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# Comparison of Topical and Subcutaneous Bupivacaine Infiltration with Subcutaneous Ketamine on Postoperative Pain in Total Abdominal Hysterectomy

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## ABSTRACT

**Introduction:** Hysterectomy is one of the most common surgical procedures. Problems such as severe pelvic pain, irregular or heavy bleeding and uterine cancer from those that may be used to treat them no choice but to remove the uterus by surgery. Abdominal pain after abdominal hysterectomy, the most common complaints of patients undergoing this type of surgery is considered. **Aim:** This study aimed to compare the effects of bupivacaine into the subcutaneous tissue and skin ketamine for pain control after surgery in patients undergoing abdominal hysterectomy was performed under general anesthesia. **Methods:** This study is a randomized, double-blind clinical trial involving 99 women scheduled for TAH referred to tertiary centers was performed. Group A: 5 mL of 0.25% bupivacaine into the subcutaneous tissue and, Group II: 100 mg ketamine skin and subcutaneous tissue with cc5 volume injection, groups of three: cc5 distilled water was injected into the subcutaneous tissue and. The average duration of analgesia and pain and pain score were recorded. **Results:** The average duration of analgesia in group K  $65.1 \pm 8.8$ , in the bupivacaine group  $65.4 \pm 8.7$  and in the placebo group  $57.6 \pm 5.5$ , which, according to  $P \text{ Value} \leq 0.01$  is a significant difference between the three groups were observed, so that the pain in the placebo group for a significant period of ketamine and bupivacaine groups is lower, while that between ketamine and bupivacaine in terms of the average duration of analgesia was no significant difference not. **Conclusion:** The results of our study indicate that the use of bupivacaine and ketamine effective in reducing postoperative pain in patients undergoing abdominal hysterectomy tissue and further doses of ketamine and bupivacaine single dose resulted in a significant reduction of postoperative pain patients were compared to the placebo group.

**Keywords:** Bupivacaine, Ketamine, pain, abdominal hysterectomy, general anesthesia.

## 1. INTRODUCTION

Hysterectomy is one of the most common types of operation. Following Caesarian, hysterectomy is considered to be the second major operation. The highest rate of hysterectomy is observed among women aging 40 to 49 years old. Sometimes the only way to deal with problems such as acute pelvic pain, intense or irregular monthly bleeding or affliction with uterus cancer is to remove uterus (1). In most cases, hysterectomy is used to treat a certain category of gynecological diseases not responding very well to medical treatments. This is an ideal method for those women who are not going to have any more babies and are fed up with fruitless treatments. Uterine

leiomyomas, endometriosis, cervical dysplasia, menstrual disorders, uterine prolapse, cancer, endometrial hyperplasia (2, 3), Endometriosis, cervical dysplasia, menstrual disorders, uterine prolapse, cancer, endometrial hyperplasia (2, 3).

Post-abdominal operation pain is one of the most common problems of patients (1). As hysterectomy is one of the most common gynecological operations, post-hysterectomy pain is one of the most common complaints among patients undergoing this type of operation (2, 3). Using certain analgesic diets can help reduce the complications and death toll caused by this operation (4). To this end, using local anesthetizers is a cheap, safe, and easy method which

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requires further attention (5). Failing to control post-operation pain will have acute and chronic effects and can even increase the death toll among patients (6, 7). It may also result in high blood pressure and pulse rate and increase oxygen consumption and cause heart attacks (4, 6, 7). Appropriate post-operation analgesia can help reduce many complications (8, 9). One of the post-operative analgesic methods is using narcotic pain killers such as intravenous morphine sulfate that have their influence on nervous system ( $\mu$ ) through central receptors. However, these medicines have several complications and side effects including nausea, vomiting, drowsiness, urinary retention, pruritus and constipation, and respiratory depression (4, 9, 10). Constant use of intravenous morphine or other types of narcotic analgesics has several complications such as low blood pressure, urinary retention, nausea, and pruritus and pulse rate reduction. However, using intradermal bupivacaine can help reduce consumption of morphine and its side effects (9, 11, 12, 13). Further to the better toleration achieved by local anesthetizers, they will reduce nausea and vomiting among patients. So, it has been used as the analgesic method in different operations (6, 9, 14).

**2. AIM**

This study aimed to compare the effects of bupivacaine into the subcutaneous tissue and skin ketamine for pain control after surgery in patients undergoing abdominal hysterectomy was performed under general anesthesia

**3. METHODS**

This is a double-blind, randomized clinical trial conducted on ladies candidates for abdominal hysterectomy who had resorted to Taleghani center. As many as 99 patients were randomly divided into 3 groups. Using the following formula, the samples were calculated and divided into 3 equal groups in accordance with the principles of randomized sampling method and table of randomized numbers. Each group consisted of 33 participants.

$$N = \frac{\left(\frac{\gamma_1 + \gamma_2}{2}\right)^2 (Z_{1-\alpha/2} + Z_{1-\beta})^2}{(\mu_1 - \mu_2)^2} = 33$$

$\mu_1 = 4.82$        $\gamma_1 = 3.80$        $Z_{1-\alpha/2} = 1.96$   
 $\mu_2 = 6.44$        $\gamma_2 = 1.22$        $Z_{1-\beta} = 2.33$

The topical and subcutaneous injection of 5 cc bupivacaine 0.25% was used for the first group, while the second group was topically and subcutaneously injected with 100 mg (reduced to 5 cc) intradermal ketamine. The third group received 5cc topical and subcutaneous injections of normal saline. Having been confirmed by anesthesiologists, the patients who had applied for total abdominal hysterectomy (TAH) entered operation room. Following full examination and recording their blood pressure and pulse rate and percentage of oxygen saturation, patients received 3-5 cc/kg Crystalloid. Then, they assumed a supine position and prepared them-

selves for general anesthesia. When the operation was over, the first group received topical and subcutaneous injections of 5cc bupivacaine 0.25%. The second group was topically and subcutaneously injected with 100 mg (reduced to 5 cc) intradermal ketamine. The third group received 5cc topical and subcutaneous injections of normal saline. Using VAS ruler, the pain score of patients was recorded in recovery room, 4 hours, 12 hours, and 24 hours after operation. If, in any phases of pain measurement, the pain score was  $\geq 5$ , Pethidine (a narcotics) would be injected to patients. The first dose of pethidine given was 25 mg and two other doses would follow if the patient failed to respond to the medicine. Those patients with pethidine doses  $\geq 100$  were excluded. To determine the average duration of analgesia, we recorded the time when patients requested their first analgesic. The average amount of opioid used by these patients in 24 hours, the side effects of these medicines, and patients' vital signs during operation were recorded in terms of BP and PR every 5 minutes. The information was recorded in questionnaires and the resulting data was analyzed by SPSS 19, ANOVA, T-test, and  $\chi^2$  statistical tests.

**4. RESULTS**

The following lengths of analgesia were observed for each group:  $65.1 \pm 8.8$  for ketamine group,  $65.4 \pm 7.8$  for bupivacaine group, and  $57.6 \pm 5.5$  for placebo. As P-value  $\leq 0.01$ , a significant difference was observed between the two groups and duration of analgesia in placebo group was significantly shorter than what was observed in the other two groups. However, no statistically significant difference was observed between ketamine and bupivacaine groups in terms of length of analgesia (Table 1). No significant difference was observed between the three groups in terms of pain score (P-value  $> 0.05$ ) (Table 2).

Groups studied	Average length of analgesia (in terms of hour)	Statistical test
Ketamine	$65.1 \pm 8.8$	T-test
Bupivacaine	$65.4 \pm 7.8$	$P \leq 0.01$
Placebo	$57.6 \pm 5.5$	Significant

**Table 1. Comparing post-operation length of analgesia among patients candidated for hysterectomy in topical ketamine and bupivacaine groups (in terms of hours)**

Pain score / groups	Ketamine	Bupivacaine	Placebo	Statistical test
In recovery	$9.2 \pm 0.33$	$9.4 \pm 0.66$	$9.5 \pm 0.68$	$P \geq 0.05$ Not significant
2 hours after operation	$7.8 \pm 0.66$	$7.6 \pm 0.31$	$8.9 \pm 0.32$	$P \leq 0.05$ Significant
4 hours after operation	$6.9 \pm 0.71$	$6.7 \pm 0.82$	$7.5 \pm 0.89$	$P \leq 0.05$ Significant
12 hours after operation	$5.1 \pm 0.84$	$4.5 \pm 0.65$	$5.6 \pm 0.55$	$P \leq 0.05$ Significant
24 hours after operation	$2.3 \pm 0.86$	$2.1 \pm 0.85$	$3.2 \pm 0.77$	$P \leq 0.05$ Significant

**Table 2. Comparing post-operation pain score among patients candidated for hysterectomy in topical ketamine and bupivacaine groups (in terms of VAS). ANOVA test  $4.5 \pm 0.65$**

Groups studied	Average levels of opioid taken (in terms of mg)	Statistical test
Ketamine	24.1 ± 1.2	T-test
Bupivacaine	25.1 ± 1.5	P≥0.05
Placebo	25.5 ± 1.1	Not significant

**Table 3. Comparing average levels of opioid consumed within 24 hours after operation among patients candidates for hysterectomy in topical ketamine and bupivacaine groups (in terms of mg)**

Blood pressure and pulse rate	Ketamine	Bupivacaine	Placebo	Statistical test
Average MAP prior to operation	105/1± 9/4	114/5± 8/8	113/2± 7/8	p≥0.05 no significant
Average PR prior to operation	91/9± 6/8	89/8± 8/2	91/4± 9/4	p≥0.05 no significant
Average MAP during operation	95/2± 8/5	95/4± 6/6	96.2 ± 8.8	p≥0.05 no significant
Average PR during operation	79.8 ± 7.8	80.1 ± 8.7	81.5 ± 8.6	p≥0.05 no significant
Average MAP during recovery	96.1 ± 8.8	97.1 ± 6.3	99.5 ± 7.4	p≥0.05 no significant
Average PR during recovery	86.1 ± 4.3	87.7 ± 5.4	94.6 ± 7.4	p≥0.05 no significant

**Table 4. Comparing blood pressure and pulse rate before operation, during operation, and during recovery time among patients candidates for hysterectomy in topical ketamine and bupivacaine groups. ANOVA test**

Within 2, 4, 12, and 24 hours after operation, a significant difference was observed between the three groups in terms of pain score. As the results indicate, a higher pain score was observed in placebo group than what was observed in the other 2 groups (P-value < 0.05). No significant difference was observed between ketamine and bupivacaine groups. The average amount of opioid taken within 24 hours after operation was equal in all 3 groups (P-value > 0.05) (Table 3). The average MAP and PR before induction, during the operation and during recovery was equal in all three groups. As P-value > 0.05, no significant difference was observed between the three groups (4). The only significant difference observed between these three groups was the average PR in recovery. As P-value < 0.05, the average PR in recovery room for placebo group was more than what was observed for other two groups (Table 4).

## 5. DISCUSSION

Exploring the results of adding topical bupivacaine and ketamine in controlling post-operation pain of patients candidates for total abdominal hysterectomy showed that the average analgesic length in ketamine and bupivacaine groups was longer than placebo group (P-value ≤ 0.01). In other words, topical injection of bupivacaine and ketamine as auxiliary medicines is really useful to control pain in patients candidates for total abdominal hysterectomy. However, no statistically significant difference was observed between ketamine and bupivacaine groups. The results achieved in our research are nearly in line with similar studies. A similar research conducted by Bon-Nyeo Koo and Seung Ho Choi (2008) compared the effectiveness of remifentanyl and fentanyl in controlling

post-operation pain of total abdominal hysterectomy and fentanyl turned out to be significantly more effective (P ≤ 0.05). However, remifentanyl had less side effects and complications than fentanyl group. This research underlined the need to use opioids particularly those with durable effects or pain control methods based upon regional or local block to reduce post-abdominal hysterectomy pains (15). Concerning post-operation pain control through topical and subcutaneous injections, similar studies have been conducted with results similar to ours. A research conducted by Soltan Zadeh M, Behin K et al., topical injection of ketamine could significantly increase the length of post-operation analgesia in the sample group (16). Another research conducted by Mc Donnel, John G, John MB, Carney MB et al, it was concluded that using bupivacaine and TAP Block was really effective in reducing the post-operation pain of patients candidates for abdominal hysterectomy (16). This study was conducted on 50 patients candidates for elective abdominal hysterectomy. As P-value < 0.01, it can be said that using bupivacaine in TAP Block is really effective in reducing post-operation pain (17). In a research conducted by Anil, Gupta, FRCA et al (2004), the effect of intraperitoneal local anesthetics on controlling post abdominal hysterectomy pain was compared to placebo. It turned out that intraperitoneal local anesthetics were useful and effective in controlling post-operation pain (P ≤ 0.05) (18). Naime Yalsin, Sema Tuncer Uzun et al (2012) conducted a research in Turkey and concluded that IV injection of 5.0 mg/kg ketamine was more effective than IV infusion of 1000 mg paracetamol and helped reduce post-operation pain among patients candidates for elective abdominal hysterectomy (as P-value < 0.05). The pain score in ketamine group within 2, 4, 6, and 12 hours after operation was less than the levels observed in placebo group (19). In another research conducted by Vegard MD, Dahl et al (2002) in Norway on 90 women candidates for abdominal hysterectomy, it turned out that using topical ketamine to control post-operation pain is more effective (20). However, there are certain researches indicating that a small dose of ketamine cannot significantly reduce post-operation pain of women candidates for abdominal hysterectomy (21). A similar research confirming these results was conducted by Ali Katen (2000) asserting that topical bupivacaine infiltration has no clear influence on reducing the post-operation pain of those patients candidates for hysterectomy (8). Two groups (including 25 participants in each one) were studied in this research. The difference observed between the results of this research and our study is probably due to lower dose of Marcaine used in this research compared to the research we conducted. The smaller sample size in that research is probably another cause of disagreement between results.

The other method which can enhance the effectiveness of topical injection of bupivacaine or ketamine in reducing post-operation pain of patients is using infusion catheter. Causing no further costs to patients, no need for further treatment by nurses, no possibility of infection caused by catheter ulcer, and using a single dose of Ketamine and Bupivacaine are some advantages of our



research compared to those studies which utilize infusion catheter. It shows that using a single but more doses of Ketamine and Bupivacaine (100 mg of topical ketamine and 20 mg of topical bupivacaine) can help significantly reduce post-operation pain of patients compared to placebo group. The amount of opioid used within 24 hours after operation in three groups of ketamine, bupivacaine and placebo were similar and no significant difference was observed between them. It is recommended to conduct a similar research with a larger population to make up for possible errors and enhance the accuracy. In another research conducted by Kamran Motaghi and Farhad Safari (2013) in Iran, 60 women with class I and II A.S.A candidates for abdominal hysterectomy were divided into bupivacaine and placebo groups. The results of their research showed that (P-value < 0.001) the average use of morphine 4, 24 and 48 hours following the operation in bupivacaine group was significantly less than what was observed in placebo group (22). As p-value < 0.001, fewer cases of nausea and vomiting were observed in bupivacaine group than placebo. Consequently, topical injection of a single dose of Marcaine and bupivacaine resulted in effective analgesia following abdominal hysterectomy and less morphine was used within 24 hours after operation (22). The results of this research were in line with the results we achieved in our research.

## 6. CONCLUSIONS

The results of our research also show that using topical ketamine and bupivacaine is a really effective measure to reduce post operation pain of those patients undergoing abdominal hysterectomy. Of course, no statistically significant difference was observed between bupivacaine and ketamine groups in terms of pain score and duration of analgesia after operation. Future researches are recommended to focus on a comparison between the effect of a single dose of these medicines and infusion of them on reducing post-operation pain levels.

- **Authors' contributions:** All the authors were involved during the investigation process in all stages of this study including a primary data collection, analysis and the documentation of the collection. They read and approved the final version of the manuscript.
- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Conflict of interest:** None declared.
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