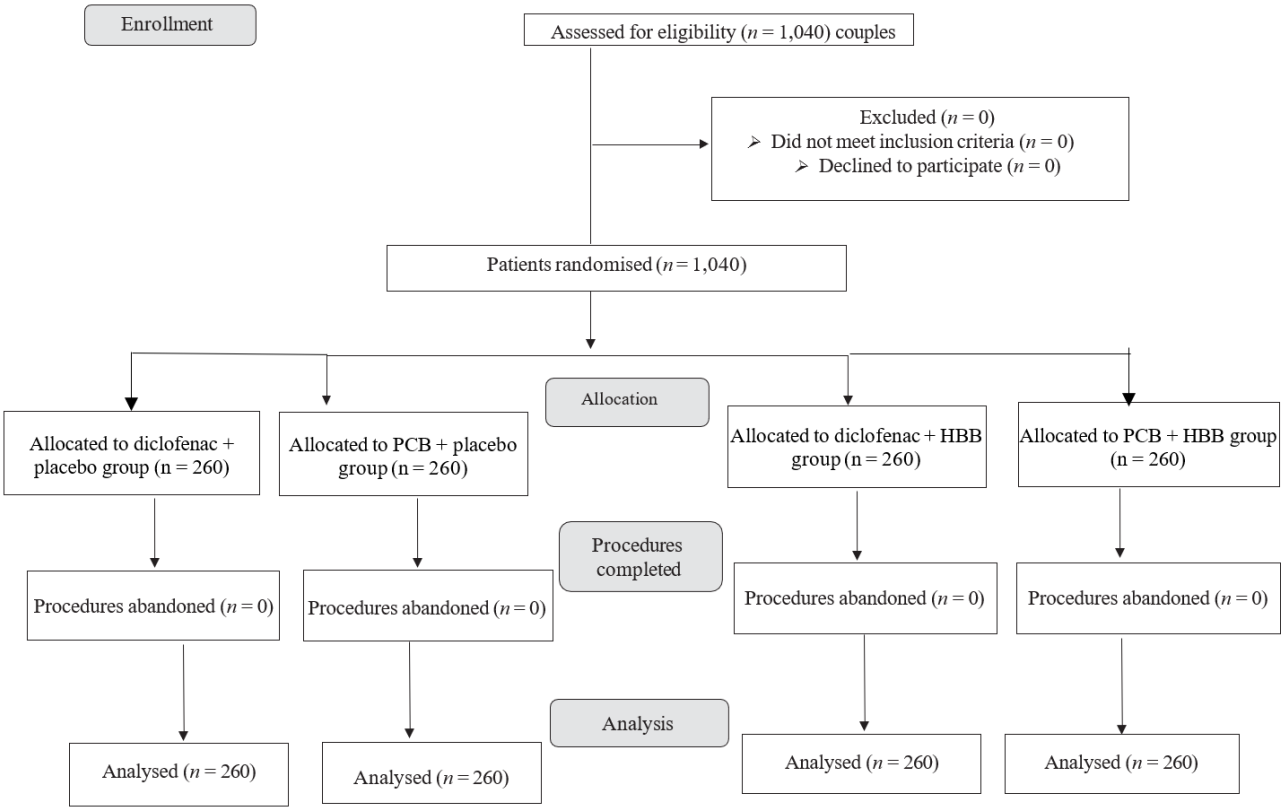

Figure 3: CONSORT flow diagram.

After hand-washing and putting on sterile gloves, under a good light source, a sterile Cusco's speculum was inserted into the vagina to expose the cervix. The ecto-cervix was cleaned with savlon solution, and paracervical block with 10 ml (200 mg) 2% lignocaine hydrochloride was administered to the women in Groups II and IV. After 60 seconds, the anterior lip of the cervix was then grasped with a tenaculum. A self-retaining

hysterosalpingography cannula was inserted into the cervix, and the speculum was removed for the patient's comfort. Urographin, a water-soluble, high osmolar contrast medium (10-20 ml) was warmed to body temperature, and injected slowly into the endometrial cavity. Three radiographs to outline the endometrial cavity, fallopian tubes and intraperitoneal spillage were obtained respectively. At completion of the procedure, the cannula was removed, the woman's vulva cleaned, and she was asked to dress up. The hysterosalpingography films were reported by the Consultant Radiologist. The outcome of the procedure was discussed with the women. Thirty minutes after the procedure, the level of pain that the women felt were recorded with the use of the Numerical Rating Scale (Figure 2).[23] This is the commonest scale used in the grading of pain. The patient rates the level of pain on a scale of 0-10. A score of 0 indicates no pain, 1-3 suggests mild pain, 4-6 suggests moderate pain, and 7-10 suggests severe pain.[23]

Outcome measures

The primary outcome measures were pain scores at the different steps of the procedure, and 30 minutes and 24 hours after the procedure. The secondary outcomes included differences in pain scores, and presence of any adverse effect in the women in any of the groups.

Data analysis

Data obtained were entered into a pre-designed proforma, and were analysed using Statistical Product and Service Solutions for Windows® version 25 (SPSS Inc.; Chicago, USA). The results were presented in frequencies and percentages for categorical variables, and mean and standard deviation for continuous variables. Student's t-test was used to compare sample means, while the chi-square test was used to compare the proportion of women who expressed pain at the different steps of the procedure, including 30 minutes and 24 hours after the procedure, between the two groups, $p<0.05$ was considered statistically significant. CONSORT flow diagram for this study is depicted in (Figure 3).

RESULTS

Sociodemographic characteristics and anthropometric measurement of the women

The study involved a total of one thousand and forty women investigated for infertility. The mean±SD age of the women was 34.5±4.3 years. The modal age group with 416 women (40.0%), was 35-39 years. Almost one-half of the women (512, 49.2%) had tertiary level of education, with a mean body mass index of 27.9±5.1kg/m^2 (Table 1).

Table 1: Sociodemographic characteristics of participants in the four study groups (n=260).

Characteristics	Study groups				Total
	Diclofenac N (%)	PCB N (%)	Diclofenac+Hyoscine N (%)	PCB+Hyoscine N (%)	N (%)
Age group (years)					
25-29	48 (18.5)	26 (10.0)	52 (26.0)	27 (10.4)	153 (14.7)
30-34	90 (34.6)	81 (31.2)	78 (30.0)	81 (31.2)	330 (31.7)
35-39	90 (34.6)	106 (40.8)	95 (36.5)	125 (48.1)	416 (40.0)
≥40	32 (12.3)	47 (18.1)	35 (13.5)	27 (10.4)	141 (13.6)
Mean age±SD	33.7±3.9	35.7± 4.7	34.1±4.9	34.1±3.4	34.5±4.3
Level of education					
Primary	34 (13.1)	26 (10.0)	40 (15.4)	27 (10.4)	127 (12.2)
Secondary	103 (39.6)	96 (36.9)	98 (37.7)	104 (40.0)	401 (38.6)
Tertiary	123 (47.3)	138 (53.1)	122 (46.9)	129 (49.6)	512 (49.2)
Occupation					
Unemployed	30 (11.5)	29 (11.2)	26 (10.0)	23 (8.8)	108 (10.4)
Civil Servant	66 (25.4)	104 (40.0)	70 (26.9)	125 (48.1)	365 (35.1)
Trader	88 (33.8)	26 (10.0)	100 (38.5)	23 (8.8)	237 (22.8)
Self-employed Professional	44 (16.9)	26 (10.0)	38 (14.6)	26 (10.0)	134 (12.9)
Farmer	0 (0.0)	26 (10.0)	0 (0.0)	28 (10.8)	54 (5.2)
Artisan	32 (12.3)	49 (18.8)	26 (10.0)	35 (13.5)	142 (13.7)
Body mass index categories					
Normal weight	67 (25.8)	82 (31.5)	78 (30.0)	79 (30.4)	306 (29.4)
Overweight	170 (65.4)	77 (29.6)	144 (55.4)	77 (29.6)	468 (45.0)
Mild Obesity	16 (6.2)	49 (18.8)	28 (10.8)	53 (20.4)	146 (14.0)
Moderate Obesity	7 (2.7)	52 (20.0)	10 (3.8)	51 (19.6)	120 (11.5)
Weight (kg)	71.4±8.2	70.5±14.9	74.0±13.6	71.7 ±14 1	71.8±12.9
Height (m)	1.66±0.03	1.58±0.04	1.61±0.08	1.60±0.07	1.60±0.06
Body mass index (kg/m^2)	27.5±3.7	27.2±5.4	28.7±5.1	28.3±6.2	27.9±5.1

Table 2: Gynaecological features and infertility related factors among participants in the four study groups.

Characteristics	Study groups				Total
	Diclofenac N (%)	PCB N (%)	Diclofenac+Hyoscine N (%)	PCB+Hyoscine N (%)	N (%)
Parity					
Nulliparity	155 (59.6)	126 (48.5)	156 (60.0)	130 (50.0)	567 (54.5)
Primiparity	49 (18.8)	68 (26.2)	58 (22.3)	81 (31.2)	256 (24.6)
Multiparity	56 (21.5)	66 (25.4)	46 (17.7)	49 (18.8)	217 (20.9)
Median parity (IQR)	0 (0-1)	1 (0-2)	1 (0-1)	0 (0-1)	0 (0-2)
Age of menarche (years)					
11-14	155 (59.6)	192 (73.8)	156 (60.0)	210 (80.8)	713 (68.6)
15-19	105 (40.4)	68 (26.2)	104 (40.0)	50 (19.2)	327 (31.4)
Mean age of menarche ±SD in years	13.7±1.7	14.0±1.8	14.7±1.8	13.5±1.0	13.9±1.6
Duration of marriage (years)					
1-5	168 (64.6)	154 (59.2)	156 (60.0)	158 (60.8)	636 (61.2)
6-10	83 (31.9)	98 (37.7)	94 (36.2)	96 (36.9)	371 (35.7)
>10	9 (3.5)	8 (3.1)	10 (3.8)	6 (2.3)	33 (3.2)
Marriage duration±SD in years	4.0±2.7	5.5±3.2	5.8±3.0	5.2±2.3	5.1±2.8
Number of children					
No children	174 (66.9)	184 (70.8)	156 (60.0)	179 (68.8)	693 (66.6)
1-2 children	86 (33.1)	76 (29.2)	104 (40.0)	81 (31.2)	347 (33.4)
Median number of children (IQR)	0 (0-1)	0 (0-1)	1 (0-1)	0 (0-1)	0 (0-1)
Type of infertility					
Primary	37 (14.2)	26 (10.0)	26 (10.0)	27 (10.4)	116 (11.2)
Secondary	223 (85.8)	234 (90.0)	234 (90.0)	233 (89.6)	924 (88.8)
Duration of infertility±SD in years	1.1±0.2	4.6±2.4	1.4±0.5	4.2±2.4	4.0±2.2

Table 3: Duration of procedure and Pain intensity scores among participants in the four groups.

Characteristics	Study groups; mean±SD				F statistics (p value)
	Diclofenac N (%)	PCB only N (%)	Diclofenac+hyoscine N (%)	PCB +hyoscine N (%)	
Duration of procedure	5.20±1.17	5.28±1.18	4.43±1.02	4.73±1.12	33.21 (0.001)
Insertion of Speculum	1.30±1.10	0.70±.456	0.44±.67	0.51±0.50	74.70 (0.001)
Grasping of the cervix	2.40±1.43	1.00±.63	1.56±.85	0.80±0.60	150.74 (0.001)
Insertion of canula	3.30±1.49	1.70±1.01	2.61±1.49	1.05±1.09	153.91 (0.002)
Instillation of contrast media	5.50±0.67	5.00±.63	3.90±1.51	3.09±1.04	289.88 (0.001)
30 minutes post-procedure	2.90±0.70	2.10±.70	2.00±1.16	1.57±0.66	116.19 (0.001)
24 hours post-procedure	0.80±0.75	0.50±.50	0.39±0.70	0.37±0.48	26.70 (0.001)

Gynaecological features and infertility related factors among participants

There were 126 (48.5%), 130 (50.0%), 155 (59.6%), and 156 women (60.0%) in the PCB only, PCB+hyoscine, diclofenac only and diclofenac+hyoscine groups, respectively who were nulliparous forming the highest parity group (54.5%) in the study (Table 2). Primiparous and multiparous women made up 24.6% and 20.9% of the study population respectively (Table 2). Mean age of menarche among participants was 13.9 years with a standard deviation of 1.6 years, while participants had been married averagely for 5.1±2.8 years (Table 2). The majority of women (88.8%) were investigated for secondary infertility (Table 2).

Duration of procedure

The mean duration for the procedure was longest (5.28±1.18 minutes) among women who had PCB only while it was shortest (4.43±1.02 minutes) among women in the diclofenac+hyoscine group (Table 3). The difference reported in the mean duration for the procedure was statistically significant (f-test = 33.21; p value=0.001).

Pain intensity scores among participants in the study groups

The least intensity of pain was recorded 24 hours after the procedure in the four groups (Table 3, Figure 3). Pain related to the procedure was lowest at the insertion of the speculum, the least mean pain intensity score (0.44±0.67 cm) at this point was recorded by women who got diclofenac+hyoscine while those who got diclofenac only recorded the highest pain score (1.30±1.10 cm) at the point during the procedure.

The highest intensity of pain was associated with the instillation of contrast media ranging from a mean pain score of 3.09±1.04 cm among women who received PCB+hyoscine to 5.50±0.67 cm among women who got diclofenac only. The PCB+hyoscine appeared to be most effective agent for pain relief in the study as women receiving this medication indicated the least pain intensity scores at all levels of the procedure except at the insertion of the speculum (Table 3, Figure 4). The differences observed in the indicated pain intensity scores were also statistically significant (p<0.05).

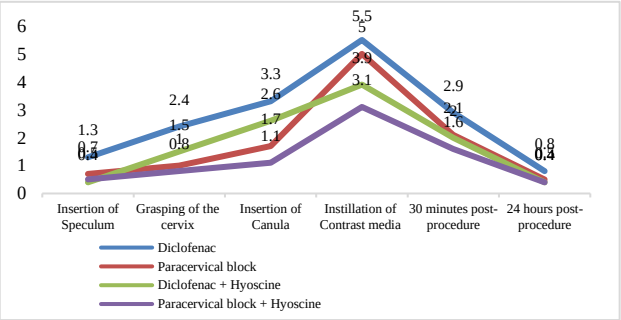

Figure 4: Pain intensity measured by VAS among study participants.

Table 4: Level of pain intensity at different points of the procedure among participants in the four study groups.

Characteristics	Diclofenac N (%)	PCB Only N (%)	Diclofenac+Hyoscine N (%)	PCB+Hyoscine N (%)	Chi-square (p value)
Perception of pain at point of insertion of speculum					
No pain	78 (30.0)	77 (29.6)	157 (60.4)	128 (49.2)	80.6 (0.001)
Mild pain	182 (70.0)	183 (70.4)	101 (38.8)	132 (50.8)	
Moderate pain	0 (0.0)	0 (0.0)	2 (.8)	0 (0.0)	
Perception of pain at point of grasping of the cervix					
No pain	0 (0.0)	52 (20.0)	52 (20.0)	77 (29.6)	
Mild pain	256 (98.5)	208 (80.0)	208 (80.0)	183 (70.4)	304.4 (0.001)
Moderate pain	2 (.8)	0 (0.0)	0 (0.0)	0 (0.0)	
Severe pain	2 (.8)	0 (0.0)	0 (0.0)	0 (0.0)	
Perception of pain at point of insertion of canula					
No pain	0 (0.0)	0 (0.0)	2 (0.8)	103 (39.6)	
Mild pain	154 (59.2)	233 (89.6)	222 (85.4)	157 (60.4)	482.1 (0.001)
Moderate pain	104 (40.0)	27 (10.4)	36 (13.8)	0 (0.0)	
Severe pain	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	
Perception of pain at point of instillation of contrast media					
Mild pain	0 (0.0)	0 (0.0)	99 (38.1)	183 (70.4)	530.4 (0.001)
Moderate pain	260 (100.0)	260 (100.0)	140 (53.8)	77 (29.6)	
Severe pain	0 (0.0)	0 (0.0)	21 (8.1)	0 (0.0)	
Perception of pain 30 minutes post procedure					
No pain	0 (0.0)	0 (0.0)	15 (5.8)	0 (0.0)	
Mild pain	208 (80.0)	260 (100.0)	239 (91.9)	260 (100.0)	211.1 (0.001)
Moderate pain	52 (20.0)	0 (0.0)	2 (0.8)	0 (0.0)	
Severe pain	0 (0.0)	0 (0.0)	4 (1.5)	0 (0.0)	
Perception of pain at point 24 hours post-procedure					
No pain	104 (40.0)	129 (49.6)	186 (71.5)	164 (63.1)	62.1 (0.001)
Mild pain	156 (60.0)	131 (50.4)	74 (28.5)	96 (36.9)	

Level of pain intensity among participants in the four study groups

Three out of every five women (60.4%) in the diclofenac+hyoscine group felt no pain at the insertion of speculum while about half (49.2%) indicated no pain in the PCB+hyoscine group. Only 78 (30.0%) and 77 (29.6%) indicated same in the 'diclofenac only' and PCB only groups respectively (Table 4). All participants in the diclofenac only and PCB only complained of moderate pain at the instillation of contrast media, while only 77 women (29.6%) and 140 53.8%) felt the same level of pain among PCB+hyoscine group and diclofenac+hyoscine group respectively (Table 4). Other women in these two groups (diclofenac+hyoscine and PCB+hyoscine groups) indicated mild pain at the point of instillation of contrast media (Table 4). The observed differences in proportions of pain intensity levels was statistically significant across the groups (p<0.05).

DISCUSSION

Our study found a significant reduction in pain scores at all steps during and after HSG with the use of HBB in addition to diclofenac and paracervical block. This contrasts with the finding of Abbas et al, who reported no benefit in using HBB for the prevention of pain during HSG.[16] Jitchanwichai and Soonthornpun and Aboshama et al however corroborated our study findings in their RCT and systematic review and meta-analysis, respectively.[15,17] HBB has antispasmodic and peripheral anticholinergic effects on gastrointestinal, biliary and genitourinary system smooth muscle.[24] HBB reduces HSG-associated pain by relieving uterine spasm and blocking transmission of pain impulses in parasympathetic ganglia.[16]

Patients who had paracervical block had significantly less pain compared to those who were administered diclofenac. Paracervical anaesthesia blocks pain transmission through sympathetic, parasympathetic, and sensory fibers at the level of the internal cervical os before these fibers enter the uterus, and is therefore effective for pain relief during HSG.[25] Evidence on the efficacy of paracervical block for pain relief during HSG is however varied. A Cochrane review by Tangsiriwatthana et al did not show whether paracervical block was inferior, equivalent, or superior to alternative analgesic agents in terms of efficacy and safety for women undergoing cervical dilatation and uterine interventions.[26] On the other hand, whereas Jain et al. showed that paracervical block had no benefit for pain relief in women undergoing HSG, de Mello et al and Robinson et al both found that paracervical block was beneficial for relieving the pain associated with cervical grasping during HSG, but had no benefit during instillation of contrast media, while Unlu et al found a beneficial effect for topical anesthesia only during dye instillation.[11,25,27,28]

Our study showed that compared to diclofenac, paracervical block was associated with a significant reduction in pain perception at all steps of HSG. The addition of HBB in the group of patients that had HBB in addition to paracervical block could have been a possible confounder influencing our study finding, as we also found that the intensity of pain perception significantly further reduced with the addition of HBB to paracervical block. The addition of HBB to paracervical block may however exacerbate the side effects of paracervical block, including nausea, vomiting and dizziness, all of which are also associated with HBB.[16]

This study also found that the duration of HSG was significantly increased in patients who had paracervical block. It takes approximately an additional 5-10 minutes to inject and allow paracervical block take effect before HSG. This increases the duration of the procedure. However, the significant pain reduction at all steps of the procedure outweighs the additional time spent carrying out the procedure. Other drawbacks of paracervical block are that it requires skilled personnel with a good knowledge of the anatomy of the cervix and proper understanding of injection technique to administer. The extra cost of injection needle and syringe and local anaesthesia also adds to the cost of HSG when paracervical block is used.[25]

The strength of this research is domiciled in the fact that it is a prospective randomized control trial where both the participants and radiologists were blinded to the intervention used for each group of women that participated in the study. Only four consultant radiologists performed the hysterosalpingography, and therefore reduced bias, and increased the reproducibility of the report of this investigative modality. The allocating team and the team performing the hysterosalpingography were different, to help prevent selection bias. The limitation of this study is domiciled in the fact that it is hospital-based. Therefore, the findings may not reflect what is obtainable in the general population of infertile women. An international multi-centre randomized control trial is recommended.

CONCLUSION

It is the conclusion of our study that adding HBB, an antispasmodic agent, to diclofenac and paracervical block significantly reduces pain perception during HSG compared to using diclofenac and paracervical block alone. Consideration should therefore be given to adding an antispasmodic agent to local and systemic analgesics for pain relief during HSG. Paracervical block with HBB showed superior analgesic effect compared to diclofenac and HBB.

ACKNOWLEDGEMENT

We appreciate all the patients and staff of our health facilities for all the roles they played in making this research successful. For the analysis of the data for this research, our profound gratitude goes to Dr. Adedotun Daniel Adesina.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Research and Ethics Committee

REFERENCES

1. Kiridi EK, Oriji PC, Abasi IJ. Effect of pre-procedure anxiety levels on post-procedure pain scores in women undergoing hysterosalpingography in South-South Nigeria. Int J Trop Dis Health. 2022;43(2):33-43.
2. Schankath AC, Fasching N, Urech-Ruh C, Hohl MK, Kubik-Huch RA. Hysterosalpingography in the workup of female infertility: indications, technique and diagnostic findings. Insights Imaging. 2012;3(5): 475–83.
3. Oriji PC, Kiridi EK, Allagoa DO, Omietimi JE, Orisabinone IB, Makinde OI. Pattern of tubal pathology in infertile women undergoing

hysterosalpingography at the Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria. Yen Med J. 2020;2(1):11-7.
4. Kiridi EK, Oriji PC, Abasi IJ, Ubom AE, Ugwoegbu JU. Predictors or abnormal findings in infertile women undergoing hysterosalgography in Bayelsa State, South-South Nigeria. Int J Clin Obstet Gynaecol. 2022;6(2):22-30.
5. Kiridi EK, Oriji PC, Ugwoegbu JU, Abasi IJ. Hysterosalpingography Findings among Women Presenting for Infertility Evaluation in Bayelsa State, South-South Nigeria. J Adv Med Med Res. 2022; 34(5):7-17.
6. De Neubourg D, Janssens L, Verhaegen I, Smits E, Mol BW, Roelant E. Live birth after additional tubal flushing with oil-based contrast versus no additional flushing: a randomised, multicentre, parallel-group pragmatic trial in infertile women with at least one patent tube at hysterosalpingo-foam sonography (HYFOIL study). BMJ Open. 2021;11(11):e054845.
7. Oriji PC, Kiridi EK, Abasi IJ, Ubom AE, Ugwoegbu JU. Predictive factors for the severity of procedure-associated pain in infertile women undergoing hysterosalpingography in Bayelsa State, South-South Nigeria. Int J Trop Dis Health. 2022;43(5):43-54.
8. Kiridi EK, Oriji PC, Ugwoegbu JU, Abasi IJ. Effectiveness of paracervical block for pain relief in women undergoing hysterosalpingography in Bayelsa State, South-South Nigeria: a randomized control trial. Int J Clin Trials. 2022;9(2):53-9.
9. Omidiji OA, Toyobo OO, Adegbola O, Fatade A, Olowoyeye OA. Hysterosalpingographic findings in infertility - what has changed over the years? Afr Health Sci. 2019;19(2):1866-74.
10. Ahmad G, Duffy J, Watson AJS. Pain relief in hysterosalpingography. Cochrane Database Syst Rev. 2007;(2):CD006106.
11. Unlu BS, Yilmazer M, Koken G, Arioz DT, Unlu E, Dogan Baki E. Comparison of four different pain relief methods during hysterosalpingography: a randomized controlled study. Pain Res Manag. 2015; 20(2):107-11.
12. Hassa H, Oge T, Aydin Y, Burkankulu D. Comparison of nonsteroidal anti-inflammatory drugs and misoprostol for pain relief during and after hysterosalpingography: prospective, randomized, controlled trial. J Minim Invasive Gynecol. 2014; 21(5):762-6.
13. ytgat GN. Hyoscine Butylbromide: A Review of its Use in the Treatment of Abdominal?? Cramping and Pain. Drugs. 2007;67(9):1343-57.
14. Sekhavat L, Karbasi SA, Fallah R, Mirowliai M. Effect of hyoscine butylbromide first stage of labour in multiparus women. Afr Health Sci. 2012;12(4):408-11.
15. Jitchanwichai A, Soonthornpun K. Effect of Premedication hyoscine-n-butylbromide before hysterosalpingography for diagnosis of proximal tubal obstruction in infertile women: A randomized double-blind controlled trial. J Minim Invasive Gynecol. 2019;26(1):110-6.
16. Abbas A, Abo-Elela N, Mosa E. Effect of oral hyoscine-N-butyl bromide on pain perception during hysterosalpingography: A randomized, double-blind, placebo controlled trial. Middle East Fertil Soc J. 2017;23(1):57-62.
17. Aboshama RA, Shareef MA, AlAmodi AA, Kurdi W, Al-Tuhaifi MM, Bintalib MG, et al. The effect of hyoscine-N-butylbromide on pain perception during and after hysterosalpingography in infertile women: a systematic review and meta-analysis of randomised controlled trials. Hum Fertil Camb Engl. 2020;3:1-8.
18. Chalazonitis A, Tzovara I, Laspas F, Porfyridis P, Ptohis N, Tsimitselis G. Hysterosalpingography: technique and applications. Curr Probl Diagn Radiol. 2009;38(5):199–205.
19. Kilcoyne A, O'Shea A, Gervais DA, Lee SI. Hysterosalpingography in endometriosis: performance and interpretation. Abdom Radiol. 2020;45(6):1680-93.
20. Zhong B. How to calculate sample size in randomized controlled trial? J Thorac Dis. 2009;1(1):51-4.
21. Oriji PC, Kiridi EK, Ubom AE, Okoye CN, Oriji VK, Awotundun B. Pattern of infertility among infertile couples in a tertiary health institution in Bayelsa State, South-South Nigeria. Int J Sci Rep. 2022;8(6): 23-9.
22. History of the Wong-Baker FACES Pain Rating Scale. Available at: https://wongbakerfaces.org/us/wong-baker-faces-history/. Accessed on 20 October 2021.
23. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. Ann Rheum Dis. 1978;37(4):378-81.
24. Hotwani J, Ainapure SS. Hyoscine Butyl bromide Suppositories. Indian Med Gaz. 2000;1:217-9.
25. Jain S, Inamdar DB, Majumdar A, Jain DK. Effectiveness of paracervical block for pain relief in women undergoing hysterosalpingography. J Hum Reprod Sci. 2016;9(4):230-5.
26. Tangsiriwatthana T, Sangkomkamhang US, Lumbiganon P, Laopaiboon M. Paracervical local anaesthesia for cervical dilatation and uterine intervention. Cochrane Database Syst Rev. 2013;9: CD005056.
27. de Mello JFL, Abrao MS, Cerri GG, de Barros N. Evaluation of pain in three hysterosalpingography techniques: metal cannula with and without paracervical blockage and balloon catheter. Am J Roentgenol. 2006;187(1):86-9.
28. Robinson RD, Casablanca Y, Pagano KE, Arthur NA, Bates GW, Propst AM. Intracervical block and pain perception during the performance of a hysterosalpingogram: a randomized controlled trial. Obstet Gynecol. 2007;109(1):89-93.

Cite this article as: Kiridi EK, Oriji PC, Ubom AE, Ugwoegbu JU, Ojanerohan AA, Abasi IJ, et al. Effect of addition of antispasmodic to local and systemic analgesics on pain perception during hysterosalpingography: a randomised controlled trial. Int J Clin Trials 2022;9(4):243-50.