Efficacy of Centrally Acting Neuromodulators During Management Hyperemesis Gravidarium: Hospital Based Study

Original Article

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ABSTRACT

Background: Hyperemesis gravidarum (HG), chemotherapy-induced nausea and vomiting, and postoperative nausea and vomiting were among the disorders alleviated by gabapentin's anti-nausea and anti-emetic properties.
Aim: To investigate the comparative impact of gabapentin versus standard treatment protocols for HG.
Methods: This randomized controlled open-label trial involved 160 pregnant women aged over 18 with HG. Participants were assigned to two equal groups: Group A, receiving 300mg of gabapentin, and Group B, receiving 7.5mg of metoclopramide.
Results: On days 2 and 3 after initial therapy, group A showed substantially lower Pregnancy-Unique Quantification of Emesis and Nausea (PQUE) scores than in group B (P <0.05). Eating scores over the first week were similar between the two groups. Urine acetone levels on day 7 were significantly different between groups (P= 0.042). Group A had considerably lower urine output on admission and days 1, 5, 6, and 7 (P <0.05), as well as lower fluid input on day 4 (P= 0.05). Fluid loss was higher in group A on admission and days 2 and 3 (P <0.05).
Conclusion: Gabapentin is a good alternative to metoclopramide in management of HG cases after initial standard replacement therapy for three days especially in lowering acetone in urine on day seven and decreasing PQUE score.

Key Words: Gabapentin, hyperemesis Gravidarum, neuromodulators.

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INTRODUCTION

Hyperemesis gravidarum (HG) is the most severe form of nausea and vomiting during pregnancy (NVP) .It is recognized by its usual clinical symptoms and by ruling out other possible causes of nausea and vomiting in pregnant women's. it is a leading cause of hospitalization in the first trimester of pregnancy[1].Typically it is characterized by More than three vomiting episodes per day, the presence of ketonuria, and weight loss of more than 3kg or 5% of body weight[2].

The exact cause of HG is still unknown but it has been linked to specific risk factors, such as multiple pregnancies or larger placental mass in molar pregnancies[3].

Many hormones are believed to be linked to the etiology of HG mainly beta human chorionic gonadotropin (B-HCG) which is reported in many researches to be higher in women with HG rather than the matched controls[4].

HG is more likely to develop among women who have had nausea and vomiting outside pregnancy, especially if they have a history of motion sickness or headaches. Additionally, some research indicates that HG runs in families especially in first degree relatives[5].

The modified Pregnancy-Unique Quantification of Emesis and Nausea (PUQE) index score was used to rate the intensity of nausea and vomiting during pregnancy. This tool is validated and objective for determining how severe various conditions are[6].

In order to prevent hospitalization, pregnant women with HG who are hemodynamically stable and able to tolerate oral intake can be treated at home with oral antiemetics[7].

Metoclopramide has antiemetic actions via inhibiting serotonin 5-hydroxytryptamine (5-HT3) and dopamine D2

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receptors in the chemoreceptor trigger zone (CTZ) of the brain's area postrema[8]. gabapentin was found to reduce nausea and vomiting in many conditions like chemotherapy induced nausea and vomiting (CINV), postoperative induced nausea and vomiting (PONV) and HG[9].

Gabapentin, a structural equivalent of gamma-aminobutyric acid (GABA), is believed to reduce neuropathic pain by interacting with voltage-gated N-type calcium ion channels, however its precise mode of action is unclear[10].

This study aimed to compare the gabapentin's therapeutic benefits and the standard-of-care therapy (metoclopramide) for treating HG.

PATIENTS AND METHODS

This randomized controlled open label study involved 160 pregnant women aged >18 years old, with one or more ketonuria, serum potassium levels <3.4mmol, lost >5% from their pre-pregnancy weight, tried one or more of antiemetics and failed, pregnant women with a normal, singleton pregnancy of under 14 weeks' gestation, as verified by fetal ultrasound, who had experienced daily vomiting for the last seven days.

In the 24 hours prior to enrollment, the mothers' PUQE scores were 13or higher. The Mansoura University Hospitals' Ethical Committee gave its approval for the study, which was carried out between March 2023 and March 2024 in Dakahlia, Egypt. Every patient provided written, informed consent. Pregnant women with serum potassium levels greater than 3.5 mmol, weight loss below 5%, and a history of gastrointestinal tract conditions, including peptic ulcers, gastroesophageal reflux disease, and others, were excluded.

Randomization and blindness:

Randomization was performed using an online program (http://www.randomizer.org), with each patient's code sealed in an opaque envelope. Patients were randomly assigned in a parallel fashion to two groups, with a 1:1 allocation ratio: Group A: received gabapentin 300mg and Group B: received metoclopramide 7.5mg[11].

At first, pilot study on 20 cases with severe hyperemesis was conducted at found that not suitable to take oral forms of gabapentin and metoclopramide as a start. As it is not ethical to leave a patient without definitive treatment and dehydrated all that time. So, we started rehydration using intravenous (IV) fluids of 2500ml\24hr divided as 1000ml saline 0.9%, 1000ml ringer lactate and 500ml 5% dextrose, multivitamins such as B-complex(B1, B3, B6, B12), anticoagulant such as low molecular weight heparin (LMWH), serum electrolyte monitoring and correction to reach a PQUE score ≤30% at day 3. Then study started after 3 days.

Beginning with one capsule bid, the study capsules were gradually increased to two capsules tid by day five. For days 6–7, patients who have troublesome nausea or vomiting but no bothersome side effects such as allergic reaction, clumsiness, unsteadiness, sleepiness and fatigue in gabapentin and allergic reaction, diarrhea, drowsiness, myalgia, fatigue and confusion in metoclopramide may increase to taking two capsules per day. The maximum daily doses were 2400mg for gabapentin and 60mg for metoclopramide, respectively. Follow up of the patients were by daily PQUE scoring system , eating score , serum potassium level monitoring, arterial blood gas (ABG) and urine output (UOP).

For data collection, an interviewer-administered questionnaire was used, which had two sections: one focusing on sociodemographic factors and the other on the PUQE score, with translations available when needed. The English version of the scale was provided upon request. The questionnaire included simple, closed-ended questions for ease of understanding, and it gathered essential sociodemographic information and details on nausea and vomiting in pregnancy.

PUQE scoring system:

Using a 5-point rating system, the 24-hour PUQE-24 is a self-assessment instrument for nausea (measured in hours during the last 24 hours), vomiting (number of episodes of vomiting during the previous 24 hours), and retching (number of episodes of retching during the previous 24 hours). More severe NVP is indicated by a higher score. There are three primary components to this interviewer-administered assessment. Five levels are available for each PUQE-24 scale component to score the intensity of nausea, vomiting, and retching or dry heaving within the previous 24 hours. The score might be as low as three or as high as fifteen. A PUQE score of less than six indicates mild hyperemesis gravidarum. Moderate hyperemesis is defined as a total PUQE score of 7–12, and severe hyperemesis is defined as a score of 13–15. The study did not include any patients younger than 18 years old. It took around 30 minutes on average to administer the PUQE score and perform the interview. The lead investigator used the PUQE score to reduce the possibility of data collection errors.

The consultant obstetrician's assessment of the intensity of nausea and vomiting comprised the second part of the evaluation. Within 24 hours of the patient's admission, both components of the evaluation were completed on the same day.

The change in Mother Risk-PUQE total scores from baseline to days 5 and 7 was the main outcome that was measured. A validated measure for evaluating NVP is the Mother Risk-PUQE diary. Baseline scores were derived from the 24-hour period prior to enrollment, based on patient recall. Following enrollment, participants

documented their daily Mother Risk-PUQE scores in a paper diary for a period of 7 days. The secondary outcomes consisted of the Mother Risk-PUQE sub-scores for nausea, vomiting, and retching, and a daily oral eating score. Each meal (breakfast, lunch, and dinner) received a score between 0 and 5, where 0 denoted nothing consumed, 1 only a small amount of liquids, 2 a small amount of food (such as bread or crackers), 3 slightly more than a small amount of food, 4 moderate food intake, and 5 normal or nearly normal food intake. Other secondary outcomes included clinical improvement in skin turgor which is the skin elasticity assessed in glabella and back of the hand, buffy eyelid, jaundice which is evaluated in the sclera of the eye and pallor which is assessed in conjunctivae and mucous membranes all are recorded daily as (present\ absent) and laboratory improvements such as K+ levels, acetone in urine by dipstick test, ABG results, and urine output assed in 24h according to fluid chart (normal range is (0.5-1ml/kg/hr.)).

Sample Size Calculation:

Sample size calculation was conducted using G*Power version 3.0.10, based on the mean difference in total Mother Risk-PUQE scores between Gabapentin-treated cases and control groups, as found in previous research[11]. With an effect size of 0.448, a 2-tailed test, a significance level of 0.05, and 80% power, the minimum required sample size per group was 79.

Statistical analysis

SPSS v26 was used to analyze the data (IBM Inc., Chicago, IL, USA). Histograms and the Shapiro-Wilk test were used to evaluate the data distribution's normality. The unpaired Student's *T*-test was used to compare the parametric quantitative data, which were displayed as mean and standard deviation (SD). The Mann-Whitney test was used to assess non-parametric data, which were presented as median and interquartile range (IQR). The Chi-square test or Fisher's exact test, as applicable, were used to assess the qualitative variables, which were displayed as frequency and percentage (%). Statistical significance was defined as a two-tailed *P* value of less than 0.05.

RESULTS

After 143 participants had their eligibility evaluated, 5 patients declined to take part in the study, and 8 patients did not fit the requirements. The remaining patients were divided into two equal groups of 80 at random. Every patient assigned was monitored and statistically examined (Figure 1).

PQUE scores on day 2 and 3 after initial therapy were significantly lower in group A than group B (P <0.05). PQUE score on admission, on day 1, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups. Eating score on admission, day 1, 2, 3, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups (Table 1).

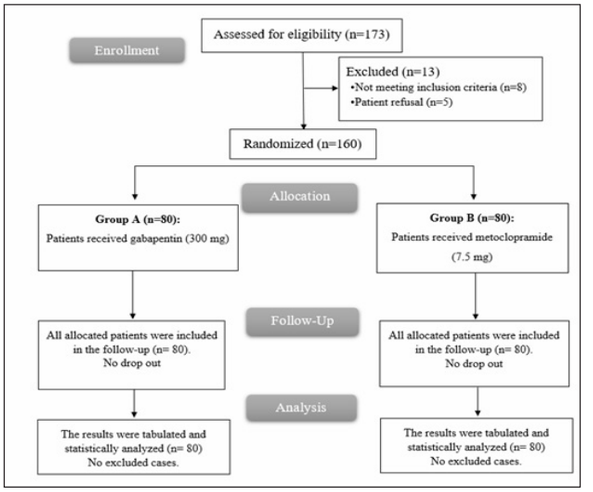

Fig. 1: CONSORT flowchart of the enrolled patients.

Table 1: PQUE and eating score of the studied groups:

	On admission	Day 1 after initial therapy	Day 2 after initial therapy	Day 3 after initial therapy	Day 4 after initial therapy	Day 5 after initial therapy	Day 6 after initial therapy	Day 7 after initial therapy
PQUE score								
Group A (*n*= 80)	13(13-14)	12(11-13)	10(10-12)	10(7-10)	8(7-10)	7(5-9)	7(5-9)	5(3-7)
Group B (*n*= 80)	14(13-14)	13(12-13)	12(10-13)	10(8-11)	8(7-10)	7(6-8)	7(6-8)	5(3-7)
P	0.638	0.203	0.025*	0.015*	0.191	0.960	0.310	0.312
Eating score								
Group A (*n*= 80)	0(0-0)	1(1-1)	1.5(1-3)	2(2-3)	3(2-4)	3(3-4)	3(3-5)	3(2-3)
Group B (*n*= 80)	0(0-0)	1(1-1)	2(1-3)	2(2-3)	3(2-4)	4(3-3.75)	3(3-5)	3(2-4)
P	0.317	0.162	0.717	0.534	0.703	0.330	0.827	0.344

Data is presented as median (IQR); *: Significant *P* value <0.05; PQUE: Pregnancy-unique quantification of emesis and nausea.

Five levels are available for each PUQE-24 scale component to score the intensity of nausea, vomiting, and retching.

A PUQE score of less than 6 indicates mild hyperemesis gravidarum. Moderate hyperemesis is defined as a total PUQE score of 7–12, and severe hyperemesis is defined as a score of 13–15.

In eating score each meal (breakfast, lunch, and dinner) received a score between 0 and 5, where 0 denoted nothing consumed, 1 only a small amount of liquids, 2 a small amount of food (such as bread or crackers), 3 slightly more than a small amount of food, 4 moderate food intake, and 5 normal or nearly normal food intake

Demographic data, medical, surgical history and gestational age on admission were insignificantly different between both groups. The type of current pregnancy whether it was spontaneous, or by assisted reproductive techniques (ART) or by ovulation induction significantly different between both groups (P= 0.049) it showed that spontaneous pregnancy and pregnancies by ovulation induction was higher in group B (96.25%) and (2.5%) respectively compared to (88%) and (1.25%) in group A while pregnancies by ART was higher in group A (10%) compared to (1.25%) in group B. The presence of GS was positive in all patients in both groups. No. of GS was one sac in all patients in both groups. All patients had fetal pole and pulsation (Table 2).

Table 2: Demographic, medical, surgical history, current pregnancy evaluation data of the studied groups:

		Group A (n= 80)	Group B (n= 80)	P
Age (years)		26.05±4.71	26±4.37	0.945
Body weight (kg)		66.47±6.91	68.62±7.33	0.058
BMI (kg/m^2)		22.11±2.77	22.53±3.53	0.398
Previous history of HEG		31(38.75%)	35(43.75%)	0.521
Gravidity	Primigravida	20(25.0%)	19(23.75%)	0.853
	Multigravida	60(75.0%)	61(76.25%)	
Parity		1.03±0.95	1.19±0.98	0.290
Abortion		0.64±1.02	0.44±1.03	0.219
Past medical history	Hypothyroidism	2(2.5%)	3(3.75%)	1
	Hyperthyroidism	4(5.0%)	3(3.75%)	1
	Chronic hypertension	1(1.25%)	0(0.0%)	1
	FMF	1(1.25%)	3(3.75%)	0.620
	Free	72(90.0%)	71(88.75%)	0.797
Past surgical history	Thyroidectomy	1(1.25%)	1(1.25%)	1
	Myomectomy	0(0.0%)	1(1.25%)	1
	Uterine metroplasty	2(2.5%)	1(1.25%)	1
	Free	77(96.25%)	77(96.25%)	1
Current pregnancy evaluation data				
Type of current pregnancy	Spontaneous	71(88.75%)	77(96.25%)	0.049*
	Ovulation induction	1(1.25%)	2(2.5%)	
	ART	8(10.0%)	1(1.25%)	
Gestational age on admission (weeks)		9.38±1.84	9.6±1.93	0.452
Presence of GS		80(100.0%)	80(100.0%)	--
Number of GS	One sac	80(100.0%)	80(100.0%)	--
Presence of fetal pole		80(100.0%)	80(100.0%)	--
Presence of pulsation		80(100.0%)	80(100.0%)	--
CRL (weeks)		9.49±1.76	9.6±1.85	0.694

Data are presented as mean±SD or frequency (%); *: Significant P value <0.05; BMI: Body mass index; HEG: Hyperemesis gravidarum; FMF: Familial mediterranean fever; ART: Assisted reproductive technology; GS: Gestational sac; CRL: Crown-rump length.

Skin turgor, buffy eyelid, jaundice and pallor on admission, on day 1, 2, 3, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups. UOP on admission, day 1, 6, 5 and 7 after initial therapy was substantially lower in group A than group B (P <0.05) and on day 2, 3, 4 after initial therapy were insignificantly different between both groups. Fluid input on day 4 after initial therapy was substantially lower in group A than group B (P= 0.05) and on admission, on day 1, 2, 3, 5, 6 and 7 after initial therapy were insignificantly different

between both groups. Fluid output on day 5 after initial therapy was significantly lower in group A than group B (P= 0.042) and on admission, on day 1, 2, 3, 4, 6 and 7 after initial therapy were insignificantly different between both groups. Fluid loss on admission, day 2 and 3 after initial therapy were considerably higher in group A than group B (P <0.05) and on day 1, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups (Table 3).

Table 3: Clinical examination signs and fluid management chart parameters of the studied groups all over the treatment period:

	On admission	Day 1 after initial therapy	Day 2 after initial therapy	Day 3 after initial therapy	Day 4 after initial therapy	Day 5 after initial therapy	Day 6 after initial therapy	Day 7 after initial therapy
Skin turgor								
Group A (n= 80)	52(65.82%)	52(65.82%)	50(63.29%)	49(62.03%)	49(62.03%)	49(62.03%)	49(62.03%)	49(62.03%)
Group B (n= 80)	40(51.28%)	40(51.28%)	40(51.28%)	40(51.28%)	40(51.28%)	40(51.28%)	40(51.28%)	50(64.1%)
P	0.064	0.064	0.128	0.174	0.174	0.174	0.174	0.787
Buffy eyelid								
Group A (n= 80)	4(5.06%)	4(5.06%)	4(5.06%)	4(5.06%)	4(5.06%)	4(5.06%)	4(5.06%)	4(5.06%)
Group B (n= 80)	2(2.56%)	2(2.56%)	2(2.56%)	2(2.56%)	2(2.56%)	2(2.56%)	2(2.56%)	2(2.56%)
P	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681
Jaundice								
Group A (n= 80)	6(7.5%)	6(7.5%)	7(8.75%)	8(10.13%)	7(8.86%)	7(8.86%)	7(8.86%)	7(8.86%)
Group B (n= 80)	9(11.25%)	9(11.25%)	9(11.39%)	9(11.54%)	9(11.54%)	7(8.97%)	6(7.69%)	7(8.86%)
P	0.416	0.416	0.580	0.776	0.579	0.980	0.791	1
Pallor								
Group A (n= 80)	25(31.25%)	27(33.75%)	26(32.5%)	25(31.25%)	25(31.65%)	26(32.91%)	26(32.91%)	26(32.91%)
Group B (n= 80)	19(23.75%)	19(23.75%)	18(22.78%)	18(23.08%)	18(23.08%)	18(23.08%)	18(23.08%)	18(23.08%)
P	0.288	0.162	0.171	0.248	0.229	0.170	0.170	0.170
UOP (ml\24hr)								
Group A (n= 80)	727.5±231.52	806.25±234.44	891.88±249.74	959.13±250.58	1034.62±252.82	1071.15±198.29	1119.49±223.97	1172.73±235.02
Group B (n= 80)	786.88±193.36	895.5±225.94	1073.54±1038.97	983.33±224.28	1094.49±247.34	1144.03±207.96	1219.23±145.99	1244.23±186.36
P	0.080	0.015*	0.130	0.524	0.137	0.027*	0.001*	0.037*
Fluid input (ml\24hr)								
Group A (n= 80)	1379.38±388.74	1349.38±360.16	1385.63±367.1	1380±349.1	1380.77±306.66	1401.28±202.26	1620.51±1543.85	1444.23±182.33
Group B (n= 80)	1325±275.82	1347.5±255.93	1347.47±230.23	1364.1±210.73	1457.05±148.53	1456.41±148.23	1483.33±117.79	1485.9±73.37
P	0.309	0.970	0.434	0.730	0.050*	0.054	0.435	0.063
Fluid output (ml\24hr)								
Group A (n= 80)	1088.75±1034.8	1025±241.57	1073.13±278.44	1253.13±1024.4	1366.67±1470.88	1265.38±206.91	1478.21±1562.62	1333.97±220.76
Group B (n= 80)	1107.5±1026.4	1089.38±218.41	1147.72±218.33	1171.43±233.74	1274.74±236.92	1326.28±160.3	1364.23±199.2	1397.44±164.93
P	0.909	0.079	0.062	0.496	0.587	0.042*	0.524	0.044*
Fluid loss (ml\24hr)								
Group A (n= 80)	435.63±380.8	339.38±315.6	429.5±959.63	248.75±207.3	226.28±387.86	162.18±200.19	142.95±153.47	118.59±165.75
Group B (n= 80)	330±226.64	271.88±201.71	201.01±184.92	175.64±195.36	170.38±193.26	137.05±189.29	98.33±151.34	94.23±140.26
P	0.035*	0.109	0.039*	0.024*	0.256	0.422	0.069	0.323

Data are presented as mean±SD or frequency (%); *: Significant P value <0.05; UOP: Urine output.

Level of acetone in urine by dipstick on admission, on day 1, 2, 3, 4, 5, and 6 after initial therapy were insignificantly different between both groups. Level of acetone in urine on day 7 after initial therapy was considerably different between both groups (P= 0.042) (Table 4).

PH on day 1 after the initial therapy was substantially lower in group A than group B (P= 0.045) and PH on admission, day 2, 3, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups. Serum K, SGPT, SGOT, albumin and serum bilirubin on admission, day 1, 2, 3, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups. Serum Na and serum creatinine on admission were significantly lower in group A than group B (P <0.05). Serum Na and serum creatinine on day 1, 2, 3, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups. RBG on days 2, 3, 4 and 5 was significantly lower in group A than group B (P <0.05) and on admission, day 1, 6 and 7 were insignificantly different between both groups (Table 5).

Table 4: Level of acetone in urine of the studied groups:

			Group A (n= 80)	**Group B (n= 80)**	***P***
On admission		+1	0(0.0%)	2(2.5%)	
		38(47.5%)	31(38.75%)		
+2					0.357
+3		41(51.25%)	45(56.25%)		
+4		1(1.25%)	2(2.5%)		
		+1	16(20.0%)	12(15.0%)	
		+2	45(56.25%)	37(46.25%)	
	On day 1 after initial therapy	+3	18(22.5%)	28(35.0%)	0.237
		+4	0(0.0%)	2(2.5%)	
		Nill	1(1.25%)	1(1.25%)	
		+1	21(26.25%)	23(29.11%)	
		+2	28(35.0%)	26(32.91%)	
	On day 2 after initial therapy	+3	12(15.0%)	17(21.52%)	0.542
		Nill	19(23.75%)	13(16.46%)	
		+1	29(36.25%)	39(50.0%)	
		+2	25(31.25%)	24(30.77%)	
	On day 3 after initial therapy	+3	6(7.5%)	4(5.13%)	0.214
		Nill	20(25.0%)	11(14.1%)	
		+1	40(51.28%)	39(50.0%)	
		+2	13(16.67%)	17(21.79%)	
Follow-up	On day 4 after initial therapy	+3	6(7.69%)	1(1.28%)	0.253
		+4	1(1.28%)	0(0.0%)	
		Nill	18(23.08%)	21(26.92%)	
		+1	28(35.9%)	32(41.03%)	
		+2	13(16.67%)	7(8.97%)	
	On day 5 after initial therapy	+3	5(6.41%)	0(0.0%)	0.061
		+4	1(1.28%)	0(0.0%)	
		Nill	31(39.74%)	39(50.0%)	
		+1	16(20.51%)	27(34.62%)	
		+2	8(10.26%)	5(6.41%)	
	On day 6 after initial therapy	+3	6(7.69%)	1(1.28%)	0.066
		Nill	48(61.54%)	45(57.69%)	
		+1	9(11.54%)	22(28.21%)	
		+2	6(7.69%)	4(5.13%)	
	On day 7 after initial therapy	+3	4(5.13%)	1(1.28%)	0.042*
		+4	2(2.56%)	0(0.0%)	
		Nill	56(71.79%)	51(65.38%)	

Data is presented as frequency (%); *: Significant P value <0.05.

Table 5: Laboratory findings of the studied groups:

	On admission	Day 1 after initial therapy	Day 2 after initial therapy	Day 3 after initial therapy	Day 4 after initial therapy	Day 5 after initial therapy	Day 6 after initial therapy	Day 7 after initial therapy
Ph								
Group A (*n*= 80)	7.4±0.07	7.37±0.05	7.39±0.04	7.39±0.04	7.39±0.03	7.39±0.03	7.39±0.02	7.39±0.03
Group B (*n*= 80)	7.39±0.07	7.39±0.05	7.39±0.04	7.4±0.06	7.39±0.03	7.4±0.03	7.39±0.03	7.4±0.02
P	0.362	0.045*	0.509	0.111	0.349	0.303	0.439	0.414
Serum K (mmol/L)								
Group A (*n*= 80)	2.8±0.45	3.01±0.46	3.22±0.47	3.38±0.48	3.55±0.5	3.68±0.43	3.85±0.57	4±0.6
Group B (*n*= 80)	2.96±2.86	2.94±0.42	3.22±0.49	3.37±0.54	3.98±3.36	3.75±0.47	3.9±0.48	3.99±0.4
P	0.618	0.304	0.972	0.916	0.272	0.365	0.544	0.925
Serum Na (mmol/L)								
Group A (*n*= 80)	140.08±5.67	140.03±4.66	140.04±3.86	138.51±11.62	137.79±14.5	139.74±2.43	139.71±2.73	140.14±2.86
Group B (*n*= 80)	143.05±5.54	141.16±3.87	140.94±3.8	153.49±113.76	157.23±147.04	140.24±2.33	138.27±14.81	140.06±2.43
P	<0.001*	0.095	0.141	0.243	0.247	0.192	0.401	0.857
Serum creatinine (mg/dL)								
Group A (*n*= 80)	0.63±0.11	0.64±0.13	0.63±0.1	0.62±0.1	0.61±0.09	0.61±0.1	0.6±0.1	1.26±4.11
Group B (*n*= 80)	0.67±0.11	0.65±0.09	0.64±0.09	0.63±0.11	0.69±0.62	0.62±0.1	0.63±0.12	0.69±0.62
P	0.009*	0.409	0.240	0.265	0.247	0.634	0.196	0.225
SGPT (IU/L)								
Group A (*n*= 80)	47.5±82.52	38.53±36.32	37.11±41.4	32.53±28.27	70.94±341.08	28.97±19.04	28.71±14.62	27.78±12.82
Group B (*n*= 80)	41.76±41.18	39.91±39.71	35.86±39.5	48±129.29	33.37±37.78	33.62±35.35	33.91±24.2	31.4±21.01
P	0.579	0.818	0.846	0.297	0.335	0.309	0.106	0.197
SGOT (IU/L)								
Group A (*n*= 80)	40.49±61.67	35.3±27.73	38.01±72.1	33.86±35.25	31.46±29.18	31.05±29.01	30.4±29.08	29.51±25.25
Group B (*n*= 80)	39.45±43.02	32.83±30	30.14±22.99	28.62±16.98	27.15±16.14	27.19±13.43	27.37±10.72	27.14±9.94
P	0.902	0.589	0.356	0.237	0.256	0.288	0.390	0.441
Albumin (g/dL)								
Group A (*n*= 80)	4.11±0.49	3.96±0.43	3.86±0.45	3.85±0.46	3.92±0.51	4.5±4.35	4.04±0.45	4.06±0.47
Group B (*n*= 80)	4.13±0.55	3.92±0.63	3.91±0.58	3.95±0.5	4±0.43	4.55±4.43	4.09±0.4	4.08±0.42
P	0.820	0.668	0.532	0.215	0.263	0.944	0.511	0.786
Serum bilirubin (mg/dL)								
Group A (*n*= 80)	0.64±0.38	0.67±0.37	0.66±0.39	0.65±0.34	0.63±0.35	0.63±0.38	0.66±0.43	0.65±0.44
Group B (*n*= 80)	0.72±0.67	0.71±0.65	0.7±0.66	0.68±0.71	0.63±0.48	0.59±0.39	0.58±0.31	0.57±0.31
P	0.368	0.605	0.630	0.781	0.985	0.537	0.190	0.227
RBG (mg/dl)								
Group A (*n*= 80)	77.58±11.98	79.19±13.15	82.14±13.59	83.7±14.52	85.33±16.27	87.5±14.45	89.56±18.72	93.97±15.3
Group B (*n*= 80)	76.29±9.02	81.05±13.74	87.42±19.51	90.45±16.36	94.41±14.86	93.74±16.44	91.77±13.17	104.17±103.6
P	0.444	0.382	0.049*	0.007*	<0.001*	0.013*	0.396	0.391

Data are presented as mean±SD; *: Significant *P* value <0.05; K: Potassium; Na: Sodium; SGPT: Serum glutamic pyruvic transaminase; SGOT: Serum glutamic-oxaloacetic transaminase; RBG: Random blood glucose.

DISCUSSION

In an open-label experiment including nine patients with breast cancer, gabapentin was first demonstrated to alleviate medically resistant CINV in (2003). Later, several RCTs confirmed the effectiveness of gabapentin in managing postoperative nausea as well as CINV[12].

Our analysis revealed that Group A had a significantly lower PUQE score on days 2 and 3 after treatment, in comparison to Group B. However, no significant differences were found between the two groups on admission, day 1, or on days 4 through 7 following the initial therapy. These results are consistent with the work of Guttuso *et al*.,[11] Who found a significant reduction in the PUQE score for the gabapentin group compared to the active comparator group (oral ondansetron or oral metoclopramide)[13]. Also observed greater reductions in the Motherisk-PUQE scores in the gabapentin group than in the comparator group.

Furthermore, there was a significant difference in the type of pregnancy between the two groups in our study as it showed that spontaneous pregnancy and pregnancies by ovulation induction was higher in group B (96.25%) and (2.5%) respectively compared to (88%) and (1.25%) in group A while pregnancies by ART was higher in group A (10%) compared to (1.25%) in group B.

However, there were no significant differences in gestational age on admission and CRL between the groups. The presence of a gestational sac (GS) was confirmed in all patients in both groups, and each patient had one sac. All patients also had a fetal pole and pulsation. Guttuso *et al*.,[11] similarly reported no significant difference in gestational age between the gabapentin and active comparator groups. Additionally, Grant *et al*.,[14] showed that gabapentin is effective in reducing postoperative nausea, vomiting, and the need for rescue antiemetic medications.

In our study, there were no significant differences in clinical examination signs between the two groups at various time points after initial therapy. Group A had significantly lower urine output (UOP) on admission, day 1, day 5, day 6, and day 7 compared to Group B, but no considerable differences were found on days 2, 3, and 4. Fluid input was significantly lower in Group A on day 4, while no differences were observed on other days. Fluid output which is UOP plus insensible water loss through sweating and inhalation was lower in Group A on day 5, but there were no differences on other days. Fluid loss was higher in Group A on admission, and on days 2 and 3, with no differences on other days. Acetone levels in urine showed no significant differences between groups until day 7, when they were substantially different. In agreement with our findings, Guttuso *et al*.,[11] showed no significant difference in ketonuria grades between the gabapentin and active comparator groups on admission.

A study looked into the connection between the severity of HG and urinary ketone levels, finding that women with more severe HG, as indicated by the 24-hour Pregnancy Unique Quantification of Emesis (PUQE-24), showed a slightly higher median level of ketones in their urine[15].

In our study, Group A had a significantly lower pH on day 1 after therapy compared to Group B (P= 0.045). However, no significant differences were found in pH on admission or on days 2-7 after therapy. Other lab values, including potassium, SGPT, SGOT, albumin, and bilirubin, did not differ considerably between the groups at any point. On admission, Group A had lower serum sodium and creatinine levels than Group B, but no significant differences were found later. Additionally, random blood glucose levels were significantly lower in Group A on days 2-5, but no differences were seen on admission, day 1, day 6, or day 7. Also, Elarby *et al*.,[16] found that the serum creatinine of the studied patients with a mean value 0.7±0.14mg/dl. SGPT with a mean value 46.2±55.99U/L. SGOT with a mean value 36±23.03U/L. HCO3 with a mean value 18.68±3.32mEq/L. PaCO2 with a mean value 32.2±7.33mmHg. pH with a mean value of 7.37±0.06.

In the current study, eating scores on admission, day 1, 2, 3, 4, 5, 6 and 7 after initial therapy were insignificantly different between both groups. In contrast, Guttuso *et al*.,[11] showed that the nutrition score improved substantially in the Gabapentin group compared to the active comparator group. The varying outcomes could originate from the various dosages of both medications used; our trial provided gabapentin at 300mg and metoclopramide at 7.5mg, in contrast to the Guttuso investigation, which used oral gabapentin, oral ondansetron, and oral metoclopramide. Moreover, Guttuso *et al.,*[17] showed that with the treatment of gabapentin at 300mg po tid for patients with HG could substantially lower nausea and emesis from baseline to days 12–14 by 80% and 94%, respectively, and by 84% and 98%, respectively, from baseline to days 19–21.

LIMITATIONS

Limitations of the study included that the study was in a single center. It did not evaluate the long-term effect of the drug used on the pregnant women.

CONCLUSION

Gabapentin is a good alternative to metoclopramide in management of HG cases after initial standard replacement therapy for three days especially in lowering acetone in urine on day seven and decreasing PQUE score.

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CONFLICT OF INTERESTS

There is no conflict of interests.

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