Effects of Gabapentin on Pain Relief and Need for Opiates after Total Abdominal Hysterectomy



ARTICLE INFO

Article Type Original Research

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How to cite this article

Forough Javanmanesh, Maryam Kashanian, Vajihe Zamani, Narges Sheikhansari. Effects of Gabapentin on Pain Relief and Need for Opiates after Total Abdominal Hysterectomy. Journal of Obstetrics, Gynecology and Cancer Research. 2018;3(3):99-103.

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Article History

Received: April 24, 2018 Accepted: May 03, 2018 ePublished: September 22, 2018

ABSTRACT

Aims Pain is the main concern after surgery. Gabapentin was recently suggested as a pain killer to be used after various surgeries. The purpose of the present study was to evaluate the effects of gabapentin on pain relief and need for opiates after total abdominal hysterectomy. **Materials & Methods** This randomized double-blind placebo-controlled clinical trial was performed on 85 women who underwent total abdominal hysterectomy from March 2014 to March 2016 in Akbarabadi teaching hospital and Firoozgar teaching hospital in Tehran, Iran. Samples were selected using consecutive sampling method and were randomly assigned into the 2 groups. In case group (n=44) gabapentin (800mg) was orally administered one hour before surgery and in the placebo group (n=41) placebo which was similar to gabapentin administered. The pain score was assessed in 2, 6, 12 and 24 hours after surgery. Nausea and vomiting were also compared between the 2 groups. Data were analyzed by SPSS 19 software using statistical tests.

Findings The two groups did not have significant differences according to pain score in the recovery room (point 0). Mean score of pain was lower in the case group in 2, 6, 12 and 24 hours after surgery (p=0.005). Meperidine (pethidine) use was less in the case group (p=0.003). There was no difference between the 2 groups for nausea and vomiting. **Conclusion** Using gabapentin before surgery can lower the pain after surgery and reduces

the need for opiates. However, it doesn't have an effect on nausea and vomiting.

Keywords Pain; Opioids; Gabapentin; Hysterectomy; Surgery; Postoperative Period

CITATION LINKS

[1] Gabapentin and postoperative pain: a qualitative and quantitative systematic review ... [2] A randomized study of the effects of single-dose gabapentin versus placebo on postoperative pain ... [3] Gabapentin blocks and reverses antinociceptive morphine ... [4] Study of the effect of oral gabapentin used as preemptive analgesia to attenuate post-operative pain in patients ... [5] The analgesic effects of gabapentin after total abdominal ... [6] A randomized, double-blind, controlled trial of perioperative administration of gabapentin ... [7] Gabapentin attenuates late but not acute pain after abdominal ... [8] Preemptive use of gabapentin significantly decreases postoperative pain and rescue ... [9] The effect of pre-operative administration of gabapentin on post-operative ... [10] Evaluation of efficacy of the perioperative administration of Venlafaxine or gabapentin on acute and chronic ... [11] Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar diskectomy ... [12] Effect of preemptive gabapentin on postoperative pain relief and morphine consumption following ... [13] The Postoperative analgesic effects of low-dose gabapentin ... [14] Effect of Gabapentin on morphine demand and pain after ... [15] Preemptive gabapentin reduces postoperative pain and ... [16] Preoperative gabapentin decreases anxiety and improves early ... [17] Premedication with gabapentin: the effect on tourniquet pain and ... [18] Gabapentin for the prevention of postoperative ... [19] Gabapentin: an alternative to the cyclooxygenase-2 inhibitors for ... [20] The post-operative analgesic effects of a combination of gabapentin ... [21] Gabapentin enhances the analgesic effect of morphine in ... [22] A systematic review and metaregression analysis of prophylactic gabapentin ... [23] Effect of gabapentin on postoperative pain: A randomized, placebo-controlled ... [24] A comparison of gabapentin and ketamine in acute and chronic... [25] Gabapentin inhibits high-threshold calcium channel currents in ... [26] Anaesthesia, surgery, and challenges in postoperative ... [27] Preemptive use of gabapentin in abdominal ... [28] Effects of gabapentin on postoperative morphine consumption ... [29] A single preoperative dose of gabapentin (800 milligrams) does not ... [30] Effects of a single 1200-mg preoperative dose of gabapentin ... [31] Gabapentin prophylaxis for postoperative nausea ...

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Effects of Gabapentin on Pain Relief and Need for Opiates after ... Introduction

Pain relief after surgery is an important matter in post-operative care and can reduce the risk of psychiatric and neurotic consequences of surgery and therefore encourage patients to undergo surgery in obligatory cases, because fear of pain may be an obstacle for deciding to undergo surgery in many cases and therefore can threaten the health and life of patients. Also, it can help with early ambulation of the patients. Many different drugs have been used for this purpose including opiates that constitute the most frequently used pain killers after operation (surgery), however, their adverse effects which including respiratory depression, nausea and vomiting and intestinal ileus, have limited their usages. Other types of pain killers have been used alone or in combination with opioids to relieve the post-operative pain and reduce need for opioids in order to lessen the adverse effects. Gabapentin is an antiepileptic and anticonvulsive drug which has been used for neuropathic pains ^[1, 2] and is a gamma-aminobutyric acid (GABA) analog that can reduce pain through different mechanisms [3]

In many different studies, the effects of gabapentin on pain relief have been evaluated using different routes of administration [4], different dosages [2, 4-11], on different surgeries [1, 2, 6, 8-18], alone or in combination with the other pain killers [6, 19-21], as a single dose or in multiple doses [10], pre-operative or post-operative [1, 10, 16, 17, 22, 23] and almost in all mentioned studies, it could reduce the postoperative pain and amount of needed pain killers. Also, it has been compared with the other pain killers like venlafaxine [10] paracetamol [20], ketamine ^[24] and cyclooxygenase -2 inhibitors ^[19]. Sutton *et al*. showed in their study that gabapentin inhibits highthreshold calcium channel currents in cultured rat dorsal root ganglion neurons ^[25]. Also, it has been used in different chronic pain conditions and has been shown that it is effective for these situations without considerable side effects [1, 7].

Hysterectomy is one of the most common gynecological surgeries and is the second most frequently done surgery after cesarean section in many countries; therefore, pain relief after hysterectomy can help with early ambulation, lowering complications including ileus, impaired pulmonary function and post-operative fatigue, increasing patient satisfaction and preventing delayed convalescence ^[26].

The purpose of the present study was to evaluate the effects of gabapentin on pain relief and need for opiates after total abdominal hysterectomy (TAH). Also, its effects on nausea and vomiting were evaluated.

Materials and Methods

This study was performed as a double-blind

randomized placebo-controlled clinical trial on women who were candidates for total abdominal hysterectomy from March 2014 to March 2016 in Akbarabadi teaching hospital and Firoozgar teaching hospital in Tehran, Iran.

Exclusion criteria were an allergy to meperidine or gabapentin, chronic using of analgesics and sedatives, drug abuse, having chronic systemic disorders including cardiovascular, liver, renal, respiratory disorders and chronic pain, hysterectomy due to malignancies, history of psychiatric disorders and complicated surgery.

85 eligible women entered the study using consecutive sampling method and were randomly assigned into the 2 groups. In case group (n=44) gabapentin (800mg) was orally administered one hour before surgery and in the placebo group (n=41) placebo which was similar to gabapentin as in taste, smell, shape, and color was administered. All women had general anesthesia for their operation.

At the end of surgery, the patients were reversed by neostigmine $40\mu g/kg$ and atropine $20\mu g/kg$. In the recovery room, all women received 30mg meperidine (pethidine) and severity of pain was determined and recorded using visual analogue scale (VAS) in 0, 2, 6, 12 and 24 hours after surgery. In these intervals according to severity of pain and VAS score, extra meperidine was administered intra muscularly. For VAS score of 4-6, 25mg and for VAS score of 8-10, 50mg meperidine was administered. Total used sedative and also, severity of nausea and vomiting were evaluated and recorded for both groups and were compared.

Data were analyzed by SPSS 19 software using Kolmogorov–Smirnov test, student t-test, Mann-Whitney U test, Fisher exact test, chi-square test, Cochran test and repeated measures analysis of variance.

Findings

The mean of age was 46.64 ± 8.40 and 48.00 ± 5.50 years old in gabapentin and placebo groups, respectively. The mean of body mass index (BMI) was 30.64 ± 3.50 Kg/m² in gabapentin group and 30.02 ± 3.30 Kg/m² in the placebo group. Also, the duration of surgery was 147.20 ± 60.60 and 151.40 ± 44.40 minutes in gabapentin and placebo groups respectively. There was no significant difference between two groups based on age, BMI, duration of surgery, history of previous surgery, type of surgery, and gravidity (p>0.05; Table 1).

The level of pain reported by the patients in both groups was decreasing within groups during 0, 2, 6, 12 and 24 hours, and the severity of pain was significantly lower in the case group. The women who needed pain killer in 2, 6, 12 and 24 hours after surgery and, the total administered dosages of

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meperidine were less in the case group. Moreover, the total administered dosage of opioid was declined within both groups (Table 2).

The rate of nausea and vomiting did not show significant difference between the 2 groups (Table 3).

The number of previous surgeries, the reason for surgery, type of surgery and, gravidity did not show any significant effect on need for pain killer in both groups (p>0.05; Table 4).

Table 1) Frequency distribution of characteristics in gabapentin (n=44) and placebo (n=41) groups (the numbers in parentheses are percentage)

Characteristics	Gabapentin group	Placebo group		
History of previous surgery				
-	17 (38.6)	13 (31.7)		
type of surgery				
TAH+BSO	14 (31.8)	14 (34.1)		
ТАН	22 (50.0)	21 (51.2)		
TAH+R/LSO	8 (18.2)	6 (14.6)		
Gravidity				
0	6 (13.6)	4 (9.8)		
1	3 (6.8)	4 (9.8)		
2	10 (22.7)	11 (26.8)		
3	12 (27.3)	11 (26.8)		
4	7 (15.9)	6 (14.6)		
5≤	6 (13.6)	5 (12.2)		

BSO: Bilateral salpingo-oophorectomy; R/LSO: Right/Left salpingo-oophorectomy

Table 2) Pair	l levels and need to pain killer in gabapenti	n
(n=44) and pl	acebo (n=41) groups	

Variables	Gabapentin group	Placebo group	P.value	
Mean sore o	of pain in differen	t points		
0	9.12±0.87	9.08±0.75	0.9	
2 hour	7.64±0.92	8.63±0.96		
6 hour	5.23±1.32	6.44±2.48	0.005	
12 hour	3.45±1.85	4.73±3.21	0.005	
24 hour	1.98±0.33	2.83±1.16		
Frequency of	of need to opioid			
2 hour	37 (84.1%)	39 (95.1%)		
6 hour	33 (75.0%)	38 (92.7%)	0.001	
12 hour	20 (45.5%)	29 (70.7%)	0.001	
24 hour	6 (13.6%)	12 (29.3%)		
Mean of tota	a <mark>l used opioid</mark> (mg	g)		
-	81.82±37.49	109.26±45.03	0.0312	
Mean of need to opioid (mg)				
2 hour	38.07±19.05	44.5±13.12		
6 hour	26.70±18.98	33.54±15.42	0.002	
12 hour	13.07±5.70	21.95±16.95	0.005	
24 hour	3.98±0.70	9.15±5.56		

Table 3) Frequency distribution of vomiting in gabapentin (n=44) and placebo (n=41) groups (the numbers in parentheses are percentage)

Hours after	Gabapentin	Placebo	P.value
2	9 (20.5)	6 (14.6)	0.4
6	9 (20.5)	4 (9.8)	0.1
12	8 (18.2)	5 (12.2)	0.4
24	2 (4.5)	0	0.1

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Table 4) The mean of used opioid in different conditions

Characteristics	Opioid (mg)	P.value
No. of previous surgeri	es	
0	124.18±37.77	
1	121.70±51.52	0.6
2	133.57±39.33	0.0
≥3	122.60±76.37	
Reason for surgery		
Муота	124.42±41.81	
AUB	123.13±39.39	0.9
Others	130.00±86.6	
Type of surgery		
TAH	125.93±44.63	
TAH+R/LSO	113.92±36.17	0.6
TAH+BSO	125.86±39.38	
Gravidity		
0	115.00±28.50	
1	130.71±39.83	
2	128.80±40.67	0.8
3	116.95±54.8	0.0
4	130.00 ± 27.00	
≥5	114.16±36.79	

AUB: Abnormal uterine bleeding

Discussion

In the present study, a single dose of 800mg oral gabapentin, which was administered one hour before surgery could reduce the pain and need for opioids in women undergoing total abdominal hysterectomy without any effects on nausea and vomiting.

Regarding the importance of pain relief after surgery for reducing the complications, including early ambulation, preventing thromboembolism, patient satisfaction and well-being and prevention from respiratory complications ^[26], different studies have been performed. Opioid analgesics are the main analgesics which have been used. However, with respect to their side effects, the researchers try to reduce need for opioid agents after surgery. Therefore, many clinical trials and studies, are under process on different agents. Gabapentin is one of these agents that has been shown its analgesic effects and approved by FDA (Food and Drug Administration) ^[1].

Abdominal hysterectomy is one of the most common surgeries in obstetrics and gynecology and after cesarean section, is the second most frequently done surgery in the field of obstetrics and gynecology, therefore, pain relief after this surgery is important both for patients and surgeons.

In a study by Turan *et al.* ^[5], 1200mg oral gabapentin, one hour after surgery, could reduce post-operative tramadol consumption in women after abdominal hysterectomy. Another study with 600mg gabapentin, one hour before abdominal surgery, showed similar results and could reduce need for tramadol and diclofenac for pain relief ^[4]. In the other study ^[1], gabapentin could decrease the pain score and need for opioids both in the cases of spinal surgery and abdominal hysterectomy. Also,

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nausea was reported to be reduced after abdominal hysterectomy in this study ^[1]. A meta-analysis on 448 cases, which used gabapentin before abdominal hysterectomy, showed decreased pain score and nausea and vomiting after surgery ^[27].

Combination of gabapentin and paracetamol and gabapentin alone, also decreased the opioid requirement after abdominal hysterectomy [20]. Continual use of gabapentin after surgery, in addition to pre-operative administration, has also been studied [28]. Dierking et al. [28] used 1200mg gabapentin, one hour before surgery and continued it as 600mg, 8, 16 and 24 hours after surgery (total dose of 3000mg) and could reduce the use of morphine about 32%. In a comparison between ketamine and gabapentin ^[24], gabapentin could lower acute pain after hysterectomy better than ketamine, when was used pre-operative. Also, gabapentin decreased the pain in the first 6 months after surgery (chronic effects). Therefore, it had better effect on chronic pain [24]. Gabapentin also has decreased pain after laparoscopic sterilization [14], and vaginal hysterectomy [18], however, it did not have effects on frequency of nausea and vomiting similar to the present study.

In contrast, some studies have had doubts about the effect of gabapentin and reported that the effects of gabapentin may have been overestimated ^[22]. Another study reported that 800mg oral gabapentin pre-operative, had no effects on post-operative pain ^[29]. In some studies, it has been reported that gabapentin has effects on acute pain after surgery ^[17] and not on chronic pain ^[10]. However, another study reported that it does not have pain relief effects on immediate pain after abdominal hysterectomy, but it has effects on chronic pain 1-month post operation ^[7].

Pre-operative gabapentin has been reported to reduce pre-operative anxiety ^[16, 30], however, in the other study, 15mg oxazepam was more effective than 1200mg gabapentin for decreasing preoperative anxiety ^[18]. The optimal dose of gabapentin also, is not clear, and different dosages have been used in different studies, but one study has compared different doses of 300, 600, 900 and 1200mg gabapentin, and concluded that 600mg is the optimal dose ^[11]. Also, it has been reported that gabapentin can reduce nausea and vomiting in abdominal surgeries ^[31]. However, the present study and the other study ^[15], could not show this effect for gabapentin.

Regarding the above-mentioned studies, it seems that gabapentin can be considered as a good pain relief agent in the cases of abdominal hysterectomy, but the optimum dose, the frequency of administration both pre and post operation, should be studied further. It might be used as an alternative to opioids and could be a substitute for them in the higher doses. Also, its effects on nausea and vomiting should be researched further.

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Conclusion

Using gabapentin before surgery can lower the pain after surgery and reduces need for opiates. However, it doesn't have an effect on nausea and vomiting.

Acknowledgments: There is nothing expressed by the authors.

Ethical Permission: The ethical permission code is 93/3393/105.

Conflict of Interests: There was no conflict of interests.

Authors' Contribution: Javanmanesh F. (First author), Introduction author/ Methodologist/ Original researcher (30%); Kashanian M. (Second author), Introduction author/ Methodologist/ Original researcher/ Statistical analyst/ Discussion author (30%); Zamani V. (Third author), Introduction author/ Assistant (20%); Sheikhansari N. (Fourth author), Introduction author/ Assistant/ Discussion author (20%)

Funding: There is no funding.

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