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Gabapentin versus Midazolam as premedication for anxiolytics in Total Abdominal Hysterectomies

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ABSTRACT

Background and Objectives: The uterus can frequently be surgically eliminated through an abdominal incision in an abdominal hysterectomy. During the process, pre-operative anxiety in patients in response to unfavorable conditions can lead to physiological changes such as heart arrhythmias, tachycardia, and hypertension, which can impact patient's surgery experience and result in adverse effects and a brief hospital stay following surgery. Therefore, it is fundamental to reduce a patient's anxiety by performing a thorough pre-anesthetic treatment. The present study aimed at elucidating the comparison between Gabapentin and Midazolam in reducing pre-operative anxiety in patients undergoing abdominal hysterectomy. **Material and methods:** A double-blinded a controlled trial occurred at the Department of Anesthesia, Services Hospital Lahore. 52 cases entirety, divided into two groups (G group and M group) with 26 treatments each. Non-probability, sequential sampling was the method used. **Results:** According to the study's findings, the Midazolam group's mean systolic and diastolic blood pressures were considerably lower than those of the Gabapentin group. Similarly, the Gabapentin group's mean heart rates were 98.30 ± 14.09 bpm, whereas the Midazolam group's was 83.55 ± 8.08 bpm.The mean respiratory rate was slightly higher in the Midazolam group (18.55 ± 15.22 breaths/min) compared to the Gabapentin group (16.15 ± 2.46 breaths/min), but this difference was not statistically significant (t = 0.696, p = 0.491). The mean Hamilton Anxiety Scoring Time was significantly lower in the Midazolam group (4.85 ± 0.88 min) compared to the Gabapentin group (7.45 ± 2.69 min). The study has indicated that both drugs significantly reduced Hamilton Anxiety scores, indicating effective anxiolytic properties. **Conclusions:** Gabapentin group had a higher as well as inconsistent anxiety reduction while Midazolam showed comparatively reliable anxiolytic effects.

INTRODUCTION

After cesarean births and deliveries, hysterectomy, or the surgical removal of the uterus, is the second most common treatment performed on women globally[1]. It is performed vaginally or abdominally[2]. The hysterectomy can be done with or without the removal of cervix and adnexa, depending upon the indications, disease, and patient's condition[3]. The most common form of therapy for removal of the uterus through an abdominal incision is abdominal hysterectomy, frequently referred to as extra fascial hysterectomy. This procedure is indicated in conditions like abnormal or excessive uterine bleeding, endometriosis, malignancy, uterine leiomyoma, and pelvic organ prolapse[4].

Pre-operative anxiety in patients in response to unfavorable conditions can lead to physiological changes such as hypertension, tachycardia, and cardiac arrhythmias which can affect the patient's surgical experience[5] and lead to poor outcomes and prolonged patient stay at hospital after surgery[6]. Therefore, it is fundamental to reduce a patient's anxiety by performing a thorough pre-anesthetic treatment[7]. It is reported in many studies that anxiolytic premedication is generally preferred over pharmacological interventions per-operatively for the reduction of anxiety[8,9]. Different medications such as benzodiazepines, Gabapentin, opioids, NSAIDS etc. are given to the patient within a short period prior to surgery for anxiolysis[10]. On the other hand, Midazolam, a benzodiazepine, is one of the most reliable medicines for anxiolysis, retrograde amnesia, and sedation owing to its immediate effect[11]. Tablet Midazolam, the

trade name for Midazolam, is a short acting sedating and anxiolytic agent used in pre-surgical treatments by inhibiting neurotransmitter gamma-aminobutyric acid[12]. Tablet Gabapentin and Pregabalin, belonging to Gabapentinoids and having structural analogy with y-aminobutyric acid, exhibit anti-hyperalgesic, and anti-allodynic properties. They are also used in post-operative pain relief treatment and widely in premedication for preoperative anxiolysis due to their high binding affinity for the alpha-2-delta sub-unit of the calcium channel, which releases excitatory neurotransmitters[14]. Studies have shown mixed results on the efficacy of Gabapentin for anxiolysis. Although the literature has shown enough evidence of the efficiency of Gabapentin in post-operation pain relief treatments, there is a limited clinical experience of its use and efficacy in pre-operative medication. The novel benzodiazepine midazolam (Midazolam) has enough experience being injected through the muscle and via the gastrointestinal tract but less is known about how to give it orally[15]. Therefore, present study is aimed at elucidating the comparison between Gabapentin and Midazolam in reducing pre-operative anxiety in patients undergoing abdominal hysterectomy.

MATERIALS AND METHODS

After receiving ethical authorization from the Committee on Ethics and obtaining written consent from each participant, a randomized controlled experiment with a double-blind study was conducted at the Department of the use of anesthesia Services Hospital Lahore. The study was carried out from October 1, 2024, to March 31, 2025, with a 95% confidence level and 5% confidence limit and 80% testing power at (www.openepi.com) we determined the necessary values such as time to first analgesic (min, mean±SD). Non-probability sampling proved most suitable because of its use of consecutive sampling technique.

Inclusion and Exclusion Criteria

Fifty-two female patients aged 35-45 years scheduled for day-case surgery in Services Hospital Lahore elective surgery admitted during October 1, 2024 to March 31, 2025 were included in the study having ASA-I and ASA-II. Patients were randomly allocated to two groups (26 patients in each); gabapentin (Group G) and midazolam (Group M). Exclusion from the study applied to the patients with neurologic disorders, bleeding diastheses, emergency surgery, hypertension, ischemic heart disease, ASA-III/IV and history of diabetes mellitus. Exclusion from the study also applied to patients who were taking β-blockers, Ca++ channel blockers and also benzodiazepines since their hospital admission.

Data Collection Procedure

52 patients receiving optional abdominal surgery with salpingo-oophorectomy from the operating room of the Faculty of Obstetricians & Gynecology Services hospital, Lahore, will be included in this study following approval from the hospital ethics committee. Patient's informed consent will be obtained. Patient's bio data (name, age, gestational age, BMI, hemoglobin level, ASA status, parity, number of previous cesarean sections) will be noted.

A computer-generated table was used to randomly assign the patients to either of the two groups receiving treatment (Midazolam and Gabapentin). Prior to beginning treatment, vital signs such as heart rate, blood pressure, respiration rate, and saturation were recorded. After that, the gabapentin group received gabapentin dose and the midazolam group received midazolam dose before incision. The vitals of patients were checked again in order to note any change in the aforementioned factors, thereby indicating the levels of anxiety in the patients treated with either of the two anxiolytics. For blinding purposes, all of the infusions were given the same label. One hour prior to surgery, the first dose of the study drug was given. The hospital pharmacy produced all of the research medications, and each patient was given a unique code number. After that, the data was collected. Anxiety score was assessed at 45 min minutes after surgery. Data was collected on Performa (attached).

Statistical Analysis

Researchers utilized IBM SPSS 24.0 (IBM Chicago SPSS Inc) software for statistical analysis of compiled systematic data collection. The researchers compiled their findings through the platform. The statistical analysis showed Mean ± SD as the representation format for age, weight, and anxiety score variables. Research conducted through independent samples t-test enabled the examination of mean variable differences. The statistics for qualitative variables including patient ASA status appeared as frequencies together with corresponding percentages. The Chi-square method determined treatment relationship patterns. The study used $p < 0.05$ as its significant threshold at a 5% level of significance. The study employed 95% confidence level as its standard significance measure throughout all statistical assessments. The study findings were presented as mean and standard deviation in addition to number and percentages. There was a comparison of anxiety score parameters against each other using "unpaired t -test". The P value determined whether the findings reached statistical significance; $P < 0.01$ indicated significance at 1% level while $P < 0.001$ indicated high significance.

RESULTS

52 female patients, whose ages ranged from 35 to 45 on average, were scheduled for day surgery. Two groups of 26 patients each were randomly assigned to either gabapentin (Group G) or midazolam (Group M). The baseline anxiety scores of both groups were comparable. The patients with neurologic disorders, bleeding diastheses, emergency surgery, hypertension, ischemic heart disease, ASA-III/IV and history of diabetes mellitus were excluded from the study. Patients who received β-blockers, Ca++ channel blockers and took benzodiazepines starting from hospital admission were excluded from this research. The comparison between the systolic blood pressure of the patients exposed to gabapentin as well as midazolam have been shown in the table 1.

The mean systolic blood pressure was significantly lower in the Midazolam group (117.00 ± 12.18 mmHg) compared to the Gabapentin group (127.00 ± 9.79 mmHg). This

difference was statistically highly significant (t = 2.86, p = 0.007) as depicted in table 1.

Table 1

The Comparison between Gabapentin and Midazolam regarding Systolic Blood Pressure

	Group	
	Gabapentin	Midazolam
N	26	26
Mean	127.00	117.00
A Std. Deviation	9.787	12.183
A Std. Error Mean	2.188	2.724
The t-value	2.86**	
Prob.	0.007	

* denotes Significant value at (P<0.05); ** denotes highly significant value at (P<0.01); NS denotes Non-significant value at (P>0.05)
SD (Standard Deviation), SE (Standard Error)

Table 2

The Comparison between Gabapentin and Midazolam regarding Diastolic Blood Pressure

	Group	
	Gabapentin	Midazolam
N	26	26
Mean	85.50	73.50
A Std. Deviation	7.592	9.333
A Std. Error Mean	1.698	2.087
The t-value	4.46**	
Prob.	0.000	

The mean diastolic blood pressure was significantly lower in the Midazolam group (73.50 ± 9.33 mmHg) compared to the Gabapentin group (85.50 ± 7.59 mmHg). This difference was statistically highly significant (t = 4.46, p = 0.000) as shown in Table 2.

Table 3

The Comparison between Gabapentin and Midazolam regarding Heart Rate

	Group	
	Gabapentin	Midazolam
N	26	26
Mean	98.30	83.55
Std. Deviation	14.094	8.082
Std. Error Mean	3.152	1.807
t-value	4.06**	
Prob.	0.000	

The mean heart rate was significantly lower in the Midazolam group (83.55 ± 8.08 bpm) compared to the Gabapentin group (98.30 ± 14.09 bpm). This difference was statistically highly significant (t = 4.06, p = 0.000).

Table 4:

Comparison between Gabapentin and Midazolam regarding Respiratory Rate

	Group	
	Gabapentin	Midazolam
N	26	26
Mean	16.15	18.55
A Std. Deviation	2.455	15.223
A Std. Error Mean	0.549	3.404
t-value	0.696^{NS}	
Prob.	0.491	

The mean respiratory rate was slightly higher in the Midazolam group (18.55 ± 15.22 breaths/min) compared to the Gabapentin group (16.15 ± 2.46 breaths/min), but this difference was not statistically significant (t = 0.696, p = 0.491) as depicted in Table 4.

Table 5

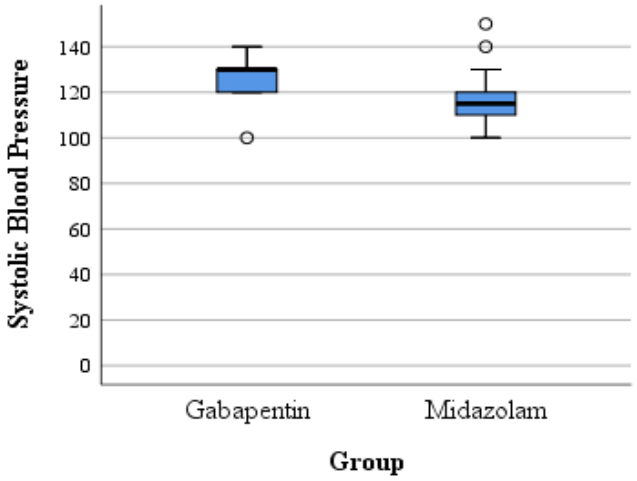
Comparison between Gabapentin and Midazolam regarding Hamilton Anxiety Scoring Time (min)

	Group	
	Gabapentin	Midazolam
N	26	26
Mean	7.45	4.85
A Std. Deviation	2.685	0.875
A Std. Error Mean	0.600	0.196
t-value	4.12**	
Prob.	0.000	

The Hamilton Anxiety Scoring Time mean score in the Midazolam group (4.85 ± 0.88 min) proved lower than the Gabapentin group mean score (7.45 ± 2.69 min). The statistical results indicated a highly important difference (t = 4.12, p = 0.000) according to Table 5.

Figure 1

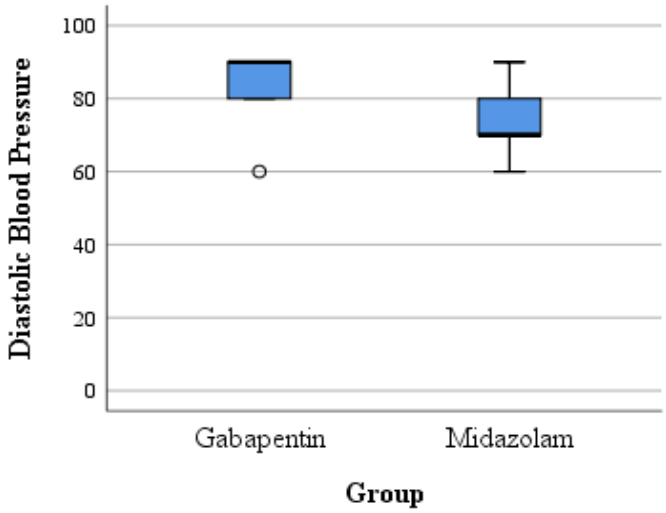
Mean plot representation of Gabapentin and Midazolam in Systolic Blood Pressure



The graph shows higher median systolic blood pressure in the Gabapentin medication group when compared to the Midazolam medication group. The difference was statistically highly significant (t = 2.86, p = 0.007), indicating that Midazolam significantly reduced systolic blood pressure more than Gabapentin.

Figure 2

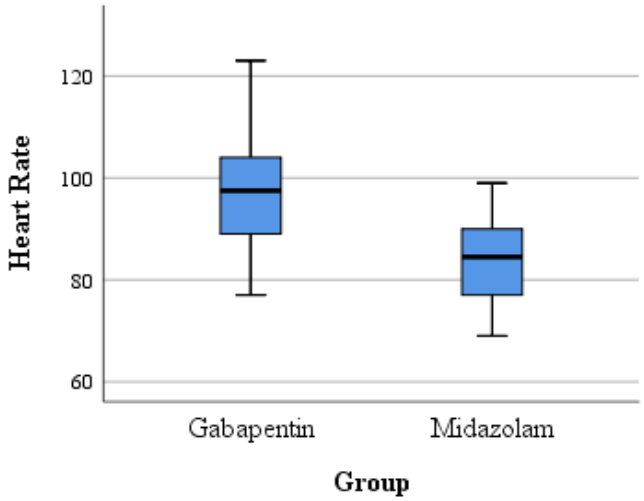
Mean plot representation of Gabapentin and Midazolam in Diastolic Blood Pressure



The graph shows that the diastolic blood pressure was higher in the Gabapentin group compared to the Midazolam group. This difference was statistically highly significant (t = 4.46, p = 0.000), indicating that Midazolam significantly reduced diastolic blood pressure more effectively than Gabapentin.

Figure 3

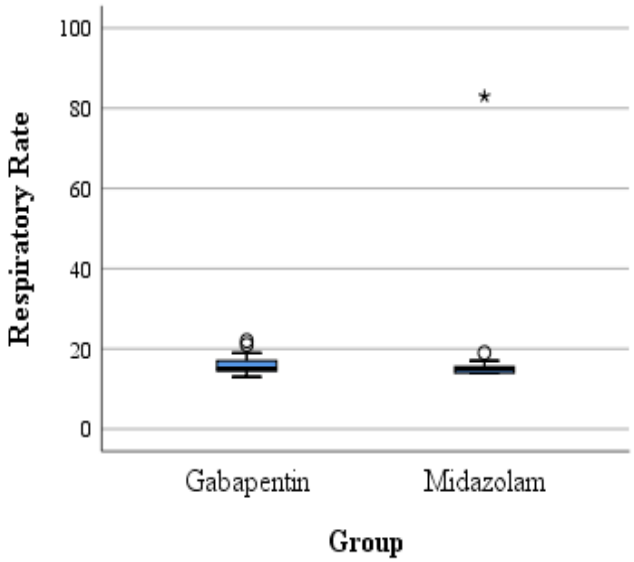
Mean plot representation of Gabapentin and Midazolam in Heart Rate



The graph illustrates that the Gabapentin group exhibited a higher median heart rate with a wider range and greater variability compared to the Midazolam group, which had a lower and more consistent heart rate. This suggests that Midazolam may offer better autonomic control and stability during treatment.

Figure 4

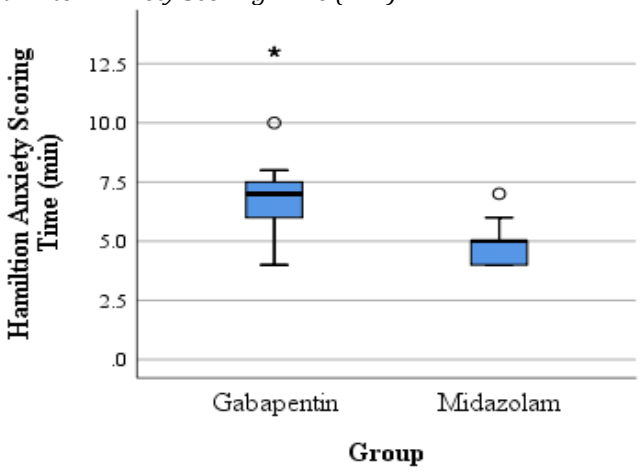
Mean plot representation of Gabapentin and Midazolam in Respiratory Rate



The graph shows that respiratory rates in both groups were generally similar, with slightly lower variability in the Gabapentin group. However, the Midazolam group displayed a notable outlier, suggesting occasional extreme values, though most participants remained within a normal range.

Figure 5

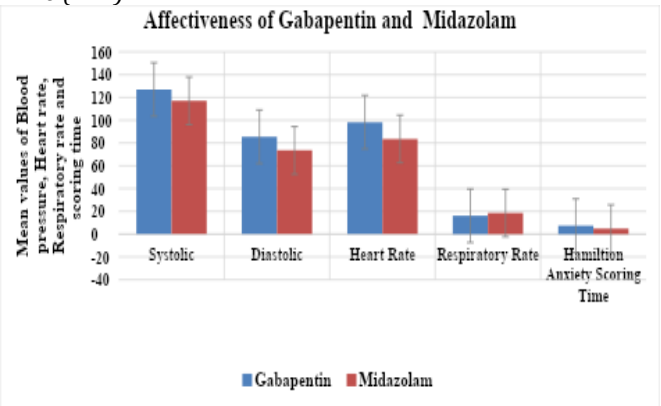
Mean plot representation of Gabapentin and Midazolam in Hamilton Anxiety Scoring Time (min)



The graph reveals that the Gabapentin group had a higher and more variable Hamilton Anxiety Score, including several outliers, suggesting inconsistent anxiety reduction. In contrast, the Midazolam group showed lower and more consistent scores, indicating superior and reliable anxiolytic effects.

Figure 6

Comparative Mean plot representation of Gabapentin and Midazolam in Systolic and diastolic Blood Pressure, Respiratory Rate , Heart Rate and Hamilton anxiety Scoring Time (min)



The bar graph illustrates that both Gabapentin and Midazolam resulted in reductions across systolic and diastolic blood pressure, respiratory rate and heart rate, with Gabapentin generally showing slightly higher values. Additionally, both drugs significantly reduced Hamilton Anxiety scores, indicating effective anxiolytic properties.

DISCUSSION

Preoperative anxiety refers to a condition of stress or restlessness related to any malady, environmental factors like the condition of ward, fears and doubts about anesthesia or surgery before operation. This state to mind may lead to dyspnea, abdominal pain, diarrhea, sweating, sleep disturbances or palpitations. Preoperative anxiety is more common in women than men[17]. After surgery, analgesics are frequently used to manage moderate to severe pain, although their use has declined because of the negative consequences they cause [18].

Randomized controlled trial with double-blind study was performed over a period of six months. The sampling technique was non-probability, consecutive sampling. The effects of pregabalin combined with famotidine were evaluated by Saadat et al., 2023 through a research approach identical to that used for studying pregabalin along with diphenhydramine effects on postoperative abdominal pain. [19].

The results of our study have suggested that both Gabapentin and Midazolam resulted in reductions across systolic and diastolic blood pressure, respiratory rate, and heart rate, with Gabapentin generally showing slightly higher values. Additionally, both drugs significantly reduced Hamilton Anxiety scores, indicating effective anxiolytic properties. The findings of this investigation align with the findings published by Khezri et al., 2013 who evaluated the influence of melatonin and gabapentin on anxiety and discomfort linked to retrobulbar eye block use for cataract surgery. Gabapentin demonstrated effectiveness in reducing pain intensity along with a better sedation score observed during retrobulbar placement according to the experimental study[20]. Moreover, a growing number of evidences have suggested that gabapentin does not cause significant drug interactions. Ménigau et al., 2006 suggested that gabapentin premedication (1200mg) improved the postoperative analgesia and preoperative anxiolysis significantly in case of knee surgery [21].

Similar results have been reported by Pandey et al., depicting that gabapentin significantly reduces the need of analgesic and ameliorates the postoperative pain in case of laparoscopic cholecystectomy[22]. Athanassoglou et al., showed in their work that midazolam application during surgery led to more patient falls yet fewer cardiac problems. Studies indicate that using midazolam with gabapentinoids leads to a dramatic improvement in the probability of respiratory failure and delirium disorders. The high use of benzodiazepines throughout perioperative periods calls for improved definition of therapeutic risks and benefits to assist surgical decision making[23].

The results have revealed that Gabapentin group had a higher and more variable Hamilton Anxiety Score, including several outliers, suggesting inconsistent anxiety reduction. In contrast, the Midazolam group showed lower and more consistent scores, indicating superior and reliable anxiolytic effects. Moreover, a growing number of evidences have suggested that gabapentin does not cause significant drug interactions as illustrated by Salraian et al. [24]

While considering the research gaps in the study, it should be mentioned that gabapentin and midazolam combinations can be studies in order to investigate the synergistic effects of both analgesics. Moreover, the study included two groups with 26 patients each, it should be conducted on even greater number of patients in order to further validate the results of the study.

CONCLUSION

This study demonstrates that Midazolam is significantly more effective than Gabapentin in reducing pre-operative anxiety, as evidenced by greater reductions in systolic and diastolic blood pressure and heart rate among patients undergoing abdominal hysterectomy. The statistically significant differences ($p < 0.01$) highlight Midazolam's superior anxiolytic effect. Although Gabapentin showed some anxiolytic properties, its impact was less pronounced. Respiratory rate changes were not statistically significant between the groups. These findings support the use of Midazolam as a preferable premedication agent for anxiolysis in surgical patients, potentially contributing to better perioperative outcomes and improved patient stability during abdominal hysterectomy procedures.

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