Original Article

Effectiveness of Gabapentin Compared to Acetaminophen for Pain Control in Postpartum Patients Following Vaginal Delivery in Phramongkutklao Hospital

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Objective: The study aimed to evaluate the effectiveness of pain reduction between acetaminophen and gabapentin among postpartum patients, who undergo vaginal delivery.

Materials and Methods: The present research was a randomized-controlled trial, enrolling term pregnant women with informed consent, who came to Phramongkutklao Hospital for vaginal delivery, between October 10, 2019 and March 15, 2020. Women with acetaminophen or gabapentin allergy, previously diagnosed with mood disorder or epilepsy, undergoing operative vaginal delivery, receiving epidural block or pudendal nerve block, not being able to understand Thai or English, need for general anesthesia, and taking other sedative agents within two hours before delivery were excluded. The participants were randomized into two groups by blocks of four and took medications, which were oral acetaminophen (500 mg) or gabapentin (300 mg). The medication was given at 30 minutes and six hours after delivery and the visual analog scale (VAS) was assessed at 30 minutes, 2- , 6- , and 12-hours. Side effects of each medication were also obtained. After 24 hours, postpartum depression was evaluated, using the Edinburgh postnatal depression scale. Data were statistically analyzed using SPSS and manifest mean ± standard deviation (SD).

Results: Two hundred twenty patients randomly received either gabapentin (n=110) or acetaminophen (n=110). The VAS reduction of both groups and postpartum depression rate did not differ significantly (p=0.428). Women, taking gabapentin complained more about dizziness. Moreover, those taking acetaminophen experienced more drowsiness (p=0.757).

Conclusion: Gabapentin and acetaminophen are not different, considering the effectiveness of pain control. In addition, side effects and efficacy of postpartum depression decrease were mostly similar.

Keywords: Vaginal delivery, Postpartum depression, Pain, Gabapentin, Acetaminophen

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Vaginal delivery is one of the greatest concerns for all pregnant women, especially regarding pain[1]. Pain is caused by three main compositions, breast engorgement, uterine contraction, and pain from a perineal wound or the episiotomy wound[2]. Much evidence indicated that experiencing more pain, leads to a greater risk of postpartum depression[3]. The rate of postpartum depression rate can reach 58.5% and is affecting their daily life activities[4]. Following vaginal delivery, women, receiving anesthesia injection to the cervix, had a four times lower rate of postpartum depression[5]. Many pain killers can be used to relieve pain. Medications that are widely used include acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs)[6]. Most research[7-9] stated that the effectiveness of pain control by NSAIDs was better than acetaminophen. No study has compared gabapentin and acetaminophen. As a result, the authors focused on research using NSAIDs[7-9].

Gabapentin is another pain killer that could decrease pain up to 50%, compared with placebo[10]. This medication increases the activity of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) by adding a cyclohexyl group and therefore, it affects directly the central nervous system to reduce pain and stabilize the mood[11]. Taking gabapentin in doses of 300 mg to 1,800 mg daily, showed that 37% of patients were able to cope with depressive mood[12]. Consequently, the authors' attention was caught by gabapentin, which is not just another pain killer but can also be used to control depressive mood. Therefore, the authors focused on this medication

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that can be used to both relieve the pain and decrease depression rate and hopefully, that can change the traditional way to reduce pain in these postpartum women along with decrease depression.

The goal of the present study was to compare between using acetaminophen and gabapentin to reduce pain, side effects, and postpartum depression.

Materials and Methods

The present study involved an open label, randomized-controlled trial and was approved by the Ethics Committee of the Institutional Review Board of the Royal Thai Army, Medicine Department, IRBRTA1036/2562. The authors enrolled term pregnant women with informed consent, who attended Phramongkutklao Hospital for vaginal delivery between October 10, 2019 and March 15, 2020. All participants were older than 18 years old and term singleton pregnant. Any women with acetaminophen or gabapentin allergy, previously diagnosed with mood disorder or epilepsy, undergoing operative vaginal delivery, receiving epidural block or pudendal nerve block, not being able to understand Thai or English, having postpartum complications and need for general anesthesia, retained placenta, vulvar hematoma, and taking other sedative agents within two hours before delivery were excluded. The randomization was performed using blocks of four, generated using a computer by random sequence. All subjects were assigned to receive either acetaminophen or gabapentin following the timing of vaginal delivery using sealed envelopes. Doctors and nurses acknowledged the medication used for each subject. Concurrently, the participants were blinded to the name of the given drugs. Sample size was calculated following that of the Akil et al study[13] with power of 80%, 0.05 alpha error, and allowing 10% of missing data included. Each group needed 110 subjects.

After vaginal delivery, participants received medication as prescribed in each sealed envelope. Postpartum women were divided in two groups, receiving acetaminophen 500 mg or gabapentin (300 mg) orally at 30 minutes and six hours after delivery, considered duration of action and onset of both medicines. The visual analog scale (VAS)[10] was written down by participants themselves at 30 minutes, 2-, 6-, and 12-hours. Side effects of each medication were also obtained and treated, when unbearable. After 24 hours, postpartum depression was evaluated, using the Edinburgh postnatal depression scale (EPDS) (Sensitivity 100%, specificity 88%)[14]. EPDS is a screening test for postpartum depression. Any woman having more than 11 points was considered as positive for postpartum depression.

The main results comprised of VAS, which referred to severity of pain. VAS was compared between acetaminophen and gabapentin at 30 minutes, 2- , 6-, and 12-hours. Other outcomes were side effects of each medication and postpartum depression.

Statistical analysis

The statistical data were analyzed using SPSS. The results were shown as mean ± standard deviation (SD). Categorical data were calculated using the chi-square test. Moreover, Kolmogorov-Smirnov was used to measure the distribution, showing the data were non-normal distribution for VAS. Consequently, Mann-Whitney U test was used to calculate the continuous data, including VAS score. A p-value of less than 0.05 was considered statistically significant.

Results

Two hundred twenty participants were included and randomly divided into two groups, using blocks of four taking either acetaminophen (n=110) as control group or gabapentin (n=110). The first table displays the demographic data of participants between acetaminophen and gabapentin groups. Maternal age, body mass index (BMI), education, and parity indicated no significant difference. One of the obstetrical complications, namely, previous preterm birth in the gabapentin and acetaminophen group was 0% and 5.5%, respectively (p=0.029) (Table 1). Mean gestational age in the gabapentin and acetaminophen group was 39.09±0.96 weeks versus 38.77±1.01 weeks (p=0.023) (Table 1). The remaining variables including other obstetrical complications, labor type, the officers who delivered and episiotomy grading were without significant difference (Table 1). Median VAS in both groups at the beginning of vaginal delivery were similar with gabapentin group at 2.80 (1.30, 4.83) and acetaminophen group at 2.85 (1.28, 1.46); (p=0.845) (Table 2). Most participants were likely to experience only mild pain with a VAS of less than 4. Nevertheless, the VAS decreased over time after taking each medication, as shown in Figure 1. The acetaminophen group surprisingly showed a higher difference of VAS than the gabapentin group, but without significance.

Postpartum participants, receiving gabapentin, felt dizzier than those receiving acetaminophen, at 60% and 33.3%, respectively (Table 3). In addition,

Table 1. Patient characteristics (n=220)

Characteristic	Gabapentin (n=110); n (%)	Acetaminophen (n=110); n (%)	p-value
Age (year)			0.702
18 to 34	93 (84.5)	95 (86.4)	
≥35	17 (15.5)	15 (13.6)	
Mean±SD	29.62±5.13	28.46±5.36	0.070
BMI (kg/m^2)			0.365
Underweight <18.5	0 (0.0)	1 (0.9)	
Normal 18.5 to 22.9	11 (10.0)	16 (14.5)	
Overweight 23 to 24.9	16 (14.5)	23 (20.9)	
Obese I 25 to 29.9	65 (59.1)	54 (49.1)	
Obese II ≥30	18 (16.4)	16 (14.5)	
Mean±SD	27.02±3.30	26.32±3.43	0.117
Education			0.997
No education	1 (0.9)	1 (0.9)	
Primary school	2 (1.8)	2 (1.8)	
Secondary school	32 (29.1)	34 (30.9)	
Vocational certificate	9 (8.2)	8 (7.3)	
Bachelor degree	63 (57.3)	62 (56.4)	
Master degree	3 (2.7)	3 (2.7)	
Parity			0.206
Nulliparous	35 (31.8)	44 (40.0)	
Multiparous	75 (68.2)	66 (60.0)	
Obstetrical complications			
Teenage pregnancy	2 (1.8)	2 (1.8)	1.000
Elderly gravida	14 (12.7)	15 (13.6)	1.000
GDM overt DM	11 (10.0)	8 (7.3)	0.471
PIH	4 (3.6)	4 (3.6)	1.000
History of preterm birth	0 (0.0)	6 (5.5)	0.029*
FGR	1 (0.9)	2 (1.8)	1.000
Oligohydramnios	4 (3.6)	4 (3.6)	1.000
GA (weeks)	39.09±0.96	38.77±1.01	0.023*
Labor type			0.230
Spontaneous labor	98 (89.1)	103 (93.6)	
Induction	12 (10.9)	7 (6.4)	
Delivery by			0.511
Attending staff	1 (0.9)	2 (1.8)	
Resident	100 (90.9)	104 (94.5)	
Medical student	6 (5.5)	3 (2.7)	
Nurse	3 (2.7)	1 (0.9)	
Episiotomy grading			0.673
Grade 1	6 (5.5)	6 (5.5)	
Grade 2	102 (92.7)	101 (91.8)	
Grade 3 (a, b, c)	2 (1.8)	1 (0.9)	
No tear	0 (0.0)	2 (1.8)	

SD=standard deviation; BMI=body mass index; GDM=gestational diabetes mellitus; DM=diabetes mellitus; PIH=pregnancy-induced hypertension; FGR=fetal growth restriction; GA=gestational age

p-value from chi-square, Fisher's exact, and Mann-Whitney U tests,
* Significance at the 0.05 level

Table 2. Comparison of VAS score between acetaminophen and gabapentin groups among postpartum participants

	Gabapentin (n=110); n (%)	Acetaminophen (n=110); n (%)	p-value
VAS at 30 minutes			0.054
0	10 (9.1)	6 (5.5)	
1 to 3.9	61 (55.5)	61 (55.5)	
4 to 6.9	28 (25.5)	40 (36.4)	
7 to 10	11 (10.0)	3 (2.7)	
Median (IQR)	2.80 (1.30,4.83)	2.85 (1.28, 4.60)	0.845
VAS at 2 hours			0.258
0	13 (11.8)	10 (9.1)	
1 to 3.9	74 (67.3)	86 (78.2)	
4 to 6.9	19 (17.3)	13 (11.8)	
7 to 10	4 (3.6)	1 (0.9)	
Median (IQR)	1.90 (0.58, 3.70)	1.70 (0.50, 2.60)	0.282
VAS at 6 hours			0.826
0	22 (20.0)	23 (20.9)	
1 to 3.9	69 (62.7)	73 (66.4)	
4 to 6.9	17 (15.5)	12 (10.9)	
7 to 10	2 (1.8)	2 (1.8)	
Median (IQR)	1.55 (0.30, 2.85)	1.20 (0.20, 2.50)	0.426
VAS at 12 hours			0.935
0	35 (31.8)	39 (35.5)	
1 to 3.9	60 (54.5)	58 (52.7)	
4 to 6.9	12 (10.9)	10 (9.1)	
7 to 10	3 (2.7)	3 (2.7)	
Median (IQR)	1.10 (0.00, 2.90)	0.35 (0.00, 1.83)	0.129
VAS at 30 minutes to 2 hours			0.444
Decreased pain	71 (64.5)	79 (71.8)	
Increased pain	28 (25.5)	24 (21.8)	
No difference (no pain 0)	11 (10.0)	7 (6.4)	
Median (IQR)	0.75 (0.13, 2.13)	0.90 (0.00, 2.53)	0.428
VAS at 30 minutes to 6 hours			0.479
Decreased pain	74 (67.3)	82 (74.5)	
Increased pain	26 (23.6)	21 (19.1)	
No difference (no pain 0)	10 (9.1)	7 (6.4)	
Median (IQR)	1.05 (0.00,2.93)	1.20 (0.00,3.10)	0.726
VAS at 30 minutes to 12 hours			0.510
Decreased pain	78 (70.9)	83 (75.5)	
Increased pain	19 (17.3)	19 (17.3)	
No difference (no pain 0)	13 (11.8)	8 (7.3)	
Median (IQR)	1.40 (0.00, 3.33)	1.90 (0.08, 3.73)	0.425

VAS=visual analog scale; IQR=interquartile range (P_{25} and P_{75})

p-value from chi-square, Fisher's exact and Mann-Whitney U tests,
* Significance at the 0.05 level

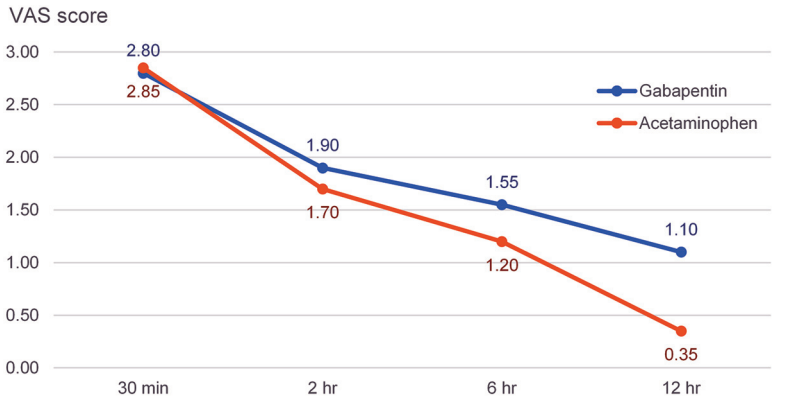

Figure 1. Chart of comparison of median VAS score between acetaminophen and gabapentin groups among postpartum participants.

Table 3. Side effects of each medication (n=220)

	Gabapentin (n=110); n (%)	Acetaminophen (n=110); n (%)	p-value
At 6 hours after delivery			0.757
No symptoms	105 (95.5)	104 (94.5)	
Developed symptoms	5 (4.5)	6 (5.5)	
• Dizziness	3 (60.0)	2 (33.3)	
• Drowsiness	2 (40.0)	3 (50.0)	
• Nausea	0 (0.0)	1 (16.7)	
At 12 hours after delivery			0.757
No symptoms	105 (95.5)	104 (94.5)	
Developed symptoms	5 (4.5)	6 (5.5)	
• Dizziness	2 (40.0)	1 (16.7)	
• Drowsiness	3 (60.0)	5 (83.3)	

p-value from chi-square test, * Significance at the 0.05 level

Table 4. Postpartum depression using Edinburgh postnatal depression scale (EPDS) (n=220)

	Gabapentin (n=110); n (%)	Acetaminophen (n=110); n (%)	p-value
EPDS score			1.000
≥11 (screening positive)	5 (4.5)	4 (3.6)	
<11	105 (95.5)	106 (96.4)	
Mean±SD	3.31±3.20	3.65±2.79	0.148

SD=standard deviation

p-value from Fisher's exact test and Mann-Whitney U test, * Significant at the 0.05 level

complaints of drowsiness and nausea was higher in the acetaminophen group, but both without significant difference. The EPDS was used to analyze postpartum depression. Those who had more than 11 points, were considered as positive for postpartum depression and were later sent to meet a psychologist. The percent was slightly higher in the gabapentin than the acetaminophen group, and again without significance (p=1.000) (Table 4).

Discussion

No previous study has compared gabapentin and acetaminophen among postpartum women, undergoing vaginal delivery. The present study might be the first, comparing these two medications. As stated in related studies[5,10,12], gabapentin might decrease pain and depression more than acetaminophen. However, the present study showed no significant difference, considering, vaginal delivery was not that painful. Timing of VAS at 30 minutes after delivery was considered as baseline pain level for each participant. Comparing to other previous study[15,16], the VAS reduction of acetaminophen 1,000 mg is less than the other medication, which is ibuprofen 400 mg. Consequently, the VAS reduction did not differ significantly between acetaminophen and gabapentin. Most participants were considered having only mild pain[6] with a VAS of less than 4. Regardless, there were few participants having severe pain with a VAS of more than 7, even more than 12 hours after delivery. Looking closely, those with severe pain experienced vaginal delivery for the first time and some had episiotomy wound grade 3 onwards, which might have caused more pain for participants. Gabapentin was known to be able to decrease pain score up to 50%[10] and depression by up to 37%[12]. Meanwhile, the present study only revealed an ability of pain reduction, but not depression. Dirks et al[17], which conducted the study of effects of gabapentin in postoperative pain, revealed no significant side effects comparing to morphine. The

result of the present study also showed no different side effects between gabapentin and acetaminophen.

The limitation of the present study was that pain perception is different for every person. Moreover, some subjects were medical officers and knew what each medication looked like without seeing their names. Thus, they knew exactly what they received. This might have affected how they felt about the pain and side effects. For the statistical analysis, the result was considered abnormal distribution, using Kolmogorov-Smirnov. Consequently, the Mann-Whitney U test was used to calculate VAS.

According to the results, using either gabapentin or acetaminophen made no difference in all aspects. The cost of gabapentin is higher than acetaminophen, at almost three times, so taking acetaminophen may be a more reasonable alternative. On the other hand, when a woman has acetaminophen allergy, gabapentin can be substituted.

Conclusion

Gabapentin and acetaminophen showed no difference about the effectiveness of pain control, side effects, and postpartum depression rate.

What is already known on this topic?

Acetaminophen is a recognized drug, used for pain control in postpartum patients. Hence, many studies have explored analgesic medications among postpartum patients. However, gabapentin has never been compared with acetaminophen.

What this study adds?

Taking gabapentin or acetaminophen exhibited no difference in pain control, side effects, and postpartum depression statistically. Using either one of these was considered acceptable.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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