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Oral dexketoprofen for pain treatment during diagnostic hysteroscopy in postmenopausal women

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Abstract

Objective: To assess the efficacy of dexketoprofen (DEX) in reducing pain at different stages of the hysteroscopic procedure in comparison with local anaesthesia in menopausal women. *Methods:* Menopausal patients affected by uterine bleeding submitted to diagnostic hysteroscopy, were randomised to receive either 25 mg DEX tablet ($n = 148$) or intracervical injection of 5 ml mepivacaine 2% ($n = 150$). Pain suffered during the procedure itself and 30, 60, 120 min after, was scored on the 11 point Visual Analogic Scale, recorded and analysed. *Results:* No statistical difference were noted during the procedure itself in both groups of treatment. Patients treated with DEX has significantly less postoperative pain. *Conclusions:* DEX is not superior to mepivacaine in reducing the discomfort of the procedure but does significantly reduce postoperative pain.

Keywords: Dexketoprofen; Hysteroscopy; Pain

1. Introduction

Comparative studies suggest the superiority of outpatient hysteroscopy over dilatation and curettage in the investigation of patients with a variety of gynaecological disorders [1,2]. It allows complete visualization of the uterine cavity, directed or guided endometrial biopsies, and more appropriate therapeutic management [3]. Most hysteroscopies are performed under general anaesthetic despite evidence suggesting it is a well tolerated and acceptable outpatient procedure [4].

Premenopausal women well tolerate the examination and topical anaesthesia or analgesia is not routinely administered in this patients [5].

Postmenopausal women badly tolerate and accept this procedure because the difficulties may be encountered when dealing with narrowed, atrophic endocervical canals.

The inability to negotiate the cervical canal can raise a very painful stimulation that could trigger threatening side effects due to systemic pathologies.

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Pain is the commonest reason for failure to complete the investigation in these patients [6,7].

Therefore Downes and Al-Azzawi [8] used routinary intracervical block to provide analgesia in 100 perimenopausal women and in this way demonstrated that outpatient hysteroscopy is well tolerate by perimenopause patients.

For the first time, Nagele et al. [9] have assessed a prostaglandin synthesis inhibitor during outpatient hysteroscopy.

The patients were instructed to take one tablet of mefenamic acid 500 mg 1 h before the hysteroscopy.

Mefenamic acid appeared to have minimal effects on the discomfort associated with the hysteroscopy itself but significantly reduced the after pains of the procedure. The partial failure of this treatment was ascribed by the authors to the relatively minor effect of the drug, with respect to uterine manipulation as well as the longer time to achieve plasma peak levels of the drug.

Dexketoprofen (DEX), the active enantiomer of the racemic compound ketoprofen, is a new nonsteroidal anti-inflammatory drug (NSAID) of the arylpropionate family.

A single oral capsule of DEX 25 mg (given as 37 mg of the trometamol salt) showed a very rapid onset of the analgesic effect associated with a long lasting activity and a level of analgesia significantly superior compared to ketoprofen [10]. Therefore it could be ipotized that this drug is appropriate for pain relief during hysteroscopy.

The aim of our randomised study was to evaluate objectively the efficacy and safety of oral treatment with DEX in the treatment of pain in postmenopausal women during outpatient diagnostic hysteroscopy.

2. Materials and methods

From December 1999 to June 2001, 305 consecutive postmenopausal women were referred to our outpatient Menopause Clinic for hysteroscopy because uterine bleeding.

The patients were randomly allocated to receive either local infiltration of the cervix by injecting of 5 ml mepivacaine 2% intracervically up to the level of the internal os or one tablet of DEX given 1 h before the procedure.

All the patients received 200 μg of misoprostol placed in the posterior vaginal fornix 2–3 h before hysteroscopy in order to render less traumatic dilatation of the cervical canal.

Randomization was achieved with sealed envelops containing computer generated block randomisation numbers.

Their informed consent were included in the study which was approved by the local medical ethics committee.

Patient with a known sensitivity to NSAIDs and prostaglandin synthesis inhibitors were excluded from the study.

Age, parity and duration of surgery did not differ significantly between the two groups (data not shown).

Hysteroscopic examination was performed in a specially prepared outpatient room with the assistance of an experienced nurse.

The examinations were performed grasping the anterior lip of the cervix with a single-tooth vulsellum after visualization and cleaning of the cervix with the aid of a vaginal speculum.

The cervical os was gradually dilatated with cervical dilators to 5 Hegar when deemed necessary.

Panoramic hysteroscopy was performed using a 4 mm telescope with a 30° fore-oblique lens and a 5 mm diagnostic sheath and an electronic Hamou CO_2 uterine insufflator set to a flow rate of 45 ml/min. and a pressure of up to 100 mmHg.

A Storz cold light source with fibre-optic cable allowed adequate illumination.

The images were observed on a high resolution color monitor using chip camera.

The TV monitor was placed so that the patient could observe if she so desired.

After assessing the endometrial cavity when the endometrium looked abnormal sampling was performed with a Pipelle device (Laboratorie CCD).

At the end of the investigation, the subject were asked to score the worst pelvic or backache or shoulder tip pain experienced during hysteroscopy and at 30, 60 and 120 min after the procedure using an 11 point Visual Analogic Scale, marking a

cross on a 10 cm line with 0 on the left side indicating no pain and 10 on the right side indicating the worst imaginable pain. Heart rate and blood pressure were monitored continuously in both groups.

The data were statistically analysed by χ^2-test and Mann–Whitney U tests, a result of $P < 0.05$ being considered statistically significant.

3. Results

Seven women were excluded from the study.

Five of these thought to be too anxious to tolerate hysteroscopy under local anaesthesia or pharmacological sedation, two because previous conization.

A total of 148 patients received DEX tablets and 150 patients received local anaesthetic drug. Age, parity and duration of surgery did not differ significantly between the two groups (data not shown).

Hysteroscopy was unsuccessful in 10 women (five in each group) because pain which caused complete cessation of the procedure and in 3 women in the DEX group because unsatisfactory view.

Fig. 1 presents values for the Visual Analogic Scale during the procedure and at 30, 60 and 120 min in both group of treatment.

The pain suffered during the procedure was similar in both groups.

Compared to local anaesthesia, values for Visual Analogic Scale scores at 30, 60 and 120 min were significantly lower in the DEX group ($P < 0.05$).

No complications attributable to the procedure occurred and no patients required admission after hysteroscopy.

4. Discussion

Metrorrhagia in menopausal women is the most frequent indication for hysteroscopy. Often, however, the procedure turns out to be difficult or impossible due to stenosis and reduction in size of the cervical canal.

We assessed the efficacy of a non-steroidal anti-inflammatory analgesic as premedication before hysteroscopy in reducing the pain in a group of postmenopausal women in the whole process and not merely during the procedure.

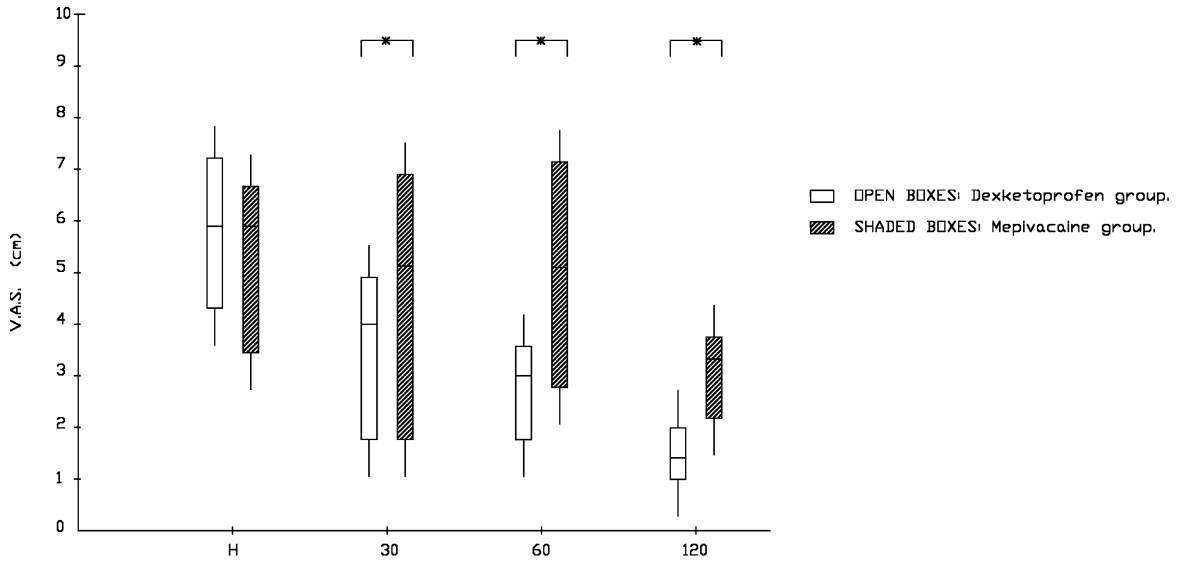

Fig. 1. Pain cores platted in the Visual Analogue Scale (VAS) The media value is represented by the horizontal bar in the box $*P < 0.05$.

Because the elevated expected rate of painful cervical dilatation in this group of patients we used in all patients vaginal misoprostol to lessen the cervical resistance [11].

Compared with local anaesthesia, DEX did not significantly affect the worst pain the women suffered during the procedure itself but reduced significantly the postoperative pain.

Intracervical anaesthesia is effective in reducing the sensitivity of the cervix but is uneffective at blocking fundal innervation of the uterus and discomfort related to prostaglandin uterine contractions [12].

DEX produces a satisfactory level of analgesia similar to that achieved with local anaesthesia during hysteroscopy; indeed 3.4% of the procedures were abandoned because pain in the mepivacaine group as well in the DEX group.

The analgesic effect lasts longer and is able in reducing the pain arising from the fundal region because its effectiveness at blocking fundal innervation of the uterus derived from the ovarian nerve plexus. Therefore patients recovered far better in the DEX group so contributing to more rapid ambulation and significantly earlier discharge.

Nagele et al. [9] first assessed a prostaglandin synthesis inhibitor during outpatient hysteroscopy found the mefenamic acid appears to have minimal effects on the pain associated with hysteroscopy itself but does significantly reduce the postoperative pain.

The positive effect of a prostaglandin synthesis inhibitor in term of postoperative pain relief has been fully documented by many authors [13,14].

Possible explanation of the failure of the intraoperative analgesic effect of prostaglandin synthesis inhibitor has been suggested due to the delayed plasma levels of mefenamic acid and possibly due to the lag time between administration of the drug and operative procedure [8].

The DEX has been demonstrated to possess a very rapid onset of action (within 30 min of administration) and a long lasting effect (at least for 6 h).

The very rapid onset of action compared with ketoprofen suggests that DEX is more appropriate for the treatment of acute pain [15–17].

Due to these characteristics, DEX revealed on the Visual Analogic Scale a similar intraoperative analgesic effect confronted with intracervical injection of mepivacaine but a significantly superior effect on the postoperative pain prevention.

Our study provide adequate evidence that outpatient diagnostic hysteroscopy under oral analgesia offers an acceptable alternative to procedures with local anaesthetic.

We eliminated discomfort not only related to the procedure itself and on the basis of our results we believe in the widespread application of this approach.

In the study presented here, the study population was exclusively postmenopausal where the chance of failed attempts due to the pain is most likely to occur compared with premenopausal women.

Therefore, we have experimented a new approach in a subgroup of patients for the treatment of pain that is far different from the one we have adopted in our department in a general population [18].

On the basis of our results we believe in the widespread application of this approach.

References

[1] Marana R, Marana E, Catalano GF. Current practical application of office endoscopy. Curr Opin Obstet Gynaecol 2001;13:383–7.
[2] Raju KS. Should outpatient hysteroscopy replace conventional diagnostic dilatation and courettage in gynecologic practice? J Gynecol Surg 1992;8(4):225–30.
[3] Roger V, Cravello L, Stolla V, d'Ercole C, Blanc B. Role of diagnostic hysteroscopy in the exploration of postmenopausal metrorrhagia. Press Med 1998;27(25):1294–5.
[4] Bellingham FR. Outpatient hysteroscopy problems. Aust NZ J Obstet Gynecol 1997;37(2):202–5.
[5] Broadbent JAM, Hill NCW, Molnar BG, Rolfe KJ, Magos AL. Randomized placebo controlled trial to assess the role of intracervical lidocaine in outpatient hysteroscopy. Br J Obstet Gynaecol 1992;99:777–9.
[6] Giorda G, Scarabelli G, Franceschi S, Carpagnutta E. Feasibility and pain control in outpatient hysteroscopy in postmenopausal women a randomized trial. Acta Obstet Gynecol Scand 2000;79(7):593–7.
[7] Cicinelli E, Didonna T, Ambrosi G, Schonauer LM, Fiore G, Matteo MG. Topical anaesthesia for diagnostic hysteroscopy and endometrial biopsy in postmenopausal

women: a randomized placebo-controlled double-blind study. Br J Obstet Gynecol 1997;104(3):316–9.
[8] Downes E, Al-Azzawi F. How well do perimenopausal patient accept outpatient hysteroscopy? Visual analogue scoring of acceptability and pain in 100 women. Eur J Obstet Gynecol Reprod Biol 1993;48:37–41.
[9] Nagele F, Lockwood G, Magos AL. Randomized placebo controlled trial of mefenamic acid for premedication at outpatient hysteroscopy: a pilot study. Br J Obstet Gynaecol 1997;104:842–4.
[10] Mc Gurk M, Robinson P, Rajayogeswaran V, De Luca M, Casini A, Artigas R, et al. Clinical comparison of dexketoprofen trometamol, ketoprofen, and placebo in postoperative dental pain. J Clin Pharmacol 1998;38(Suppl 12):46S–54S.
[11] Preutthipan S, Herabutya Y. A randomized controlled trial of vaginal misoprostol for cervical priming before hysteroscopy. Obstet Gynecol 1999;94(3):427–30.
[12] Vercellini F, Colombo A, Mauro F, Oldani S, Bramante T, Crosignani PG. Paracervical anaesthesia for outpatient histeroscopy. Fertil Steril 1994;62:1083–5.
[13] Siddle NC, Young O, Sledmere CM, Reading AE, Whitehead MI. A controlled trial of naproxen sodium for relief of pain associated with Vabra suction curettage. Br J Obstet Gynaecol 1993;82:951–4.
[14] Rvan EE, Hemrika DJ, van der Linden ThM. Pain relief following day-case diagnostic hysteroscopy–laparoscopy for infertility: a double-blind randomized trial with preoperative naproxen versus placebo. Obstet Gynecol 1993;82:951–4.
[15] Bagan JV, Lopez Arranz JS, Valencia E, Santamaria J, Eguidazu I, Horas M, et al. Clinical comparison of dexketoprofen trometamol and dipyrone in postoperative dental pain. J Clin Pharmacol 1998;38(Suppl 12):55S–64S.
[16] Beltran J, Martin-Mola E, Figueroa M, Sanmarti R, Artigas R, Torres F, et al. Comparison of dexketoprofen trometamol and ketoprofen in the treatment of osteoarthritis of the knee. J Clin Pharmacol 1998;38(Suppl 12):74S–80S.
[17] Barbanoj MJ, Gich I, Artigas R, Tost D, Moros C, Antoijoan RM, et al. Pharmacokinetics of dexketoprofen trometamol in healthy volunteers after a single and repeated oral doses. J Clin Pharmacol 1998;38(Suppl 12):33S–40S.
[18] Zullo F, Pellicano M, Stigliano CR, Di Carlo C, Fabrini A, Nappi C. Topical anaesthesia for office hysteroscopy. A prospective randomized study comparing two modalities. J Reprod Med 1999;44(10):865–9.