INTRODUCTION

INTRAPERITONEAL LIDOCAINE FOR PAIN RELIEF DURING AND AFTER TUBAL STERILIZATION

By
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ABSTRACT

We conducted a randomized, blinded, placebo-controlled study to evaluate the effectiveness of intraperitoneal lidocaine, IM meperidine, or both drugs together for pain relief (intraoperative and postoperative) in postpartum tubal ligation. Sixty postpartum patients scheduled to have tubal ligation were randomly divided into four groups to receive IM isotonic sodium chloride solution (2 mL) and intraperitoneal instillation of 40 mL of isotonic sodium chloride solution (Group I) ; IM meperidine (100 mg in 2 mL) and intraperitoneal instillation of 40 mL of isotonic sodium chloride solution (Group II) ; IM injection of isotonic sodium chloride solution and intraperitoneal instillation of 1% lidocaine in 40 mL (Group III) and both meperidine and intraperitoneal lidocaine instillation (Group IV). The minilaparotomy was performed after local infiltration with 20 ml of lidocaine. A numerical rating score was used to rate pain on a 0 – 10 scale during and after the surgical procedures. During the surgical procedures, the mean pain scores were 1.8 in group III and 0.7 in group IV. These pain scores were significantly lower than those in groups I and...
II, which were 6.4 and 6.0, respectively (p < 0.001). Postoperative mean pain scores at 24 h rest were 2.1 in group III and 0.8 in group IV. These pain scores were significantly lower than those in groups I and II, which were 6.5 and 6.4, respectively (p < 0.001). Postoperative mean pain scores at 24 h movement were 2.9 in group III and 1.6 in group IV. These pain scores were significantly lower than those in groups I and II, which were 7.5 and 7.3 respectively (p < 0.001). The plasma lidocaine concentrations reached a maximum in groups III and IV 30 min after instillation begun. The highest mean plasma lidocaine level was 2.6 ug/ml (range 1.2 – 3.6).

In conclusions pain relief was inadequate in patients undergoing post-partum tubal ligation under local anesthesia, even after the administration of IM meperidine. Intraperitoneal lidocaine, however, effectively, decreased intraoperative and postoperative pain in these patients.

INTRODUCTION

Recently, there has been interest in the instillation of local anesthetic solutions into the peritoneal cavity for treatment of pain after abdominal surgery. This technique has been described as producing effective analgesia after laparoscopic cholecystectomy by some workers (1, 2), but not by others (3). After gynaecological laparoscopy, there is a stronger evidence for effective analgesia (4, 5).

Anesthetic techniques for tubal sterilization range from local anesthesia to neuraxial or general anesthesia. Although regional anesthesia is routinely used for this minor operation in the United States (8, 9), in many parts of the world, it is performed under local anesthesia, often with inadequate pain relief (6, 10). Intraperitoneal lidocaine instillation for post partum tubal ligation was reported in 1973; however, that study had inadequate pain measurement (11). Although
previously investigated for postoperative pain relief (12, 13), IM meperidine has not been evaluated for intraoperative pain relief in patients undergoing postpartum tubal ligation under local anesthesia. The aim of this study was to evaluate whether intraperitoneal lidocaine, IM meperidine, or both drugs together can effectively decrease intraoperative and postoperative pain in postpartum tubal ligation performed under local anesthesia.

**PATIENTS AND METHODS**

After obtaining a written informed patient consent, we studied 60 patients (ASA physical status I or II) who agreed to undergo postpartum tubal sterilization within 48 h of delivery under local anesthesia. Patients were excluded if they had cardiac or vascular disease, hepatic disease, allergy to local anesthetic agents or any contraindications to local anesthesia. The patients were randomly assigned to one of four groups (15 patients per each group). Group I (placebo group) received an intramuscular (IM) injection of 2 mL of isotonic sodium chloride solution 1 h before surgery and an intraoperative intraperitoneal instillation of 40 mL of isotonic sodium chloride solution. Group II (meperidine group) received an IM injection of meperidine (100 mg in 2 mL) 1 h preoperatively, as well as the intraoperative intraperitoneal instillation of 40 mL of isotonic sodium chloride solution. Group III (Lidocaine group) received an IM injection of isotonic sodium chloride solution and an intraoperative intraperitoneal instillation of 40 mL of 1.0% lidocaine in isotonic sodium chloride solution. Group IV (meperidine plus lidocaine group) received both IM injection of meperidine and the intraperitoneal instillation of 1.0% lidocaine. During the preoperative visit, the patients were asked to practice scoring their pain verbally using the numerical rating score (NRS). Pain was rated on a scale of 0 – 10 (0 = no pain at all,

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10 = the most severe pain). One hour after the IM injection of either saline or meperidine, patients were brought into the operating room where an IV infusion of lactated ringer's solution was started and non invasive monitoring (electrocardiogram, automated blood pressure and pulse oximetry) was begun. Every patient received 20mL of 1% lidocaine infiltration of the skin and beneath the rectus sheath in a 2.5cm horizontal line just below the umbilicus. After checking the numbness of the skin with a needle, an incision was made. The solution for intraperitoneal instillation was made by mixing 20mL of the blinded solution (2% lidocaine or isotonic sodium chloride solution) with 20 mL of isotonic sodium chloride solution for a total of 40 mL. After the abdominal cavity was opened, this solution was slowly instilled into the peritoneal cavity while the patient remained supine in a horizontal plane. The abdominal opening was lifted while half of the local anaesthetic solution (20 mL) was instilled to each side of the adnexa with a 20-mL syringe without a needle. After waiting 3 min, the surgeon started searching for the uterine tubes and the patient was asked to rate the pain using a verbal NRS. If the pain score was ≤3, no analgesic drugs were given. If the pain score was >3, IV fentanyl 1 – 2 mg/Kg was given. Patients who had pain scores of 3 – 5 received only fentanyl. IV ketamine 0.5 – 2 mg/Kg was given if the pain score was ≥ 6. If the surgery could not be performed after the administration of ketamine, anesthesia was induced with propofol 1 – 2 mg/Kg and the patient's trachea was intubated with succinyl choline 1 mg/Kg, then maintained with nitrous oxide, oxygen and isoflurane. Venous blood samples were drawn 0, 5, 15, 30, 45, 60 and 120 min after the peritoneal instillation for the detection of plasma lidocaine concentration using high pressure liquid chromatography and ultraviolet detection. The limit of detection was 0.04 μg/mL.
In the postoperative period, the patient completed the numerical rating score (NRS), at 24 h, for pain at rest and during a standardized movement (sitting upright from the supine horizontal position). In the recovery room, vital signs were observed for 2h after surgery. On the postpartum ward, paracetamol (Two-500 mg tablets) was administered every 4 h if the patients required pain relief. Side effects such as vomiting, fever, or urinary retention were observed and recorded until the patients were discharged home. For statistical analysis, the $\chi^2$ test, the Kruskal-Wallis test and Mann-Whitney U test were used as appropriate.

RESULTS

There were no significant differences in demographic characteristics among the four groups and the duration of surgery was similar (table 1). As regards the intraoperative pain, the mean NRS were significantly lower ($p < 0.001$) in the groups using lidocaine (1.8 and 0.7 in group III and IV, respectively) compared with the groups in which lidocaine was not used (6.4 and 6.0 in group I and group II, respectively) (table 2). However, there were no significant differences in mean NRS between the groups receiving meperidine and the groups not receiving meperidine (6.0 vs 6.4 in group II versus group I and 0.7 vs 1.8 in group IV versus group III). As regards the postoperative pain at 24h rest, the mean NRS were significantly lower ($p < 0.001$) in the groups using lidocaine (2.1 and 0.8 in groups III and IV, respectively) compared with groups in which lidocaine was not used (6.5 and 6.4 in group I and group II, respectively (table 2).

Also, at 24 h movement the mean NRS were significantly lower in the groups using lidocaine (2.9 and 1.6 in groups III and IV respectively) compared with the groups in which lidocaine was not used (7.5 and 7.3 in
groups I and II respectively) (table 2). The percentages of patients who required fentanyl or ketamine were lower (p < 0.001) in the groups receiving lidocaine (groups III and IV) than in the groups that did not receive lidocaine (groups I and II) (table 2). There were no differences in the proportions of patients who required fentanyl or ketamine between the groups using and not using meperidine. Only two patients (13.33%) in group I and one patient (6.66%) in group III required general anesthesia with endotracheal intubation. Significantly, less fentanyl and ketamine were used in the groups III and IV compared with groups I and II (p < 0.001) (table 2). The hemodynamic changes, indicated by systolic, diastolic, mean blood pressure and heart rate during the operation were not different among the four groups (table 3).

The plasma lidocaine concentrations reached a maximum in group III and IV 30 min after instillation was begun (Fig. 1). The highest mean plasma lidocaine level was 2.6\(\mu\)g/mL (range 1.2-3.6 \(\mu\)g/mL).

There were no clinical differences in observed side effects. Vomiting occurred in 3 patients (20%) in group II and one patient (6.66%) in group IV. A decrease in oxygen saturation to <95% was found in 2 (13.33%), three (20%) and one patient (6.66%) in group I, II and IV, respectively. Urinary retention occurred in two patients (13.33%) in group II and in two patients in group IV (13.33%) (table 4).

In the postoperative period, the paracetamol tablet requirement was significantly less in groups III and IV (3.5 and 2.2) than in group I and II (6.3 and 6.7) (p < 0.001) (table 2).
Table (1) : Demographic characteristics and duration of surgery

<table>
<thead>
<tr>
<th></th>
<th>Group I (Placebo)</th>
<th>Group II (Meperidine)</th>
<th>Group III (Lidocaine)</th>
<th>Group IV (Lidocaine + meperidine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Age</td>
<td>30.3 ± 5.1</td>
<td>30.4 ± 5.4</td>
<td>30.5 ± 6.0</td>
<td>28.9 ± 4.5</td>
</tr>
<tr>
<td>- Weight (Kg)</td>
<td>55.3 ± 15.2</td>
<td>60.2 ± 10.1</td>
<td>58.2 ± 11.7</td>
<td>62.2 ± 9.5</td>
</tr>
<tr>
<td>- Height (cm)</td>
<td>155.5 ± 3.3</td>
<td>155.8 ± 5.6</td>
<td>152.7 ± 4.4</td>
<td>154 ± 3.0</td>
</tr>
<tr>
<td>- Duration of surgery (min)</td>
<td>26.8 ± 10.4</td>
<td>25.7 ± 9.8</td>
<td>26.2 ± 17.0</td>
<td>22.5 ± 13.2</td>
</tr>
</tbody>
</table>

Values are mean ± SD

Table (2) : Numerical rating score (NRS), analgesic drug, patients requiring analgesic drugs and postoperative paracetamol use.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative NRS pain scores (0-10*)</td>
<td>6.4±3.2</td>
<td>6.0±2.9</td>
<td>1.8±2.1</td>
<td>0.7±1.4</td>
</tr>
<tr>
<td>Postoperative NRS pain scores (0-10*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- At 24 h rest.</td>
<td>6.5±3.3</td>
<td>6.4±3.4</td>
<td>2.1±1.2</td>
<td>0.8±1.5</td>
</tr>
<tr>
<td>- At 24 h movement.</td>
<td>7.5±2.5</td>
<td>7.3±2.4</td>
<td>2.9±1.6</td>
<td>1.6±1.2</td>
</tr>
<tr>
<td>Patients requiring fentanyl.*</td>
<td>13 (86)</td>
<td>10(66.66)</td>
<td>2 (13.33)</td>
<td>1 (6.66)</td>
</tr>
<tr>
<td>Patients requiring ketamine.*</td>
<td>12 (80)</td>
<td>12 (80)</td>
<td>2 (13.33)</td>
<td>1 (6.66)</td>
</tr>
<tr>
<td>Patients requiring general anesthesia</td>
<td>2 (13.33)</td>
<td>0 (0)</td>
<td>1 (6.66)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Intraoperative fentanyl use (ug)*</td>
<td>85.2±34</td>
<td>83.5±33.4</td>
<td>20.5±30.3</td>
<td>10±15.2</td>
</tr>
<tr>
<td>Intraoperative ketamine use (ug)*</td>
<td>20.3±15.7</td>
<td>19.0±13.8</td>
<td>5.2±15.6</td>
<td>3.5±14.6</td>
</tr>
<tr>
<td>Postoperative paracetamol used (tablets)</td>
<td>6.3±2.8</td>
<td>6.7±2.9</td>
<td>3.5±1.8</td>
<td>2.2±1.9</td>
</tr>
</tbody>
</table>

- Values are mean ± or n (%)
- p < 0.001

Table (3) : Hemodynamic changes during operation among the four groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I Control</th>
<th>Group I Intra-operative</th>
<th>Group II Control</th>
<th>Group II Intra-operative</th>
<th>Group III Control</th>
<th>Group III Intra-operative</th>
<th>Group IV Control</th>
<th>Group IV Intra-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beat/min)</td>
<td>99±10</td>
<td>106±12</td>
<td>97±10</td>
<td>106±4</td>
<td>98±9</td>
<td>104±10</td>
<td>97±9</td>
<td>104±2</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>122±8</td>
<td>126±2</td>
<td>126±2</td>
<td>130±2</td>
<td>120±6</td>
<td>126±2</td>
<td>124±4</td>
<td>130±4</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>82±4</td>
<td>86±2</td>
<td>78±2</td>
<td>80±4</td>
<td>80±4</td>
<td>84±6</td>
<td>80±2</td>
<td>82±4</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>96±3</td>
<td>104±3</td>
<td>94±2</td>
<td>104±3</td>
<td>96±3</td>
<td>102±4</td>
<td>98±3</td>
<td>104±6</td>
</tr>
</tbody>
</table>

HR = Heart rate  SBP = Systolic blood pressure  DBP = Diastolic blood pressure  MAP = Mean arterial pressure  values = mean ± SD.

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Table (4): Postoperative side effects during the first 24h (n %).

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Vomiting</td>
<td>0 (0)</td>
<td>3 (20%)</td>
<td>0 (0)</td>
<td>1 (6.66%)</td>
</tr>
<tr>
<td>- Urinary retention</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (13.33%)</td>
<td>2 (13.33%)</td>
</tr>
<tr>
<td>- Decrease in O₂ saturation to 95%</td>
<td>2 (13.33%)</td>
<td>3 (20%)</td>
<td>0 (0)</td>
<td>1 (6.66%)</td>
</tr>
</tbody>
</table>

Fig. (1): Serum concentrations of lidocaine (mg/mL) after instillation of a dose of 400mg into the pelvic cavity after tubal ligation. Group I (placebo group; ○), group II (meperidine group; ○), Group III (lidocaine group, ■) and group IV meperidine ± lidocaine (△). There were significant differences between the groups not receiving lidocaine (group I and II) and the groups receiving lidocaine (groups III and IV) (p < 0.001). Values are mean ± SD.
DISCUSSION

These results demonstrate that intraperitoneal lidocaine instillation is effective for intraoperative and postoperative pain relief during and after postpartum tubal ligation under local anesthesia. Although the optimal volume and concentration have not been studied, we used 40 ml of a 1.0% solution, as this has been used in previous studies (11, 4, 15). The effectiveness of pain relief with intraperitoneal lidocaine in this study confirms the results of Cruikshank et al. (11) and Williamson et al. (15) who reported that most of their patients slept through the operative procedure under intraperitoneal lidocaine with heavy sedation. Their evaluations, however, were performed during the postoperative period when the patients were amnesic and may not have remembered their intraoperative pain.

Narchi and Colleagues found that (16), after gynaecological laparoscopy, the rate of absorption of lidocaine from the peritoneal cavity was relatively slow; the time to maximum concentration (± Cpmax) was reached at 29 min with plain lidocaine 400 mg, at 58 min using lidocaine 400 mg with adrenaline 1:320,000 and at 72 min with lidocaine 400 mg and adrenaline 1:800,000. In both Narchi's study and ours, the maximum concentration of lidocaine attained (Cpmax) was relatively low. Narchi and Colleagues (16), found a Cpmax value of 4.3 µg/mL with plain lidocaine 400mg (versus to 2.6 µg/mL in our study), 2.3 µg/mL with lidocaine 400 mg and adrenaline 1:320,000 and 1.89 µg/mL using lidocaine 400 mg with adrenaline 1:800,000; this suggests that the rate of absorption of lidocaine was slower after open tubal sterilization than after gynaecological laparoscopy.
The highest mean plasma lidocaine concentration in our study (2.6 ug/mL) was similar to the level of 2.2 ug/mL reported by Deeb and Viechnicki (17). The total dosage of lidocaine was 600 mg, which is also approximately similar to 500 mg used by Deeb and Viechnichi. Williamson et al. (15), found that, the final mean maximum concentration achieved at 3 h was approximately 0.4 ug/mL versus to 2.6 μg/mL in our study. This difference because Williamson et al. used a total dose of 200 mg lidocaine with 1:500,000 adrenaline. Although a precise toxic dose of local anesthetics in humans has not been established, Ryan et al., reported that the level of lidocaine that caused convulsions in a child during cardiac catheterization was 8.7 μg/mL, although non-life threatening signs of toxicity, such as light headedness, tinnitus, or circumoral numbness, were seen at 4 ug/mL and muscle twitching at 8 ug/mL (19). The plasma lidocaine concentration in our study was far below that considered to be toxic. It is possible, however, that these lidocaine concentrations, although not toxic, were still sufficient to produce analgesia through a systemic, or central effect and not only via the topical effect on the peritoneum. A follow-up study that compares intraperitoneal instillation of lidocaine with systemic infusion of lidocaine to achieve similar plasma levels could be performed to clarify this.

The few side effects observed in our patients included a mild decrease in oxygen saturation (2 cases in group I, 3 cases in group II and one case in group IV), which was most likely due to transient hypoventilation secondary to fentanyl. This was easily corrected by the administration of supplemental oxygen by mask. Urinary retention occurred in 2 cases in group III and in 2 cases in group IV due to intraperitoneal lidocaine administration. Cruikshank et al. (11), observed
two cases of urinary retention in their study. In our study, vomiting occurred in 3 cases in group II and one case in group IV, this was in accordance with the results of Williamson et al. (15).

Intravenous ketamine (2 mg/Kg) was used for postpartum tubal ligation in the retrospective study of Weerasekara et at. (22) with expected side effects, including hallucinations and transient psychotic symptoms. Because serious complications such as aspiration pneumonitis (20) and respiratory insufficiency (21), may be associated with ketamine, its use is not without risk. Two cases in group I and one case in group III in which ketamine was required plus general anesthesia with endotracheal intubation had a surgical duration of > 50 min (55.60, 70 min). It may be possible to use a more potent local anesthetic solution with a longer duration of action (e.g. bupivacaine) in prolonged cases, rather than general anesthesia. This requires a further study.

In conclusion, we have found that administration of lidocaine 400mg into the peritoneal cavity during the postpartum tubal ligation was associated with low serum concentrations of lidocaine without clinical toxic effects. Intraperitoneal lidocaine instillation, either alone or in combination with I.M. meperidine, is a safe, effective, and easy technique that should be used to decrease suffering in patients who undergo postpartum tubal ligation under local anesthesia. I.M. meperidine alone is not effective in providing pain relief during postpartum tubal ligation.

REFERENCES


