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## Tramadol as a prophylactic analgesic for hysterosalpingography in African Women

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### Summary

Hysterosalpingography (HSG) is a contrast investigation of the female reproductive tract. A major drawback to its use is pain during and after the procedure. This study was designed to evaluate the usefulness of Tramadol in alleviating the pain of the procedure and to assess the influence of tubal pathology on the degree of pain experienced. We studied 84 women; the patients were assigned randomly into two groups, group A and B. The first group, Group A (n=40) had premedication with intravenous Tramadol (100mg) and IV hyoscine N butylbromide (20 mg), The Group B (n=44) had premedication with IV hyoscine N butylbromide (20mg) only. The mean numeric rating pain score was 6.25 for the Tramadol group and 6.26 for the control group,  $P>0.05$ . This study does not show a significant decrease in pain perception during HSG in African women premedicated with Tramadol.

**Keywords:** *Hysterosalpingography, tramadol usage, pain in hysterosalpingography*

### Résumé

L'hysterosalpingographie (HSG) est une technique d'investigation opposée au fonctionnement du système reproductif femelle. L'obstacle majeur de son utilité est la douleur durant et après la procédure. Cette étude était pour évaluer l'utilité du tramadol pour atténuer la douleur pendant la procédure et évaluer l'effet de la pathologie tubale sur le degré de la douleur expérimentée. Quatre vingt quatre femmes étaient choisies au hasard et divisées en deux groupes A et B. Le groupe A (n=40) avait reçu une prémédication du tramadol intraveineuse (100mg) plus de l'hyoscine IV (20mg). Le groupe B (n=44) avait eu une prémédication intraveineuse de l'hyoscine N-butylbromide seulement. Le taux moyen

de la douleur était de 6.25 pour ceux ayant reçu le tramadol et 6.26 pour le contrôle sain ( $P>0.05$ ). Cette étude ne montrait pas de réduction significative de la perception de la douleur pendant l'HSG chez les femmes Africaine ayant une prémédication au tramadol.

### Introduction

Hysterosalpingography (HSG) is a contrast investigation of the female reproductive tract, and it is especially useful for the evaluation of tubal patency. A hysterosalpingogram is an integral part of the evaluation of infertility but is often painful. A number of alternatives have been developed over the years to replace the conventional HSG such as hysterosalpingo-contrast sonography (HyCoSy) and Three Dimensional Dynamic MR Hysterosalpingography. Despite these advances conventional HSG remains the most commonly used procedure to image the female reproductive tract [1].

Tramadol is an atypical opioid which is a centrally acting analgesic, used for treating moderate to severe pain. (Trade name, Tramal, manufactured by German pharmaceutical company Grünenthal GmbH). It is a synthetic agent, a 4-phenyl-piperidine analogue of codeine, and appears to have actions on the GABAergic, noradrenergic and serotonergic systems [2]

It relieves pain from distension of hollow viscera, superficial structures such as skin and mucous membranes, also pain in the more deep-seated structures, arising from joints, periosteum and muscles.

There has been a lot of research into pain relieve in HSG using various modalities, including the use of opiate analgesia and non-steroidal analgesic drugs in the Western world [4,5]. We are not aware of any similar study in our environment to study the effects of Tramadol on pain relief during HSG in African Women. In this environment various non-steroidal analgesic drugs are used to relieve pain after the procedure, this study was designed to evaluate the usefulness of Tramadol in alleviating the pain of the procedure and to assess the influence of tubal pathology on the degree of pain experienced.

### Materials and methods

This prospective randomized study was carried out in the Radiological department of LAUTECH Teaching Hospital, Osogbo, Nigeria over a 12-month period (March 2004 to April 2005). Following institutional approval and patient consent, we studied 84 women who were referred for hysterosalpingography; the patients were assigned randomly into two groups, group A and B. The first group, Group A comprising 40 patients, had premedication with intravenous Tramadol (100mg) and IV hyoscine N butylbromide (20 mg), given 5 minutes before beginning the procedure. The Second group, (Group B) comprising of 44 women had premedication with IV hyoscine N butylbromide (20mg) only. The randomization of the patients and the premedication with the appropriate drug was done by the consultant radiologist (BTO) and the hysterosalpingograms were performed by three second- year residents in the department, they also assessed the pain level of the patient using the Numeric Rating Scale.

All the patients were referred for infertility studies; a questionnaire was also designed to collate demographic data on the patients and the indication for hysterosalpingography, the degree of pain during the procedure was assessed by a 10 point Numeric Rating Scale, the scale, a modified version of the visual analog scale has been discovered to be easier for subjects to use, resulting in less missing and unclear responses [3]. The measurement of the pain perception was done five minutes after the procedure, before taking the late film.

The patients were placed in the lithotomy position, the vulva was cleaned with chlorhexidine solution, and the cervix was located with a lubricated Cusco's speculum, and cleaned with chlorhexidine solution. The cervix was held by a re-usable Volsellum forceps and a Leech Wilkinson cannula was inserted into the distal end of the cervix. About 15 mls of Urografin 76% was slowly introduced into the uterine cavity and the fallopian tubes via the Leech Wilkinson cannula.

The cannula and the tenaculum were then removed. Pelvic Radiographs were obtained in the antero-posterior, supine, and right oblique positions during the injection of the contrast medium. Immediately after these radiographs the patient was asked to assess the degree of pain, its character, and location. A late radiograph, 30 minutes after the procedure was done to assess the presence of loculation of the contrast medium within the pelvis.

Data was analyzed with SPSS11( SPSS Inc, Chigago,IL), a statistical package for data analysis. Demographic characteristics were explored using parametric and nonparametric tests to show baseline comparability among groups. Continuous data were expressed as means and standard deviation. The independent samples T- test was used to analyze the relationship between the mean visual numeric score of pain for both groups, and to study the effect of tubal pathology on the pain score. The level of significance was set at 0.05

### Results

Eighty four women were involved in the study, forty were randomly assigned to group A, and forty four women to group B. Demographic data on age, indications, and results of the hysterosalpingogram are presented in table 1.the mean age of the subjects in Group A is 32.30 years and the mean age in Group B is 30.75 years ( $P > 0.05$ ).

**Table 1:** Demographic characteristics of study groups and major findings on HSG

	Tramadol Group n=40 (%)	Control Group n=44 (%)
Age (years $\pm$ SD)	32.30	30.75
Indications		
Primary infertility	8(20%)	6(13.6%)
Secondary infertility	30(75%)	38(86.4%)
Aschermans syndrome	2(5%)	0
Results of HSG		
Bilateral patent tubes	23(57.5%)	30(68.2%)
Bilateral blocked tubes	9(22.5%)	11(25%)
Unilateral blocked tube	8(20%)	3(6.8%)

$P > 0.05$

**Table 2a:** Numeric rating pain assessment in both groups, regardless of tuba status

Tramadol Group (n=40)	6.25
Control Group (n=44)	6.27

The major indication in both groups is secondary infertility. The mean numeric pain score was 6.25 for the Tramadol group and 6.26 for the control group,  $P > 0.05$ . (Table 2A) In a subgroup analysis of those with tubal abnormality and those with bilateral normal tubes, the mean numeric pain score (MNS) score were 6.47 and 6.08 in the Control group and 6.38 and 6.03 in the Tramadol group.( Table

2B) Although there is increase in pain perception with tubal pathology in both the control and the Tramadol groups, the findings were not statistically significant.

Some other workers have evaluated the use of non-steroidal analgesic drugs, including Paracetamol to effect a reduction in pain during hysterosalpingography, but most of these studies did

**Table 2b:** Comparison of pain score assessment in patients with bilatera normal tubes and in those with a tubal pathology, either unilateral or bilateral

Group	Tubal status	N	Mean pain scores	Std. deviation	Std error mean
Group 1 (control)	Bilateral normal tubes	23	6.0870	2.10871	.43970
	A tubal pathology	17	6.4706	2.03463	.49347
Group 2 (Tramadol)	Both normal	30	6.0333	.92786	.16940
	A tubal pathology	14	6.3857	.97496	.26057

## Discussion

Pain is a sensation that is better experienced than described, measurement of pain is a function of various factors, and two persons experiencing the same level of pain may not react the same way. The established radiological tests for demonstrating fallopian tube patency include conventional hysterosalpingography, (HSG), hysterosalpingo-sonography (HyCoSy), three dimensional hysterosalpingography (3D-HyCoSy) and three-dimensional dynamic MR-hysterosalpingography (3D-MR-HSG); the new innovations of HyCoSy and 3DMR-HSG are thought to provide more information and less pain, however, recent research has shown that HyCoSy is as painful as HSG [4,5] and although 3DMR-HSG provides excellent information and less pain, it is not readily affordable and available to patients in the Africa [6]. A major disadvantage of these methods is pain, which is common with the traditional ionic contrast HSG.

The hysterosalpingogram (HSG) is an integral part of the evaluation for anatomic aetiologies of female infertility. The majority of women regard a hysterosalpingogram as acutely painful since it involves placement of a cervical tenaculum, traction on the cervix, and instillation of dye through a cervical cannula. The pain experienced during conventional HSG is mainly due to osmotic irritation of endometrial and peritoneal tissue by iodinated contrast agents.

Table 1 shows that both groups have similar demographic characteristics, including similarities in the radiographic findings on HSG. The mean numeric rating pain score for the Tramadol and Control group is 6.25 and 6.27,  $p > 0.05$ . The authors observed that there was a slight reduction in the mean numeric pain score in the Tramadol group, but it was not statistically significant.

not show any significant reduction when compared to placebo therapy [5,7]

Gary *et al* [8] conducted a randomized, double-blinded, placebo-controlled trial of intrauterine lidocaine in women undergoing hysterosalpingography (HSG), they found no difference in pain score between the intrauterine-lidocaine and placebo groups. They opined that Intrauterine lidocaine does not appear to be effective in decreasing pain in women undergoing HSG.

However, other workers such as Cicinelli *et al* [9], worked on the use of local anaesthetic injected into the cervix to relieve the pain of the procedure, they discovered that 2 mls of 2% mepivacaine injected transcervically via an 18-gauge intravenous catheter was able to reduce pain and the incidence of vasovagal reactions in women undergoing diagnostic hysteroscopy and endometrial biopsy. Similarly, Zupi *et al* [10] performed a similar study using 5 mL of 2% mepivacaine and, likewise, found a reduction in pain in women undergoing hysteroscopy with or without an endometrial biopsy. But none of these local anaesthetics relieved the pain during instillation of the dye when performing an HSG, although there was reduction in the pain associated with the application of the Volsellum and tenaculum. It is also possible that the pain associated with hysteroscopy or endometrial biopsy is different from that associated with HSG. This may be related to the underlying nature of these procedures with hysteroscopy and endometrial biopsies typically physically traumatizing the uterine cavity and, possibly, causing pain via contractions, whereas hysterosalpingogram may induce discomfort more via a stretching phenomenon. Also, the use of balloon catheters instead of metallic cannulas have been observed to reduce pain sensation significantly during the application of the tenaculum and traction on the cervix [11,12,13].

We were interested in the tubal patency of these patients because a previous study showed that pain increases with tubal occlusion [14]. In this study, we observed that patients with patent bilateral fallopian tubes in the Control and Tramadol group, had mean pain scores of 6.08 and 6.03 respectively, and with tubal pathology (either unilateral or bilateral) the mean pain scores are 6.47 and 6.38, respectively. ( $P > 0.05$ ) There is a mild increase in pain sensation with tubal pathology, but this series does not support the theory that tubal pathologies predispose to statistically increased pain level.

A limitation of the study was that the assessment was done five minutes after the procedure, and some of the patients may have confused the discomfort of the procedure with the pain assessment.

In conclusion, this study does not show a statistically significant decrease in pain perception in patients premedicated with Tramadol; we believe more studies should be done in our environment to know the technical innovation and analgesic agent that will result in significant reduction of pain experienced during HSG.

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