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Research Article

Preoperative adjuvant gabapentin with dexamethasone compared to dexamethasone alone for postoperative analgesia in cholecystectomy

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ABSTRACT

Objective: Severe postsurgical pains cause long-lasting hospital stay and are also thought to be a risk factor for the development of chronic pain. This study aimed at investigating the effect of preoperative adjuvant gabapentin with dexamethasone for postoperative analgesia in cholecystectomy compared to dexamethasone alone or compared to placebo treatment.

Methods: This study done during the period from January 2019 to May 2019. 60 patients (17-67 years old), scheduled for laparoscopic cholecystectomy, were allocated randomly into three groups, the first group (GD) administered oral gabapentin 600 mg, about one hour before surgery then 8 mg dexamethasone intravenously just before induction. The second group (D) administered only intravenous dexamethasone 8mg and the third group (C) considered as control, administered placebo treatment, which is same looking as treatment. All patients trained for the pain visual analogue scale (VAS) (zero for "no pain" and 10 for "worst pain") for measurement of pain.

Findings: All groups in this study were similar concerning age, gender (male: female), height and body weight. The mean systolic and diastolic blood pressure and also heart rate were not different among the groups in any of the measured times (2h, 6h, 12h and 24h postoperatively). Meanwhile, there were statistical significant difference in oxygen pressure (p= 0.0091and p= 0.0200) after 2h and 6h from the surgery, respectively. Lower value of (VAS) found in (GD) group compared to (D) and (C) groups. The frequency of nausea and vomiting and the Tramadol and paracetamol consumption during 24h postoperatively was significantly lower in (GD) and (D) groups compared to group (C).

Conclusion: Gabapentin combination with dexamethasone causes significant reduction in the requirement of opioid postoperatively, reduction of postoperative pain and reduction of postoperative nausea and vomiting compared to the control placebo treatment.

Keywords: Gabapentin, Dexamethasone, laparoscopic cholecystectomy and postoperative analgesia.

INTRODUCTION

Severe postsurgical pains cause long-lasting hospital stay and are also thought to be a risk factor for the development of chronic pain. Postoperative pain after laparoscopic cholecystectomy is a common complaint. Pain may lead to postoperative nausea, vomiting, and urinary retention, consequently increases morbidity. Studies revealed that the cause of postoperative pain in laparoscopic surgeries is inflammation of peritoneum or may be the presence of gas. Postoperative pain is not only nociceptive but also involves inflammatory, neurogenic as well as visceral components[1-3]. Multiplicity of the mechanisms leading to postoperative pain caused the multimodal analgesic regimens been used for enhancing analgesia and to reduce the need to opioid therapy that have bad side effects[4].

Corticosteroids have shown to reduce inflammation and provide postoperative analgesia in many surgeries. Injection of single-dose dexamethasone may prevent postoperative

nausea and vomiting, greatest effect when administered before induction of anaesthesia.

Gabapentin an anticonvulsant drug is a structural analogue of γ-aminobutyric acid. Studies have found that gabapentin is effective in neuropathic pain[6]. Moreover, it is effective in treating diabetic neuropathy[7]. The mechanism of gabapentin action on neuropathic pain is supposed to be due to binding the alpha 2-delta subunit of the voltage-dependent calcium channel in the central nervous system, decreasing calcium influx into the nerve terminals and reducing the release of neurotransmitters, such as glutamate[8].

A new study determined that gabapentin has a role in preoperative anxiolysis, postoperative pain control, prevention of postoperative nausea and vomiting (PONV), reduction of hemodynamic response to intubation, and postoperative delirium[9].

The postoperative pain management aims to eliminate pain and discomfort with minimum of side effects. Improvements in postoperative systemic analgesia for pain management are useful and prognostic features for severe postoperative pain should expected in order to control pain while minimizing opioid side effects.

This study aimed at investigating the effect of preoperative adjuvant gabapentin with dexamethasone for postoperative analgesia in cholecystectomy compared to dexamethasone alone or compared to placebo treatment.

METHODS

A prospective randomized controlled study, comparing preoperative adjuvant gabapentin with dexamethasone for postoperative analgesia in cholecystectomy to dexamethasone alone or to placebo treatment, during the period from January 2019 to May 2019. The study was approved by the ethical committee and an informed consent from all patients were taken, 60 patients (17-67 years old), arranged for laparoscopic cholecystectomy, were divided randomly into three groups (20 patients each): the first group (GD) administered oral gabapentin 600 mg, about one hour before surgery then 8 mg dexamethasone intravenously just before induction. The second group (D) administered only intravenous dexamethasone 8mg and the third group (C) considered as control, administered placebo treatment, which is same looking as treatment. All patients trained for the pain visual analogue scale (VAS) (zero for "no pain" and 10 for "worst pain") for measurement of pain.

Exclusion criteria was the recognised allergy to any one of the used drugs, patients using the following drugs regularly (corticosteroids, NSAIDs, tricyclic antidepressants, benzodiazepines or other analgesics), patients administered pregabalin or gabapentin before surgery and also patients with psychiatric or neurological disorders, diabetes mellitus, or significant renal, cardiac, pulmonary or hepatic disease or peptic ulcer. Furthermore, patients excluded if their body mass index (BMI) more than 35.

Blood pressure, ECG and pulse oximetry measured routinely. Patients in group (GD) were given oral gabapentin 600 mg (Gabapentin 300 mg, Nupentin, Mylan) one hour before the operation, then 8 mg intravenous dexamethasone just before induction, while, patients in group (D) were given placebo capsules and then 8 mg intravenous dexamethasone just before induction, and the control group were given placebo capsules and then 15ml water.

Statistical analysis performed using GraphPad Prism software (version 7.0, GraphPad Software, Inc., San Diego, CA). Descriptive statistics, such as mean ± standard deviation (SD), calculated for all estimated parameters. Comparison between groups performed using ANOVA (and non-parametric analysis) with Kruskal-Wallis test.

Findings

A total of 60 patients (17-67 years old), arranged for laparoscopic cholecystectomy, were allocated randomly into three groups (20 patients each): the first group (GD) administered oral gabapentin 600 mg, about one hour before surgery then 8 mg dexamethasone intravenously just before induction. The second group (D) administered only intravenous dexamethasone 8mg and the third group (C) considered as control, administered placebo treatment.

All groups in this study were similar concerning age, gender (male: female), height and body weight. The mean systolic and diastolic blood pressure and also heart rate were not different among the groups in any of the measured times (2h, 6h, 12h and 24h postoperatively). Meanwhile, there were statistical significant difference in oxygen pressure ($p= 0.0091$and $p= 0.02$) after 2h and 6h from the surgery, respectively, (table 1).

The visual analog scale (VAS) analysis showed high statistically significant difference among the three groups after 2h, 6h and 12h from the surgery ($p< 0.001$). Lower value of (VAS) found in (GD) group compared to (D) and (C) groups. In the meantime, there were no statistical significant differences in (VAS) after 24 h from the surgery, (table 2).

Tramadol and paracetamol consumption during 24h postoperatively was significantly lower in (GD) and (D) groups compared to group (C)

(p=0.0004 for tramadol, p= 0.0165 for paracetamol and p= 0.0357 for both together). In the meantime, there was no statistically significant differences between (GD) and (D) groups (table 3).

Nausea and Vomiting at 2 h after surgery presented highly statistical significance (p= 0.0036), lower values was found in (GD) and (D) groups compared to group (C) (table 3).

Table 1: Postoperative sedation (data represented as mean ± SD or numbers).

	Group (GD) (n= 20)	Group (D) (n= 20)	Group (C) (n= 20)	p-value
Age	39.8 ± 14.3	42.8 ± 14.6	44.2 ± 12.8	0.5965
Sex Male / Female	2 /18	3 /17	3 /17	
Weight	78.1 ± 26.2	69.8 ± 21.9	69.3 ± 13.6	0.3448
Height	156.8 ± 19.4	154.9 ± 22.5	162.6 ± 5.8	0.3554
Systolic BP (mmHg)				
2 h after surgery	126.3 ± 10.6	119.5 ± 11.3	125.8 ± 19.6	0.2597
6 h after surgery	123.8 ± 11.6	116.2 ± 9.3	126.9 ± 21.4	0.0773
12 h after surgery	124.4 ± 12.4	117.4 ± 11.7	121.7 ± 12.5	0.1967
24 h after surgery	122.4 ± 12.2	120.6 ± 6.6	123.1 ± 12.9	0.7582
Diastolic BP (mmHg)				
2 h after surgery	77.4 ± 9.4	73.5 ± 9.3	76.9 ± 9.6	0.3699
6 h after surgery	76.2 ± 10.8	72.7 ± 8.3	78.3 ± 7.0	0.1384
12 h after surgery	76.8 ± 9.5	72.7 ± 9.8	68.4 ± 18.9	0.1520
24 h after surgery	77.0 ± 9.6	74.7 ± 6.3	76.7 ± 7.7	0.6147
Heart rate (min)				
2 h after surgery	84.4 ± 8.6	81.2 ± 10.7	86.7 ± 7.1	0.1565
6 h after surgery	81.5 ± 7.3	80.5 ± 8.7	84.2 ± 8.7	0.3485
12 h after surgery	78.7 ± 5.8	79.5 ± 11.5	82.8 ± 6.3	0.2602
24 h after surgery	79.9 ± 9.6	78.5 ± 9.3	81.7 ± 4.3	0.4618
O_2 Pressure (%)				
2 h after surgery	97.7 ±1.4	98.0 ± 0.9	96.6 ± 1.9	**0.0091***
6 h after surgery	97.4 ±1.3	97.7 ±1.0	96.5 ± 1.7	**0.0200***
12 h after surgery	97.8 ±1.3	97.9 ±1.1	97.3 ±1.3	0.2672
24 h after surgery	98.0 ± 0.9	96.9 ± 4.8	97.9 ±1.1	0.4180

Group (GD) = Gabapentin / Dexamethasone, Group (D) = Dexamethasone and Group (C) = control group. *Statistically significant compared to group C, ($p<0.05$).

Table 2: Postoperative VAS (data represented as median (range))

Hours (h) post-operative	Group (GD) (n= 20)	Group (D) (n= 20)	Group (C) (n= 20)	p-value
2 h postoperative	4 (4 - 5)†	5 (4 - 6) *	6 (5 - 7)	<0.0001
6 h postoperative	3 (2 - 4)†	4 (3 - 5) *	5 (4 - 6)	<0.0001
12 h postoperative	3 (2 - 4)†	4 (2 - 5) *	4 (4 - 6)	<0.0001
24 h postoperative	2 (2 - 3)	2 (2 - 3)	2 (2 - 3)	0.8148

Group (GD) = Gabapentin / Dexamethasone, Group (D) = Dexamethasone and Group (C) = control group. * Statistically significant compared to group C ($p<0.05$). † Statistically significant compared to group D and group C ($p<0.05$).

Table 3: Tramadol and paracetamol consumption during 24h postoperatively (data represented as (mean ± SD)).

Total analgesics dose during 24h (mg)	Group (GD) (n= 20)	Group (D) (n= 20)	Group (C) (n= 20)	p-value

Paracetamol (mg) only	8	8	10	0.0165*
Tramadol (mg) only	1	3	5	0.0004***
Paracetamol (mg) + Tramadol (mg)	2	2	7	0.0357*
No analgesic need	7	5	0	0.0036**
Nausea and vomiting	4	3	12	0.0036**

Group (GD) = Gabapentin / Dexamethasone, Group (D) = Dexamethasone and Group (C) = control group. *Statistically significant compared to group C ($p<0.05$).
**Statistically significant compared to group C ($p<0.005$).
***Statistically significant compared to group C ($p<0.001$).

CONCLUSION

This study is a prospective randomized controlled study, comparing preoperative adjuvant oral gabapentin with intravenous dexamethasone to dexamethasone alone or to placebo treatment for postoperative analgesia and occurrence of postoperative nausea and vomiting after laparoscopic cholecystectomy.

Diversity of the mechanisms leading to postoperative pain caused the multimodal analgesic regimens used to improve analgesia and to decrease the need to opioid therapy that have bad side effects [4]. In this study, expected that gabapentin and dexamethasone would have a synergistic effect because of their different mechanisms of action in severe pain management.

The results of this study presented high statistical significant difference between GD group and the other groups in the VAS after 2h, 6h and 12h from the surgery and also, a significant difference between (D) and (C) groups at the same time intervals. These results indicated that the administration of gabapentin with dexamethasone preoperatively is of a higher value.

The results of this study consistent with the results of earlier study presented that gabapentin, ketamine decreased opioid requirement following hysterectomies, and they have a same effect on preoperative control of pain[10]. These results also consistent with previous study stated a pain reduction in mastectomy patients after single dose of gabapentin[11]. Furthermore, this study results best correlated with another studies on gabapentin combinations with paracetamol to decrease the opioid requirement after abdominal hysterectomy[12], with dexamethasone in controlling post-operative pain after adenotonsillectomy in children[13] and with dexamethasone in controlling post-operative pain after abdominal hysterectomy[14].

In conclusion, Gabapentin combination with dexamethasone significantly reduced the requirement to opioids after surgery along with postoperative pain and postoperative nausea and vomiting, in comparison with the control or placebo treatment.

AUTHOR'S CONTRIBUTION

None.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

No data used to support this study.

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