

STUDY OF PROPHYLACTIC ROLE OF ORAL MIDODRINE ON INCIDENCE OF HYPOTENSION AFTER SUBARACHNOID BLOCK IN ELECTIVE LOWER ABDOMINAL SURGERY

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ABSTRACT

Background and Aim: Hypotension is a common and significant complication following subarachnoid block (SAB), resulting from sympathetic blockade and peripheral vasodilation. Oral midodrine, an $\alpha 1$ -adrenergic agonist, may help maintain hemodynamic stability and reduce the incidence of spinal anaesthesia-induced hypotension. This study aimed to evaluate the prophylactic role of oral midodrine in preventing hypotension following subarachnoid block in patients undergoing elective lower abdominal surgery and to assess its associated adverse effects.

Materials and Methods: This prospective randomized controlled trial was conducted in a tertiary care hospital. Seventy ASA I–II patients undergoing elective lower abdominal surgery under subarachnoid block were randomized into two groups (n=35 each). Group M received oral midodrine 5 mg, while Group C received an identical placebo tablet 60 minutes before spinal anaesthesia. Hemodynamic parameters, incidence of hypotension, vasopressor requirement, and adverse effects were recorded and compared between the groups.

Results: Baseline demographic characteristics were comparable between the groups. Heart rate was similar before drug administration and before SAB; however, Group M demonstrated significantly lower HR values from 6 minutes onward ($p < 0.05$). Mean arterial pressure was significantly better maintained in Group M following SAB, with higher MAP values observed at 3, 6, 9, and 12 minutes compared to Group C ($p < 0.05$). Rescue mephentermine was required in only 3 patients (8.57%) in Group M compared with 18 patients (51.43%) in Group C ($p < 0.0001$). The incidence of adverse effects, including nausea, vomiting, shivering, and hypothermia, was low and comparable between the groups.

Conclusion: Oral midodrine effectively reduces the incidence of spinal anaesthesia-induced hypotension, improves hemodynamic stability, and significantly decreases vasopressor requirements without increasing adverse effects. It is a safe and effective prophylactic agent for patients undergoing elective lower abdominal surgery under spinal anaesthesia.

KEYWORDS: Midodrine, Hypotension, Subarachnoid Block

INTRODUCTION

Subarachnoid block (SAB), commonly known as spinal anaesthesia, is one of the most widely practiced regional anesthetic techniques for lower abdominal, pelvic, perineal, and lower limb surgeries. It offers several advantages, including rapid onset of action, profound sensory and motor blockade, excellent muscle relaxation, reduced perioperative stress response, and avoidance of airway manipulation. Despite these benefits, Subarachnoid block is frequently associated with hemodynamic disturbances, particularly hypotension, which remains one of the most common and clinically significant complications encountered during the perioperative period [1].

The incidence of hypotension following subarachnoid block varies widely, ranging from 15% to 70%, depending on patient characteristics, anesthetic technique, and the level of sympathetic blockade achieved [2]. The primary mechanism underlying this complication is sympathetic nervous system blockade, resulting in arterial and venous vasodilation, decreased systemic vascular resistance, reduced venous return, and subsequent decline in cardiac output and blood pressure [3]. Although transient hypotension may be well tolerated in healthy individuals, severe or prolonged episodes can lead to inadequate tissue perfusion, myocardial ischemia, nausea, vomiting, dizziness, and delayed postoperative recovery [4].

Various preventive and therapeutic strategies have been employed to minimize the occurrence of spinal anaesthesia-induced hypotension. These include preloading or coloads with intravenous crystalloids and colloids, lower doses of local anesthetics, positioning maneuvers, and administration of vasopressor agents such as ephedrine, phenylephrine, and norepinephrine [5]. However, fluid administration alone often fails to completely prevent hypotension, while vasopressors administered after the onset of hypotension may not effectively avert associated symptoms and complications [6]. Consequently, attention has shifted toward prophylactic pharmacological interventions that can maintain hemodynamic stability before the development of significant hypotension.

Midodrine hydrochloride is an orally active selective $\alpha 1$ -adrenergic receptor agonist that undergoes rapid conversion to its active metabolite, desglymidodrine. It produces peripheral vasoconstriction by stimulating $\alpha 1$ -adrenergic receptors in the arteriolar and venous circulation, thereby increasing systemic vascular resistance and venous return without significant direct effects on heart rate or cardiac contractility [7]. Owing to these pharmacological properties, midodrine has been

widely used in the management of orthostatic hypotension and autonomic dysfunction [8]. More recently, its role in perioperative settings has attracted considerable interest as a potential prophylactic agent for preventing hypotension associated with neuraxial anesthesia.

Several clinical studies have suggested that preoperative oral administration of midodrine can reduce the incidence and severity of hypotension following spinal anesthesia by maintaining vascular tone during sympathetic blockade [9]. The oral route offers additional advantages, including ease of administration, cost-effectiveness, patient comfort, and reduced requirement for intravenous vasopressors during surgery. Nevertheless, the available evidence remains limited, and variations in dosage, timing of administration, patient populations, and surgical procedures necessitate further evaluation of its efficacy and safety [10].

Therefore, the present study was undertaken to evaluate the prophylactic role of oral midodrine in reducing the incidence of hypotension following subarachnoid block in patients undergoing elective lower abdominal gynaecological surgery. The findings may contribute to establishing an effective and practical strategy for improving hemodynamic stability and perioperative outcomes in patients receiving subarachnoid block.

The primary objective of the study was to evaluate the prophylactic role of oral midodrine in preventing hypotension following subarachnoid block in patients undergoing elective lower abdominal surgery and secondary objective being to assess any adverse effects associated with the drug.

MATERIALS AND METHODS

This prospective randomized controlled trial was conducted in a tertiary care hospital. After written and informed consent, 70 eligible patients were randomly allocated into two equal groups of 35 patients each using a computer-generated randomization sequence. Patients in Group M received oral midodrine 5 mg with a sip of water approximately 60 minutes before administration of subarachnoid block. Patients in Group C received an identical placebo (sugar) white colour tablet at the same time. Allocation concealment was maintained using sealed opaque envelopes to minimize selection bias.

Female patients aged 20 to 50 yrs of ASA grade 1 and 2 undergoing elective lower abdominal gynaecological surgery under subarachnoid block were included. Patients having any contraindication of midodrine (Hypersensitivity to drug, severe heart disease, Uncontrolled hypertension) or having contraindication of subarachnoid block were excluded. Any case converted to general anaesthesia during procedure were considered as drop out.

The study was conducted in a double-blind manner. Neither the patients nor the anesthesiologist responsible for intraoperative monitoring and data collection was aware of the group allocation. The study medication was prepared and administered by an independent investigator not involved in patient assessment.

Standard fasting guidelines were followed in all patients. Upon arrival in the operating room, standard monitoring including electrocardiography, non-invasive blood pressure, and pulse oximetry was instituted. Baseline hemodynamic parameters were recorded. Intravenous access was secured and patients received preloading with 10 mL/kg Ringer's lactate solution over 15–20 minutes before subarachnoid block.

Subarachnoid block was performed under strict aseptic precautions at the L3–L4 or L4–L5 intervertebral space using a 25G Quincke spinal needle. Hyperbaric bupivacaine 0.5% (3 mL, 15 mg) with 25 microgram fentanyl was administered intrathecally. Patients were then positioned appropriately for surgery. Heart rate, mean arterial pressure, incidence of hypotension, vasopressor requirement, were recorded at every 3 minutes interval for 15 minutes, then at every 5 minutes interval for 30 minutes, then at every 10 minutes interval up to 60 minutes and then at every 15 minutes till the end of surgery and analysed for comparison between the two groups. On episode of hypotension (decrease in MAP > 20% of baseline) IV bolus of 5mg of mephentermine and bolus of iv fluid 100 ml were given and if there was episode of bradycardia (decrease in HR > 20% from baseline value), dose (0.6mg) of atropine was given. Total dose of sympathomimetics drug and adverse effects intraoperatively was recorded.

Statistical Analysis: The data was put into Microsoft Excel and then used SPSS software version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5 to look at it. Normality of continuous variables was assessed using the Shapiro–Wilk test before application of parametric statistical methods. Variables following normal distribution were expressed as mean $\pm$ standard deviation and compared using the independent Student's t-test. Categorical variables were expressed as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test where appropriate. A two-sided p value < 0.05 was considered statistically significant.

Sample Size

The sample size was calculated based on the primary outcome measure, namely the incidence of hypotension following subarachnoid block. The calculation was derived from the randomized controlled trial by Mahmoud Mohammed Alseoudy et al. (2022), who reported a reduction in hypotension incidence from approximately 43% in the placebo group to 15% in the midodrine group.

Assumptions used for calculation:

- Incidence of hypotension in control group (P1) = 43%
- Incidence of hypotension in midodrine group (P2) = 15%
- Alpha error (two-sided) = 0.05
- Beta error = 0.20
- Statistical power = 80%

Formula used:

$$n = ((Z_{\alpha/2} + Z_{\beta})^2 \times [P1(1-P1) + P2(1-P2)]) / (P1-P2)^2$$

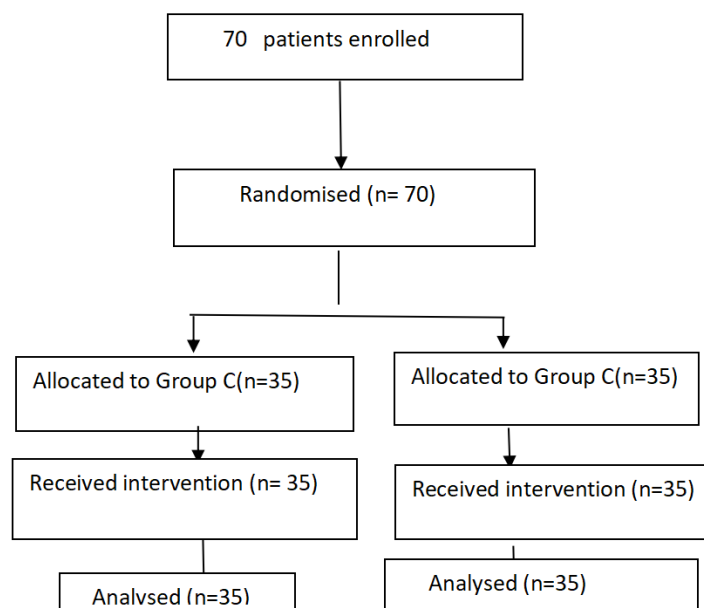
Substituting the values:

$$n = ((1.96 + 0.84)^2 \times [(0.43 \times 0.57) + (0.15 \times 0.85)]) / (0.43 - 0.15)^2$$

n = 37.2 patients per group

Therefore, approximately 35–38 patients were required in each group. Considering feasibility and recruitment targets, 70 patients (35 per group) were enrolled, providing approximately 80% power to detect a clinically significant difference in the incidence of hypotension between the groups.

Consort Diagram



RESULT

A total of 70 patients were included in the study, with 35 patients each in Group M and Group C. Baseline demographic and anthropometric characteristics were comparable between the groups (Table 1). The mean age was 40.60 ± 7.63 years in Group M and 43.08 ± 4.33 years in Group C, with no significant difference ($p=0.09$). The majority of patients belonged to the 41–50 years age group (60.0% in Group M and 71.43% in Group C). Mean body weight (54.91 ± 9.63 kg vs. 52.25 ± 6.69 kg; $p=0.18$) and mean height (154.80 ± 4.04 cm vs. 156.68 ± 5.77 cm; $p=0.11$) were also comparable between Groups M and C, respectively.

Table: 1. Comparison of Baseline Characteristics of Patients

Parameter	Category	Group M n (%) / Mean $\pm$ SD	Group C n (%) / Mean $\pm$ SD	P-Value
Age Distribution (years)	20–30	6 (17.14%)	0 (0.00%)	0.09
	31–40	8 (22.86%)	10 (28.57%)	
	41–50	21 (60.00%)	25 (71.43%)	
	Total	35 (100.00%)	35 (100.00%)	
	Mean $\pm$ SD	40.6 ± 7.63	43.08 ± 4.33	0.09
Weight (kg)	Mean $\pm$ SD	54.91 ± 9.63	52.25 ± 6.69	0.18
Height (cm)	Mean $\pm$ SD	154.8 ± 4.04	156.68 ± 5.77	0.11

Statistically significant ($p < 0.05$)

Data presented as mean $\pm$ standard deviation

Baseline heart rate (Table 2) was similar in both groups before drug administration (87.62 ± 16.17 bpm vs. 83.97 ± 10.54 bpm; $p=0.16$) and before subarachnoid block (89.05 ± 17.25 bpm vs. 87.22 ± 11.64 bpm; $p=0.60$). No significant difference was observed at 3 minutes after SAB (86.80 ± 17.44 bpm vs. 89.62 ± 10.85 bpm; $p=0.41$). However, from 6 minutes onward, Group M demonstrated significantly lower heart rates than Group C, with values of 80.82 ± 14.52 vs. 89.80 ± 9.45 bpm at 6 minutes ($p=0.002$), 76.48 ± 14.81 vs. 88.71 ± 7.08 bpm at 12 minutes ($p<0.0001$), and 74.65 ± 11.94 vs. 87.05 ± 5.92 bpm at 75 minutes ($p<0.0001$).

Table 2: Comparison of Patients According to Heart Rate at Different Time Points

Parameter	Group M Mean $\pm$ SD	Group C Mean $\pm$ SD	P-Value
Before Drug	87.62 ± 16.17	83.97 ± 10.54	0.16
Before SAB	89.05 ± 17.25	87.22 ± 11.64	0.6
At 3 min	86.80 ± 17.44	89.62 ± 10.85	0.41

At 6 min	80.82 ± 14.52	89.80 ± 9.45	0.002
At 9 min	77.45 ± 15.07	87.54 ± 9.20	0.001
At 12 min	76.48 ± 14.81	88.71 ± 7.08	<0.0001
At 15 min	78.70 ± 14.42	88.68 ± 6.96	0.0005
At 20 min	80.34 ± 13.65	87.80 ± 5.69	0.003
At 25 min	79.54 ± 10.74	87.68 ± 7.58	0.0005
At 30 min	77.57 ± 11.09	87.91 ± 7.04	<0.0001
At 40 min	73.34 ± 11.69	87.45 ± 6.06	<0.0001
At 50 min	73.23 ± 12.63	87.62 ± 6.86	<0.0001
At 60 min	75.15 ± 13.59	87.47 ± 6.56	<0.0001
At 75 min	74.65 ± 11.94	87.05 ± 5.92	<0.0001
At 90 min	71.12 ± 9.63	94.00 ± 0.00	–

Statistically significant ($p < 0.05$)

Data presented as mean ± standard deviation

Mean arterial pressure (Table 3) before drug administration was comparable between the groups (95.45±13.64 mmHg vs. 96.31±11.10 mmHg; $p=0.60$). Prior to SAB, MAP was significantly higher in Group M (98.48±14.20 mmHg) compared with Group C (92.65±8.27 mmHg; $p=0.03$). Following SAB, Group M maintained significantly higher MAP values at 3 minutes (94.31±14.98 vs. 73.60±13.14 mmHg; $p<0.0001$), 6 minutes (92.10±13.81 vs. 72.54±13.31 mmHg; $p<0.0001$), 9 minutes (91.11±13.08 vs. 78.02±9.01 mmHg; $p<0.0001$), and 12 minutes (89.94±14.36 vs. 83.65±9.23 mmHg; $p=0.03$), indicating superior hemodynamic stability. In addition to p -values, 95% confidence intervals were calculated for key outcome measures.

Table 3. Comparison of Mean Arterial Pressure (MAP) at Critical Time Points

Parameter	Group M Mean ± SD	Group C Mean ± SD	P-Value
Before Drug Administration	95.45 ± 13.64	96.31 ± 11.1	0.6
Before SAB	98.48 ± 14.20	92.65 ± 8.27	0.03
At 3 min	94.31 ± 14.98	73.6 ± 13.14	<0.0001
At 6 min	92 ± 13.81	72.54 ± 13.31	<0.0001
At 9 min	91.11 ± 13.08	78.02 ± 9.008	<0.0001
At 12 min	89.94 ± 14.36	83.65 ± 9.23	0.03
At 15 min	89.6 ± 14.92	85.74 ± 10.68	0.21
At 20 min	84.22 ± 15.02	86.48 ± 9.41	0.45
At 25 min	84.14 ± 11.33	85.25 ± 8.79	0.64
At 30 min	81.6 ± 11.47	84.94 ± 7.78	0.15
At 40 min	82.74 ± 10.51	86.88 ± 8.94	0.08
At 50 min	83.76 ± 11.69	85.71 ± 7.41	0.4
At 60 min	83.78 ± 9.08	85.61 ± 9.62	0.41
At 75 min	83.23 ± 12.25	85.47 ± 8.61	0.37
At 90 min	82.43 ± 8.27	82 ± 0	–

Statistically significant ($p < 0.05$)

For the primary outcome of hypotension, the relative risk was 0.17 (95% CI 0.05–0.52), demonstrating a statistically and clinically significant reduction in the incidence of hypotension with prophylactic oral midodrine administration. The relative risk reduction was 83.3%, and the number needed to treat was 3.

The requirement for rescue mephentermine (Table 4) was significantly lower in Group M, with only 3 patients (8.57%) requiring vasopressor support compared to 18 patients (51.43%) in Group C ($p<0.0001$).

Table 4. Comparison of Mephentermine Requirement

Mephentermine Used	Group M n (%)	Group C n (%)	P-Value
Yes	3 (8.57)	18 (51.43)	<0.0001
No	32 (91.43)	17 (48.57)	
Total	35 (100)	35 (100)	

Statistically significant ($p < 0.05$)

Data presented as mean ± standard deviation

Adverse effects (Table 5) were infrequent and comparable between groups. Hypothermia occurred in 2.86% of patients in each group, while shivering, nausea, and vomiting were observed in 5.71%, 2.86%, and 2.86% of patients in Group M compared with 8.57%, 5.71%, and 5.71% in Group C, respectively. Overall complication $p=0.34$.

Overall, both interventions demonstrated a favorable safety profile, with Group M providing significantly better hemodynamic stability and reducing vasopressor requirements.

Table 5. Comparison of Adverse Effects

Adverse Effect	Group M n (%)	Group C n (%)	P-Value
Hypothermia	1 (2.86)	1 (2.86)	0.34
Shivering	2 (5.71)	3 (8.57)	
Nausea	1 (2.86)	2 (5.71)	
Vomiting	1 (2.86)	2 (5.71)	
Overall Comparison	-	-	

DISCUSSION

The present randomized controlled study evaluated the efficacy of oral midodrine in preventing spinal anesthesia-induced hypotension among patients undergoing elective lower abdominal surgery. The findings demonstrated improved hemodynamic stability, reduced vasopressor requirement, and a comparable adverse effect profile in the midodrine group when compared with the control group.

Regarding baseline characteristics, both groups were comparable with respect to age, weight, height, and gender distribution. The mean age was 40.6 ± 7.63 years in Group M and 43.08 ± 4.33 years in Group C, with no statistically significant difference. Similar demographic comparability was reported by Sanjay et al. [11], who observed no significant differences in age, body weight, or anthropometric variables between patients receiving prophylactic midodrine and controls before spinal anesthesia. Likewise, Gunda et al. [12] reported comparable baseline characteristics between study groups, ensuring that subsequent hemodynamic differences could be attributed to the intervention rather than confounding demographic variables. The homogeneity of the study population in the present investigation strengthens the internal validity of the results.

Heart rate analysis revealed no significant differences between groups before drug administration or before spinal anesthesia. However, from the sixth minute onward, Group M exhibited significantly lower heart rates than Group C, with the difference persisting throughout the intraoperative period. This finding suggests improved autonomic stability and reduced compensatory tachycardia in patients receiving midodrine. Similar observations were reported by Agrawal et al. [13], who found that prophylactic midodrine maintained cardiovascular stability and prevented reflex tachycardia associated with spinal anesthesia-induced hypotension. A randomized trial by Prakash et al. [14] also demonstrated significantly lower fluctuations in heart rate among patients receiving oral alpha-adrenergic agonists prior to spinal blockade. The reduced heart rate variability observed in the present study may be attributed to better preservation of systemic vascular resistance and venous return.

Mean arterial pressure was significantly better maintained in Group M following spinal anesthesia. At 3 and 6 minutes after SAB, MAP remained substantially higher in the midodrine group compared with controls, indicating effective prevention of sympathetic blockade-induced hypotension. These findings are consistent with those reported by Singh et al. [15], who observed significantly higher MAP values and fewer hypotensive episodes in patients receiving oral midodrine before spinal anesthesia. Similarly, Mokhtar and El-Shmaa [16] reported superior maintenance of arterial pressure following prophylactic midodrine administration in patients undergoing regional anesthesia. The vasoconstrictive action of midodrine through selective alpha-1 adrenergic receptor stimulation likely accounts for the enhanced blood pressure stability observed in the present study.

One of the most clinically relevant findings was the markedly reduced requirement for rescue mephentermine in Group M. Only 8.57% of patients in the midodrine group required vasopressor support compared with 51.43% in the control group. This difference was highly significant and reflects the effectiveness of midodrine in preventing severe hypotensive episodes. Similar reductions in rescue vasopressor consumption have been reported by Batra et al. [17], who demonstrated a significant decrease in ephedrine requirement among patients pretreated with oral midodrine. Likewise, Kumar et al. [18] found that prophylactic midodrine significantly reduced the need for additional vasopressor interventions during spinal anesthesia. The reduced dependence on rescue vasopressors not only improves patient safety but also decreases anesthetic workload and facilitates smoother intraoperative management.

The incidence of adverse effects was low and comparable between both groups. Hypothermia, shivering, nausea, and vomiting occurred infrequently, with no statistically significant difference between the groups. These findings suggest that oral midodrine is well tolerated and does not increase perioperative complications. Similar safety outcomes were documented by Choudhary et al. [19], who reported no increase in nausea, vomiting, bradycardia, or other adverse effects following prophylactic midodrine administration. Furthermore, study done by Mokhtar et al. [20] concluded that midodrine effectively reduces spinal anesthesia-induced hypotension without significantly increasing drug-related adverse events. The favorable safety profile observed in the present study similar to Amin S et al [21] and Alseoudy et al [22] supports the routine consideration of oral midodrine as a preventive strategy in selected patients undergoing spinal anesthesia. Also it helps in early mobilization following hip and knee arthroplasty [23].

Overall, the findings of the present study are in agreement with previous literature demonstrating that oral midodrine effectively attenuates hypotension following spinal anesthesia, improves hemodynamic stability, reduces vasopressor requirements, and maintains a favorable safety profile. These results support the growing body of evidence advocating the prophylactic use of midodrine in patients at risk of spinal anesthesia-induced hypotension.

This study had multiple limitations. It was conducted at a single tertiary care center with a relatively small sample size of 70 patients, which may limit the generalizability of the findings. Only ASA Grade I and II female patients undergoing elective lower abdominal surgeries were included, restricting applicability to higher-risk patients, males, and other surgical populations. Additionally, only a single prophylactic dose of oral midodrine was evaluated, and long-term postoperative outcomes and comparisons with other vasopressors were not assessed.

Future multicenter studies with larger and more diverse patient populations are needed to validate these findings. Research should evaluate different doses and timing schedules of oral midodrine and compare its efficacy with established vasopressors such as phenylephrine, ephedrine, and norepinephrine. Further studies should also investigate its role in high-risk patients, various surgical procedures, and its impact on postoperative recovery, patient satisfaction, and long-term outcomes.

CONCLUSION

The present study demonstrates that oral midodrine is an effective prophylactic agent for preventing spinal anesthesia-induced hypotension in patients undergoing elective lower abdominal surgery. Patients who received midodrine maintained significantly higher mean arterial pressure during the critical early period following subarachnoid block and exhibited greater overall hemodynamic stability compared with the control group. The requirement for rescue mephentermine was markedly reduced in the midodrine group, indicating a lower incidence of clinically significant hypotension. Although heart rate values were lower in the midodrine group during the intraoperative period, no adverse hemodynamic consequences were observed. Furthermore, the incidence of adverse effects such as nausea, vomiting, shivering, and hypothermia was low and comparable between the groups, confirming the safety and tolerability of oral midodrine. Therefore, preoperative administration of oral midodrine represents a simple, safe, and effective strategy for minimizing spinal anesthesia-induced hypotension and reducing vasopressor requirements in elective surgical patients.

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