



To compare the fixed dose combination of drotaverine hydrochloride and mefenamic acid with intravenous sedation with injection pentazocine and diazepam in terms side effects at tertiary care hospital Rajasthan.

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background- Hysteroscopic examination with endometrial biopsy is currently the most informative investigation for patients with abnormal uterine bleeding and infertility.

Methods- This study was conducted at the department of obstetrics and gynecology, pannadhay rajkiya mahila chikitsalaya, RNT medical college, Udaipur.

Results- In our study, nausea, vomiting and dizziness were the most common symptoms which were significantly higher in patients who received intravenous sedation. Above symptoms were very less in patients with oral drotaverine and mefenamic acid. Headache was comparable in the two groups during procedure with non significant results. However, headache was significantly higher 2 hours after procedure in patients who received intravenous sedation.

Conclusion- To conclude, the present study showed that fixed dose combination of drotaverine and mefenamic acid has less side effects compared to intravenous sedation.

Keywords- Hysteroscopy or endometrial biopsy, pain, preoperative care or premedication

Introduction

Hysteroscopic examination with endometrial biopsy is currently the most informative investigation for patients with abnormal uterine bleeding and infertility. Previously, this procedure was done under general or regional anesthesia. Hysteroscopy with endometrial biopsy under local anesthesia has gained wider acceptance to avoid the risk of general anesthesia.¹ Schoenfeld et al. and Kajve et al. concluded that intravenous diazepam and pentazocine is effective for pain relief during minor gynecological operations and tubal ligation.^{2,3} A mixture of pentazocine and diazepam was used by them for minor gynecological procedures. Satisfactory operating conditions were achieved in 98% of the patients without any adverse reactions. With the advent of locally acting better drugs, many centers stopped using intravenous sedation. Various methods of local anesthesia have been studied to reduce the pain, and it was suggested that paracervical block, topical lignocaine, intracervical lignocaine may reduce the pain, but the evidence is not strong.⁴⁻⁶ It could be due to inability of the paracervical block to affect the sensitivity of the uterine fundus. Similarly techniques involving

dilatation of cervix, like introduction of hysteroscope, result in increased pain due to prostaglandin release. Therefore, it seems logical to prime the cervix and use prostaglandin synthesis inhibitors prophylactically before the procedure. Drotaverine hydrochloride, an isoquinoline derivative, is a potent spasmolytic which acts directly on the smooth muscles by inhibiting phosphodiesterase activity and is devoid of any anticholinergic side effects.⁷ Because of this antispasmodic action, it is widely used in biliary and renal colic, for augmentation of labor, dysmenorrhea and before instrumental diagnostic procedures. Mefenamic acid, a nonsteroidal anti-inflammatory drug, inhibits cyclooxygenase enzyme and exerts its anti-inflammatory and analgesic action by inhibiting prostaglandin synthesis. It is widely used in gynecology to treat dysmenorrhea and menorrhagia. By virtue of two different mechanisms of action due to different active ingredients, a fixed-dose combination of drotaverine hydrochloride with mefenamic acid would be expected to reduce the discomfort of the procedure. Both are well absorbed orally. Peak plasma concentration of drotaverine is attained within 1 hour; and that of mefenamic acid, in 2 to 4 hours. The two molecules in a fixed-dose combination provide comprehensive pain relief. Drotaverine allays the early-onset pain and potentiates the sustained analgesic effect of mefenamic acid. As the special property of fixed dose combination having synergistic effects allows achieving relief in early-onset pain by drotaverine and sustained analgesic effect by mefenamic acid, we hypothesized that oral tablet containing drotaverine and mefenamic acid will be effective in relieving pain during hysteroscopy and endometrial biopsy, cost effective and less invasive. We therefore studied the effect of fixed-dose (oral) combination of drotaverine (80 mg) with mefenamic acid (250 mg) on pain perception during hysteroscopy and endometrial biopsy and compared it with that of

paracervical block and with that of intravenous sedation, both of which are more invasive.

Material And Method

Study Centre: The study was conducted at the department of obstetrics and gynecology, pannadhay rajkiya mahila chikitsalaya, RNT medical college, Udaipur.

Type Of Study: randomized prospective comparative study

Duration: January 2014 to June 2014.

Subjects for Study:

Total 200 patients attending the OPD for minor gynecological procedures were enrolled in the group after taking informed consent. These patients were randomly divided into two groups, each group containing 100 patients.

Inclusion Criteria

- All women should be requiring any of the above mentioned gynecological procedure.
- All of them should have given written and informed consent

Exclusion Criteria

- Having a known sensitivity to NSAIDs, drotaverine, Inj pentazocine, Inj diazepam.
- Having peptic ulcer disease, inflammatory bowel disease, porphyrias, genital infections, cervical stenosis, serious cardiac disease, severe anemia.
- Patients with anxiety disorders, airway diseases, chronic medical illnesses, elderly.
- Being unable or unwilling to provide informed consent.
- Having history of cervical surgery.

Method

- i. Total 200 patients will be included in the study, after taking informed consent.
- ii. Patients will be randomly divided into two groups each of 100 patients.

- iii. Among two group there is equal number of patient with particulare procedure.
- iv. Group 1 patients will receive fixed dose oral tablet containing 80 mg of drotaverine and 250 mg of mefenamic acid one hour before the procedure.
- v. Group 2 patients will receive intravenous sedation with pentazocine (0.6mg/kg) and diazepam (0.2mg/kg) ten minutes before the procedure.
- vi. Pulse and blood pressure will be recorded during the procedure,1hr after procedure,and 2hr after procedure.
- vii. Adverse effect and VAS score also observed during the procedure,1hr after procedure,and 2hr after procedure.
- viii. The procedures will be done placing the patients in lithotomy position with proper asepsis.
- ix. Another resident doctor not aware of the group of the patient will be asked to score the worst pain felt by the patients during procedure and the discomfort felt by them 1 hour and 2 hour after the procedure.
- x. Pain will be assessed by visual analog scale (VAS; 0 cm – no pain, 10 cm – excruciating pain)
- xi. Any adverse effects will be noted like nausea, vomiting, headache and dizziness.
- xii. Statistical analysis will be done using t –test and chi-square test.
- xiii. P value less than 0.05 will be considered significant.

Observations

Table 1. Age wise distribution

Age group (years)	Group I	Group II
20-40	80 (80%)	64 (64%)
41-60	17 (17%)	30 (30%)
>60	3 (3%)	6 (6%)
Total	100	100
Mean age (years)	33.53	36.60

P value = 0.075

Highest number of patients were in the age group of 20-40 years in both the groups. The p value is non significant. So the confounding factor, age, was eliminated in the comparative study.

Table 9. Side effects

Side effects	Group I (n=100)	Group II (n=100)	P value
Nausea:			
During procedure	9 (9%)	49 (49%)	0.0001
1 hour after procedure	4 (4%)	89 (89%)	0.0004
2 hours after procedure	20 (40%)	85 (85%)	0.001
Vomiting:			
During procedure	0 (0%)	11 (11%)	0.001
1 hour after procedure	0	0	-
2 hours after procedure	0 (0%)	2 (2%)	0.00
Dizziness:			
During procedure	40 (40%)	49 (49%)	0.293
1 hour after procedure	60 (60%)	18 (18%)	0.0006
2 hours after procedure	45 (45%)	9 (9%)	0.0004
Headache:			
During procedure	16 (16%)	19 (19%)	0.467
1 hour after procedure	13 (13%)	15 (15%)	0.647
2 hours after procedure	0 (0%)	5 (5%)	0.003

In our study, nausea, vomiting and dizziness were the most common symptoms which were significantly higher in patients who received intravenous sedation. Above symptoms were very less in patients with oral drotaverine and mefenamic acid. Headache was comparable in the two groups during procedure with non significant results. However, headache was significantly higher 2 hours after procedure in patients who received intravenous sedation.

Discussion

In our study, nausea, vomiting and dizziness were the most common symptoms which were significantly higher in patients who received intravenous sedation. Above symptoms were very less in patients with oral drotaverine and mefenamic acid. Headache was comparable in the two groups during procedure with non significant results. However, headache was significantly higher 2 hours after procedure in patients who received intravenous sedation.

Similar to our study, Romics I⁸ study showed that nausea, vomiting and dizziness were significantly more in the intravenous sedation group. However, abdominal cramps were little more in the drotaverine – mefenamic acid group but it was not statistically significant.

J B Sharma⁹ study showed that 1 patient in oral drotaverine and mefenamic acid complained of epigastric pain after 2 hours of procedure; 4 complained of abdominal cramps after 1 hour of procedure and no other adverse effects were noted. In patients with intravenous sedation, 20 patients had dizziness, 4 had palpitations during procedure, 12 had dizziness after 1 hour of procedure. 7 patients had nausea and vomiting after the procedure. These results are comparable to our study.

Conclusion

To conclude, the present study showed that fixed dose combination of drotaverine and mefenamic acid has less side effects compared to intravenous sedation.

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