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RESEARCH ARTICLE

Comparison Effects of Pre-emptive Gabapentin and Meloxicam for Postoperative Pain in White New Zealand Rabbits Undergoing Ovariohysterectomy Using the Grimace Scale

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ABSTRACT

The study aimed to evaluate the effectiveness of Gabapentin in controlling postoperative pain in New Zealand white rabbits after ovariohysterectomy. Twenty sexually mature and healthy female rabbits were divided into four groups: a negative control, Meloxicam treatment, Gabapentin treatment, and Meloxicam plus Gabapentin treatment. After the surgery, the rabbits' pain levels were assessed using the Grimace Scale at various time points. The Gabapentin group consistently had the lowest Grimace Scale scores. Statistical analysis showed significant differences between the Meloxicam group and the negative control, the Gabapentin plus Meloxicam group and the negative control, the Gabapentin group and the negative control, and the Gabapentin group and the Gabapentin plus Meloxicam group. Postoperative analgesia was significantly better in the Meloxicam, Gabapentin, or combined treatment groups compared to the negative control. Gabapentin was found to be equally effective as Meloxicam in controlling pain. However, the combination of Meloxicam and Gabapentin was not as effective as Gabapentin alone. In conclusion, Gabapentin showed preventive efficacy in controlling postoperative pain after ovariohysterectomy in New Zealand white rabbits. These findings suggest that Gabapentin could be a valuable analgesic option for surgeons to provide adequate pain control in this surgical context. Further research is needed to explore optimal dosing and potential synergistic effects when combining Gabapentin with other analgesics.

Keywords: Postoperative Pain, Grimace scale, Gabapentin, Meloxicam, Ovariohysterectomy, Rabbit

INTRODUCTION

Surgical interventions are linked to central and peripheral sensitization [1]. Postoperative pain may prolong recovery time, hospital stay, and time to mobilization for patients recovering from surgery and anesthesia. In postoperative care, preventing and treating postoperative pain and its consequences, including nausea and vomiting, remains a significant concern. Opioids are routinely used to treat pain, but they have a number of adverse side effects that limit their use. A multimodal approach has been proposed to improve postoperative analgesia and prevent opioid-related adverse effects. An important area of acute pain research involves testing novel analgesics and combinations of analgesics in an attempt to decrease the need for opioids [2,3].

Gabapentin is a structural analog to aminobutyric acid (GABA), a medication that was first used as an anti-epileptic drug. It is a well tolerable anticonvulsant drug with limited side effects and drug interactions. It binds to the voltage-gated calcium channel's 2-protein subunit, which is found throughout the central (CNS) and peripheral (PNS) parts of the nervous system. This modulates excitatory neurotransmitters, such as glutamate, release and suppresses calcium influx in pain pathways [4]. Gabapentin also, promotes amino acid release in the dorsal horn of the spinal cord and reduces reactivity to neural stimuli, thus lowering or stabilizing the activity of injured nerves [5]. There are also some other possible pathways for Gabapentin, including recruiting the descending noradrenergic system [6], activating potassium channels [7], and inhibiting α2δ-1-NMDAR complexes [8]. Gabapentin can thus be used to treat chronic pain diseases such as fibromyalgia [9], diabetic neuropathy [10], postherpetic neuralgia [11], and other neuropathic conditions [12]. Gabapentin's analgesic effects

have been extensively studied in surgical settings in recent years. According to the findings of these investigations, Gabapentin has analgesic qualities in the treatment of postoperative pain [13-15].

Meloxicam, an NSAID, was originally approved for oral use in the United States in the late 20th century. Meloxicam is a member of the oxicam family of compounds that suppresses cyclooxygenase-2 more than cyclooxygenase-1, resulting in fewer gastrointestinal side effects and no interference with platelet function as compared to non-selective NSAIDs [16,17]. Its efficacy and safety have been tested in several randomized controlled studies (RCTs) after procedures such as abdominal hysterectomy, abdominoplasty, dental surgery, and other major operations [18].

We aimed to assess the preemptive efficacy of Gabapentin in controlling postoperative pain in New Zealand White Rabbits after hysterectomy and ovariohysterectomy.

Material and Methods

Ethical Statement

All procedures were carried out with the approval of the Ethical Committee of Islamic Azad University - Karaj Branch (Approval ID: IR.IAU.K.REC.1400.005).

Animals

Twenty adult female white New Zealand rabbits (Razi Institute, Karaj, Iran) entered this study. They were housed individually in suspended cages (970 × 895 × 1718 mm) and acclimatized for two weeks before the start of the experiment. There was no physical contact between the rabbits. Animals were kept on a 12:12 light-dark cycle (lights on at 06:30 AM), the room temperature was between 19-21°C, and humidity was 45±10%. Each rabbit had *ad libitum* access to water and standard rabbit food (Pellet diet, Razi Institute, Karaj, Iran). The protocol used for anesthesia in all cases included: an intramuscular injection of 35 mg/kg 10% ketamine HCl plus 5 mg/kg Xylazine HCl (K-X protocol).

Study Groups

A total of twenty white New Zealand rabbits were included into the study which were divided into four groups and each group consist of five rabbits. The rabbits were randomly assigned in one of four groups seven days before surgery. The first group, the negative control group (NG), received anesthesia according to the K-X protocol. They received no other drugs and underwent surgery. The second group received K-X anesthesia and subcutaneous Meloxicam 2% at 0.5 mg/kg one hour before surgery as a positive control group (MG). The third group received K-X anesthesia and oral Gabapentin every 12 h for five days before surgery at 10 mg/kg (GG). The last group received Meloxicam 2% (0.5 mg/kg) one hour before surgery in addition to the protocol of the third group (GMG).

Surgical Procedure

Animals were placed in a supine position, hair was removed from the area, and a median laparotomy was performed under aseptic conditions. A routine ovariohysterectomy was conducted on each animal using a No. 15 scalpel blade and a ventral midline abdominal incision that began approximately 2 cm caudal to the umbilicus. Once the uterus had been located, the fat around each ovarian pedicle was meticulously removed to allow the ovarian vessels to be identified. The broad ligament was then perforated and accessed, and the suspensory ligament was severed. The uterine horn was then made fully accessible, an incision was made in the broad ligament, and a 3-0 absorbable suture was tied around the blood vessels of the ovary and uterine horn. Uterine vessels were sutured and removed after both uterus horns were clamped and dragged out of the abdominal cavity. After ligation, each horn was removed cranial to the cervix. In the same way, the other horn was cut, and then both horns were taken and pulled slightly outwards. They were tied in order to ligate the uterine arteries located in the body of the uterus. The white line was closed with bites in a simple interrupted pattern by the use of 3-0 absorbable suture. For skin closure, an intradermal suture pattern with a 3-0 non-absorbable silk was used.

Postoperative Measurements

Finally, the surgical site was cleaned with sterile gauze and serum. The antibiotic Enrofloxacin was used prophylactically. The pain was measured using the evaluation of the rabbit grimace scale [19]. Five characteristics of rabbits, including orbital tightening, flattening of the cheeks, shape of the nostril, whisker shape and position, and ear shape and position, were considered observational indicators and were examined at eight-time points after the surgery by scoring from zero to two. The average of these scores for each rabbit was then calculated as the Grimace Scale Score (GSC).

Statistical Analysis

We used SPSS version 23 for data analysis. Numerical data was expressed as means and standard deviations. To see if a variable is normally distributed, we utilized the Shapiro-Wilk test. The equality of variances for a variable calculated for two or more groups was assessed using Levene's test. In a repeated measures ANOVA, Mauchly's test of sphericity was employed to see if the assumption of sphericity was met. If the sphericity was accepted, we directly used Pillai's trace, Wilks' Lambda, Hotelling trace, and Roy's Largest Root tests. If not, we applied Greenhouse-Geisser, Huynh-

Feldt, and Lower Bound corrections. P≤0.05 considered significant.

Results

The preoperative weight of rabbits in NG, MG, GG, and GMG was 2.33±0.06, 2.29±0.28, 2.34±0.10, and 2.31±0.17, respectively.

In all analyses, Levene's test confirmed equality of variances and the Shapiro-Wilk test confirmed normal distribution of data.

Orbital Tightening

Table 1 shows the mean and SD of orbital tightening at different time points. Mauchly's test approved the sphericity

Table 1. *Mean and SD of orbital tightening, nostril shape, cheek flattening, ear shape and position, whisker shape and position, and grimace scale score in each study groups*

Groups	After Anesthesia	Few Hours After Surgery	Night of Surgery	One Day After Surgery	Two Days After Surgery	Three Days After Surgery	Four Days After Surgery	Five Days After Surgery
Orbital Tightening								
Negative control	1.40±0.54	1.00±0.00	0.80±0.44	0	0	0	0	0
Meloxicam	1.00±0.00	0.60±0.54	0.20±0.44	0	0	0	0	0
Gabapentin	0.60±0.54	0.60±0.54	0.20±0.44	0	0	0	0	0
Meloxicam + Gabapentin	1.10±0.22	0.80±0.57	0.20±0.27	0	0	0	0	0
Nostril Shape								
Negative control	2.00±0.00	1.60±0.54	1.00±0.00	1.60±0.54	1.40±0.54	1.20±0.57	0.80±0.27	0.40±0.54
Meloxicam	1.00±0.70	0.60±0.54	0.80±0.44	1.10±0.22	1.10±0.41	0.20±0.44	0.30±0.44	0.10±0.22
Gabapentin	1.00±0.70	0.60±0.54	0.60±0.54	1.00±0.35	0.80±0.27	0.60±0.65	0.30±0.44	0
Meloxicam + Gabapentin	1.60±0.54	1.60±0.54	0.80±0.44	1.30±0.44	1.20±0.44	1.00±0.00	0.80±0.27	0.10±0.22
Cheek Flattening								
Negative control	1.20±1.20	1.00±1.00	1.20±1.20	0.80±0.80	1.00±1.00	0.80±0.80	0.70±0.70	0
Meloxicam	0.40±0.54	0.40±0.54	0.60±0.54	0.50±0.35	0.50±0.00	0.50±0.35	0.30±0.44	0
Gabapentin	0.60±0.54	0.60±0.54	0.40±0.54	0.20±0.44	0	0	0	0
Meloxicam + Gabapentin	1.00±0.00	0.60±0.54	1.00±0.70	0.60±0.54	0.50±0.61	0	0	0
Ear Shape and Position								
Negative control	2.00±0.00	1.40±0.54	0.80±0.44	0.70±0.44	0	0	0	0
Meloxicam	1.40±0.54	0.80±0.27	0.20±0.27	0.20±0.27	0	0	0	0
Gabapentin	1.40±0.30	0.20±0.20	0.20±0.20	0.20±0.07	0	0	0	0
Meloxicam + Gabapentin	2.00±0.00	1.00±0.00	0.50±0.35	0.20±0.27	0	0	0	0
Whisker Shape and Position								
Negative control	2.00±0.00	2.00±0.00	1.00±0.70	1.00±0.00	0.90±0.22	0.40±0.41	0	0
Meloxicam	2.00±0.00	1.60±0.54	0.60±0.54	0.50±0.35	0.30±0.44	0	0	0
Gabapentin	1.60±0.54	0.90±0.22	0.40±0.54	0.30±0.44	0.10±0.22	0	0	0
Meloxicam + Gabapentin	2.00±0.00	1.60±0.54	0.70±0.44	0.70±0.44	0.40±0.54	0	0	0
Grimace Scale Score								
Negative control	1.72±0.10	1.40±0.28	0.96±0.21	0.82±0.13	0.66±0.15	0.48±0.19	0.30±0.10	0.08±0.10
Meloxicam	1.16±0.16	0.80±0.23	0.48±0.31	0.46±0.15	0.38±0.16	0.14±0.11	0.12±0.17	0.02±0.04
Gabapentin	1.04±0.16	0.50±0.17	0.36±0.26	0.34±0.16	0.18±0.08	0.12±0.13	0.06±0.08	0
Meloxicam + Gabapentin	1.54±0.13	1.12±0.23	0.64±0.15	0.56±0.15	0.42±0.25	0.20±0.00	0.16±0.05	0.02±0.04

Table 2. *Repeated measures ANOVA for the orbital tightening, nostril shape, cheek flattening, ear shape and position, whisker shape and position, and grimace scale score over time*

Effect		Test	Value	F	Df1	Df2	P-value
Orbital Tightening	Time	Pillai's trace	0.63	13	2	15	0.001
		Wilks' Lambda	0.36	13	2	15	0.001
		Hotelling trace	1.73	13	2	15	0.001
		Roy's Largest Root	1.73	13	2	15	0.001
Nostril Shape	Time	Pillai's trace	0.93	22.01	7	10	0.0001
		Wilks' Lambda	0.06	22.01	7	10	0.0001
		Hotelling trace	15.40	22.01	7	10	0.0001
		Roy's Largest Root	15.40	22.01	7	10	0.0001
Cheek Flattening	Time	Pillai's trace	0.71	4.48	6	11	0.015
		Wilks' Lambda	0.29	4.48	6	11	0.015
		Hotelling trace	2.44	4.48	6	11	0.015
		Roy's Largest Root	2.44	4.48	6	11	0.015
Ear Shape and Position	Time	Pillai's trace	0.92	53.79	3	14	0.0001
		Wilks' Lambda	0.08	53.79	3	14	0.0001
		Hotelling trace	11.52	53.79	3	14	0.0001
		Roy's Largest Root	11.52	53.79	3	14	0.0001
Whisker Shape and Position	Time	Pillai's trace	0.97	110.43	5	12	0.0001
		Wilks' Lambda	0.02	110.43	5	12	0.0001
		Hotelling trace	46.01	110.43	5	12	0.0001
		Roy's Largest Root	46.01	110.43	5	12	0.0001
Grimace Scale Score	Time	Pillai's trace	0.98	127.80	7	10	0.0001
		Wilks' Lambda	0.01	127.80	7	10	0.0001
		Hotelling trace	89.46	127.80	7	10	0.0001
		Roy's Largest Root	89.46	127.80	7	10	0.0001

Table 3. *Repeated measure ANOVA test results for orbital tightening, nostril shape, cheek flattening, ear shape and position, whisker shape and position, and grimace scale score*

Parameter	Effect	Sum of Square	Df	Mean of Square	F	P	Eta Squared	Power
Orbital Tightening	Intercept	30.10	1	30.10	180.62	0.0001	0.91	1
	Group	2.97	3	0.99	5.95	0.006	0.52	1
Nostril Shape	Intercept	126.91	1	126.91	200.06	0.0001	0.92	1
	Group	11.59	3	3.86	6.09	0.006	0.53	0.90
Cheek Flattening	Intercept	42.35	1	42.35	159.70	0.0001	0.90	1
	Group	9.12	3	3.04	11.46	0.0001	0.68	1
Ear Shape and Position	Intercept	54.45	1	54.45	221.96	0.0001	0.93	1
	Group	6.12	3	2.04	8.32	0.001	0.60	0.97
Whisker Shape and Position	Intercept	91.87	1	91.87	456.99	0.0001	0.96	1
	Group	6.74	3	2.24	11.17	0.0001	0.67	1
Grimace Scale Score	Intercept	46.87	1	46.87	817.39	0.0001	0.98	1
	Group	4.87	3	1.62	28.31	0.0001	0.84	1

of orbital tightening scores (P=0.81). Pillai's trace, Wilks' Lambda, Hotelling trace, and Roy's Largest Root tests showed the effects of time on orbital tightening (P<0.001 for all) *(Table 2)*. Repeated measures ANOVA between groups to evaluate the effect of oral Gabapentin on orbital tightening showed significant changes (P<0.0001) *(Table 3)*. The post hoc Tukey test demonstrated that there was a significant difference between Meloxicam versus negative control (MD=0.46±0.14; P=0.03) and Gabapentin versus negative control (MD=0.60±0.14; P=0.005) *(Table 4)*. As shown in *Fig. 1*, orbital tightening changes were less in the Gabapentin group than in the other groups.

Nostril Shape

The sphericity of the nostril bulging scores was confirmed by Mauchly's test (P=0.48). Further tests showed the effects of time on nostril shape (P<0.0001 for all) *(Table 2)*. The effect of oral Gabapentin on nostril shape was evaluated using a repeated measures ANOVA between groups, which revealed significant differences (P<0.0001). Meloxicam versus negative control (MD=0.60±0.17; P=0.018) and Gabapentin versus negative control (MD=0.63±0.17; P=0.01) showed a significant difference *(Table 4)*. As illustrated in *Fig. 1*, the Gabapentin group had fewer nostril shape alterations than the other groups.

Cheek Flattening

The sphericity of cheek flattening alterations was verified by Mauchly's test (P=0.71). Further testing revealed that time had an influence on cheek flattening (P<0.015 for all). Repeated measures ANOVA showed significant differences between groups (P<0.0001). Post hoc Tukey test demonstrated significant difference between Meloxicam versus negative control (MD=0.50±0.12; P=0.005), Gabapentin plus Meloxicam versus negative control (MD=0.42±0.12; P=0.01), Gabapentin versus negative control (MD=0.70±0.12; P=0.0001), and Gabapentin plus Meloxicam versus Meloxicam (MD = -0.7±0.12; P=0.005) *(Table 4)*. The level of this index in the Meloxicam group was lower than in the other groups until the second time point of the experiment (a few hours after surgery). At the third time point (the night of surgery) the index in the Gabapentin group was lower than in the other groups, and the index in the Gabapentin group reached zero two days after surgery.

Ear Shape and Position

After Mauchly's test approval (P=0.45), further analysis showed the effects of time (P<0.0001 for all). Also, ANOVA showed significant changes and the post hoc Tukey test mentioned a significant difference between Meloxicam versus negative control (MD=0.57±0.15; P=0.01) and Gabapentin versus negative control (MD=0.72±0.15; P=0.001) *(Table 4)*. Ear shape and position changes were less in the Gabapentin group than in the other groups *(Fig. 1)*. Two days after surgery, all groups' ear shape and position scores reached zero.

Table 4. *Results of post hoc tukey tests for orbital tightening, nostril shape, cheek flattening, ear shape and position, whisker shape and position, and grimace scale score*

Parameter	Groups	Mean Difference ± Standard Deviation	P
Orbital Tightening	MG-NG	0.46±0.14	0.03
	GMG-NG	0.36±0.14	0.10
	GG-NG	0.60±0.14	0.005
	GMG-MG	-0.10±0.14	0.90
	GG-MG	0.13±0.14	0.80
	GG-GMG	0.23±0.14	0.42
Nostril Shape	MG-NG	0.60±0.17	0.018
	GMG-NG	0.20±0.17	0.68
	GG-NG	0.63±0.17	0.01
	GMG-MG	-0.40±0.17	0.15
	GG-MG	0.03±0.17	0.99
	GG-GMG	0.43±0.17	0.10
Cheek Flattening	MG-NG	0.50±0.12	0.005
	GMG-NG	0.42±0.12	0.01
	GG-NG	0.70±0.12	0.0001
	GMG-MG	-0.70±0.12	0.005
	GG-MG	0.20±0.12	0.39
	GG-GMG	0.27±0.12	0.16
Ear Shape and Position	MG-NG	0.57±0.15	0.01
	GMG-NG	0.30±0.15	0.26
	GG-NG	0.72±0.15	0.001
	GMG-MG	-0.27±0.15	0.32
	GG-MG	0.15±0.15	0.77
	GG-GMG	0.42±0.15	0.06
Whisker Shape and Position	MG-NG	0.38±0.11	0.02
	GMG-NG	0.31±0.11	0.06
	GG-NG	0.66±0.11	0.0001
	GMG-MG	-0.06±0.11	0.93
	GG-MG	0.28±0.11	0.10
	GG-GMG	0.35±0.11	0.03
Grimace Scale Score	MG-NG	0.35±0.05	0.0001
	GMG-NG	0.22±0.05	0.004
	GG-NG	0.46±0.05	0.0001
	GMG-MG	0.13±0.05	0.08
	GG-MG	0.11±0.05	0.21
	GG-GMG	0.24±0.05	0.05

NG = Negative control, MG = Meloxicam, GMG = Meloxicam + Gabapentin, GG = Gabapentin

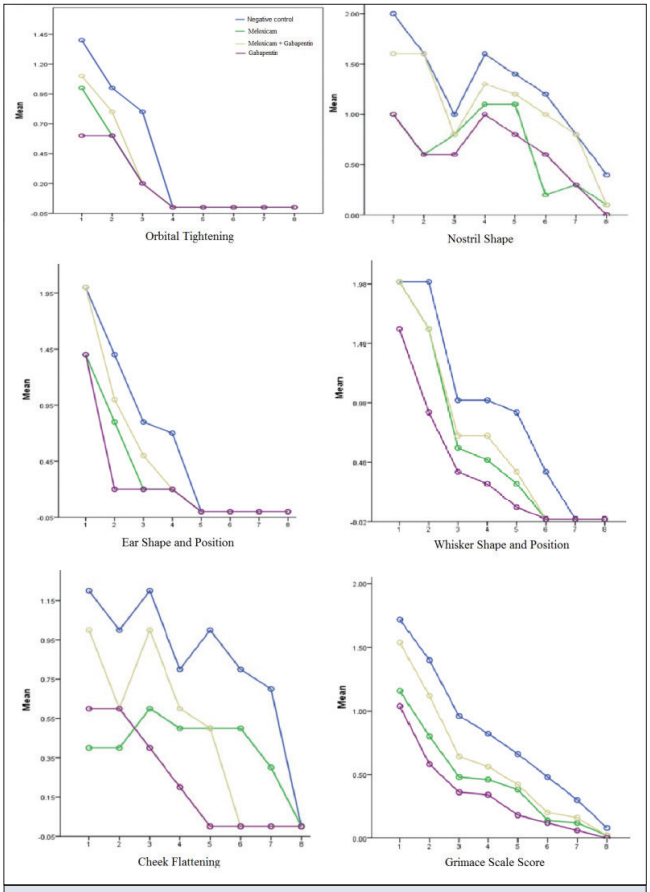

Fig 1. Mean of orbital tightening, nostril shape, cheek flattening, ear shape and position, whisker shape and position, and grimace scale score in each study groups (1: recovery period, 2: Few hours after surgery, 3: Night of surgery, 4: One day after surgery, 5: Two days after surgery, 6: Three days after surgery, 7: Four days after surgery, 8: Five days after surgery)

Table 5. *Epsilon-corrected results of whisker shape and position and Grimace Scale Score*

Whisker Shape and Position	**Corrections**	**Sum of Squares**	**Degrees of Freedom**	**Mean Sqaure**	**F**	**P-value**
Time	Sphericity	47.57	5	9.51	69.3	0.0001
	Greenhouse–Geisser	47.57	3.14	15.10	69.3	0.0001
	Huynh–Feldt	47.57	4.74	10.02	69.3	0.0001
	Lower Bound	47.57	1	47.57	69.3	0.0001
Error	Sphericity	10.98	80	0.13		
	Greenhouse–Geisser	10.98	50.38	0.21		
	Huynh–Feldt	10.98	75.92	0.14		
	Lower Bound	10.98	16	0.68		
Grimace Scale Score	**Corrections**	**Sum of Squares**	**Degrees of Freedom**	**Mean Sqaure**	**F**	**P-value**
Time	Sphericity	694.59	7	99.22	166.46	0.0001
	Greenhouse–Geisser	694.59	4.01	173.03	166.46	0.0001
	Huynh–Feldt	694.59	6.53	106.34	166.46	0.0001
	Lower Bound	694.59	1	694.59	166.46	0.0001
Error	Sphericity	66.76	112	0.59		
	Greenhouse–Geisser	66.76	64.22	1.03		
	Huynh–Feldt	66.76	104.5	0.63		
	Lower Bound	66.76	16	4.17		

Whisker Shape and Position

Mauchly's test did not approve the sphericity of whisker change scores (P=0.049). Hence, we used Greenhouse-Geisser, Huynh–Feldt, and Lower Bound corrections *(Table 5)*. Repeated measures ANOVA between groups to evaluate the effect of oral Gabapentin on whisker change showed significant changes. There was a significant difference between Meloxicam versus negative control (MD=0.38±0.11; P=0.02), Gabapentin versus negative control (MD=0.66±0.11; P=0.0001), and Gabapentin versus Gabapentin plus Meloxicam (MD=0.35±0.11; P=0.03).

Grimace Scale Score

The sphericity of grimace scale scores was not approved by Mauchly's test (P=0.046). Hence, we utilized Greenhouse-Geisser, Huynh–Feldt, and Lower Bound corrections *(Table 5)*. The effect of Gabapentin administration on grimace scale scores was evaluated using repeated measures ANOVA, which revealed significant alterations. Post hoc Tukey test demonstrated that there was a significant difference between Meloxicam versus negative control (MD=0.35±0.05; P=0.0001), Gabapentin plus Meloxicam versus negative control (MD=0.22±0.05; P=0.004), Gabapentin versus negative control (MD=0.46±0.05; P=0.0001), and Gabapentin versus Gabapentin plus Meloxicam (MD=0.24±0.05; P=0.05).

Discussion

In the present study, the analgesic effects of Gabapentin were evaluated and compared with those of Meloxicam, Gabapentin plus Meloxicam, and the negative control group. The Grimace Scale Score, as an indicator of pain, in the Meloxicam, Meloxicam plus Gabapentin, and Gabapentin groups was significantly lower than the negative control group. The Grimace Scale Score is reduced over time, and the Gabapentin group gets the lowest scores. These medications reduce opioid-related side effects and the occurrence of chronic postoperative pain [20].

The results of previous studies on postoperative pain are too controversial. An RCT on cats undergoing ovariohysterectomy compared the analgesic effects of Gabapentin-Buprenorphine, Meloxicam-Buprenorphine, and Buprenorphine alone. The two first groups did not significantly ask for rescue analgesia. However, the latter group, Buprenorphine alone, asked for more rescue analgesia [20]. Another RCT on outpatients undergoing laparoscopic cholecystectomy showed that 60-min rest pain was significantly lower with Gabapentin alone versus Meloxicam alone. Also, the combination of Meloxicam and Gabapentin did not show different results compared to Gabapentin alone. However, on postoperative days 1, 2, and 30, there were no significant effects of the treatment group on spontaneous or movement-evoked pain measures [21]. Contrary to their study, we showed that a multimodal approach is not as effective as Gabapentin alone, and Meloxicam alone showed similar efficacy to Gabapentin alone. A recent study showed that Gabapentin alone or in combination with Meloxicam could not significantly reduce neuropathic pain compared to placebo [22]. Jain et al.[23] studied the efficacy of Gabapentin (1200 mg) prior to induction of anesthesia in patients scheduled for laparoscopic cholecystectomy. They found that the pain score was significantly lower in the Gabapentin group compared to the placebo group one hour following the surgery. However, at other time points, there was no difference. Also, Karri et al.[24] showed similar results to the Jain et al.[23] study. The findings of the present study are in accordance with Karri et al.[24] and Jain et al.[23], but our study procedure was more invasive, so the pain lasted longer. A study on 100 patients who underwent laparotomy for gynecologic surgery divided them into four groups: placebo, Gabapentin 300, 600, and 1200 mg, who received drugs 2 h before surgery. The study showed that postoperative intravenous fentanyl requirement was lower with Gabapentin treatment, but there were no significant differences for the different doses [25]. Fassoulaki et al.[26] conducted a study on 60 patients undergoing abdominal hysterectomy. Patients were randomly assigned to either oral administration of 400 mg Gabapentin every 6 h for seven days plus continuous wound infusion of Ropivacaine 0.75% for 30 h or placebo. The treatment group consumed less cumulative morphine over the first 48 h and fewer lonalgal tablets on days 3-7. The visual analog score values at rest and after coughing did not differ between the groups during the first seven postoperative days. One month after the operation, fewer patients in the treatment group experienced pain than in the control group.

The current study did not look at long-term postoperative results, and this is an area where more research is needed. All pain scoring methods have limitations, and we avoided interobserver variability by having the same blinded observer perform all of the assessments throughout the trial. It's probable that having an observer around changed their behavior, as well as their pain scores and expressions.

Postoperative analgesia was significantly higher in groups that received Meloxicam, Gabapentin, or both compared to the negative control group. Gabapentin is as effective as Meloxicam. However, Meloxicam plus Gabapentin is not as effective as Gabapentin alone.

In conclusion, our results indicate that using either Gabapentin or Meloxicam as pre-operative medication can decrease post-operative pain while it may have coincidence with some adverse effects. In addition, it seems that applying these treatments can limit administration of

opioid drugs during the surgery.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author (S. Mohitmafi).

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Ethical Statement

All procedures were carried out with the approval of the Ethical Committee of Islamic Azad University - Karaj Branch (Approval ID: IR.IAU.K.REC.1400.005).

Competing Interests

The authors declared that there is no conflict of interest.

Authors' Contributions

S.M and Z.A designed the study. H.M performed the laboratory analysis and wrote the paper. S.M reviewed and revised the paper. All authors have read and agreed to the published version of the paper.

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