



A Comparative Study of the Effect of Dexmedetomidine, Clonidine and Magnesium Sulphate on Attenuation of Haemodynamic Response During Intraoperative Period and on Post- Operative Analgesia in Patients Posted for Abdominal Laparoscopic Surgeries Under General Anaesthesia

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KEYWORDS

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ABSTRACT:

Background and Aim: In this study, effectiveness of Dexmedetomidine, Clonidine and Magnesium Sulfate in attenuation of haemodynamic response to laryngoscopy and intubation in patients posted for laparoscopic abdominal surgeries under general anaesthesia was compared and their intraoperative haemodynamic response was studied along with the requirement for postoperative rescue analgesia.

AIMS AND OBJECTIVES: To compare the effect of Dexmedetomidine, Clonidine and Magnesium Sulfate on attenuation of haemodynamic response during intraoperative period and on postoperative analgesia in patients posted for abdominal laparoscopic surgeries under general anaesthesia and the requirement of rescue analgesia.

Materials and Methodology: After institutional ethical committee approval, this double-blinded randomized study consists of 105 patients divided into 3 groups who are ASA I and ASA II, aged between 18-60 years, who underwent abdominal laparoscopic surgeries lasting not more than 3 hours. Group A: Dexmedetomidine (1 mcg/kg) Group B: Clonidine (1 mcg/kg) Group C: Magnesium Sulfate(40mg/kg). Haemodynamic parameters were recorded and analysed.

Results: Fall in heart rate (H.R.) was more with Dexmedetomidine than with clonidine and Magnesium Sulfate. Fall in blood pressure (B.P.) was more significant with Clonidine. Post-operative analgesic requirement was least with Dexmedetomidine group than with Magnesium Sulfate group and most with Clonidine group.

Conclusion: All 3 groups provided adequate haemodynamic stability but Dexmedetomidine was found to be better in providing controlled haemodynamic response as well as for control of postoperative pain.

INTRODUCTION

Hemodynamic response constitutes a dynamic set of physiological adjustments within the cardiovascular system that transpire in reaction to diverse stimuli,

encompassing stress, physical exertion, discomfort, and medical procedures [1]. During surgery, the patient is subjected to a confluence of factors that evoke substantial hemodynamic shifts [2]. The commencement of anaesthesia prompts a reduction in



blood pressure as vasodilation occurs, laying the foundation for the surgery.

The perception of pain triggers the sympathetic nervous system, leading to increased heart rate, vasoconstriction, and elevated blood pressure. This response aims to redirect blood flow to essential organs and tissues, but prolonged or severe pain can strain the cardiovascular system. [3] Prioritizing pain management in the postoperative setting is pivotal not only for patient comfort but also for curbing the adverse effects of the sympathetic stress response [4].

Dexmedetomidine is the dextrorotatory S-enantiomer of medetomidine. It demonstrates rapid distribution with a distribution half-life of six minutes and a terminal elimination half-life of about 2 hours. It exhibits 8 to 10 times more selectivity towards α_2 receptors which are responsible for producing sedative effect and analgesic action [5]. It does not depress respiratory function. Apart from its sedative, analgesic, and anxiolytic actions it also enhances cognitive performance, reduces cerebral blood flow and oxygen metabolic requirements.[6]

Clonidine is an antihypertensive medication that acts as an agonist on alpha-adrenergic and imidazoline receptors. Besides its antihypertensive effect, clonidine can be used for the treatment of attention deficit hyperactivity disorder (ADHD), management of tics associated with Tourette syndrome, and adjunct therapy for severe cancer-related pain [7][8]. Clonidine, targets alpha-2 receptors, which helps in modulating pain transmission [9].

Magnesium acts as a distinctive calcium antagonist, induces arterial relaxation, lowering peripheral and cerebral vascular resistance, alleviating vasospasm, and reducing arterial blood pressure. Magnesium Sulfate has also been shown to reduce analgesic requirements and stabilize hemodynamic during laparoscopic procedures [10], though results have been variable based on dose and timing. Magnesium, as an NMDA receptor antagonist, has been investigated for its analgesic properties and it was found that perioperative use of Magnesium reduced postoperative pain scores and delayed first analgesic request. [11]

The purpose of this study was to assess and compare the effects of Dexmedetomidine, Clonidine and Magnesium

Sulfate on attenuation of haemodynamic response during intraoperative period and on postoperative analgesia in patients posted for abdominal laparoscopic surgeries under general anaesthesia.

Aims and Objectives: To compare the effect of 3 drugs dexmedetomidine, clonidine and magnesium Sulfate on attenuation of haemodynamic response during intraoperative period, their requirement as post-operative analgesia, and their adverse side effects.

METHODOLOGY:

Study Design: This Prospective randomized study was conducted in the Department of Anaesthesiology IIMSR, Lucknow

Procedure: Prior to the conduction of study, approval from the institutional ethics committee was obtained. The study included 105 participants. The patients were divided into 3 groups, Group D(Dexmedetomidine), Group C(Clonidine) and Group M (Magnesium Sulfate) with 35 participants in each group.

Informed consent was obtained and routine investigations like CBC, LFT, RFT, ECG, CHEST X-RAY (PA VIEW), RBS were done. Patients with ASA grade I and II, within age group of 18-60 years were included in the study.

The test drugs (Dexmedetomidine/Clonidine/Magnesium Sulfate) were infused were administered intravenously over a period of 10 mins before induction of general anaesthesia. The haemodynamic parameters were recorded after pre-oxygenation with 100% oxygen, at the end of infusion of the test drugs and 5 mins thereafter.

Intubation was done with cuffed endotracheal tube and haemodynamic measurements were recorded 1 min after intubation, 5 minutes, 10 minutes and every 5 minutes thereafter till the end of operative period. Muscle relaxation was provided by subsequent doses of inj. Vecuronium (0.01 mg/kg). Reversal was done with inj. Neostigmine (0.05 mg/kg.) and inj. 0.01 mg/kg of glycopyrrolate following the start of spontaneous breathing. Patients were assessed for post-operative pain using VAS score and were treated with injection nefopam as rescue analgesic when VAS Score is more than 4.



Statistical analysis: Data was analysed using SPSS software.

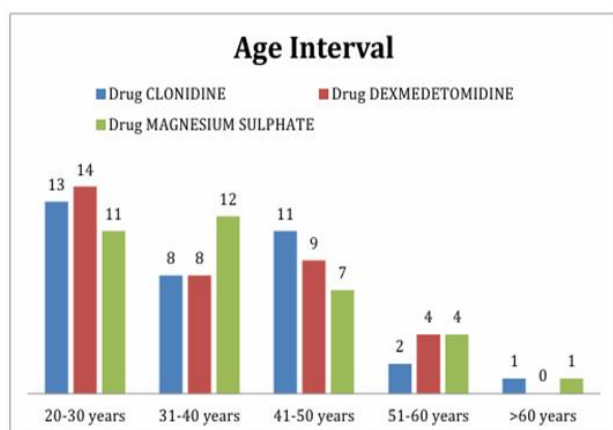
RESULTS:

Demographics:

The majority of participants in all three groups belonged to the 20–30 years age category, with the highest proportion observed in the Dexmedetomidine group (40%), followed by the Clonidine group (37.1%) and the Magnesium Sulphate group (31.4%). In the 31–40 years age group, the Magnesium Sulphate group had a slightly higher representation (34.3%) whereas a relatively balanced distribution was seen across the Clonidine and Dexmedetomidine groups with 22.9% each. The 41–50 years group accounted for the highest participants in the Clonidine group (31.4%).

Age intervals	Drug					
	CLONIDINE		DEXMEDETOMIDINE		MAGNESIUM SULPHATE	
	N	%	N	%	N	%
20-30 years	13	37.1%	14	40.0%	11	31.4%
31-40 years	8	22.9%	8	22.9%	12	34.3%
41-50 years	11	31.4%	9	25.7%	7	20.0%
51-60 years	2	5.7%	4	11.4%	4	11.4%
>60 years	1	2.9%	0	0.0%	1	2.9%
Total	35	100.0%	35	100.0%	35	100.0%

Table 1: Age-wise distribution of participants within each group



Graph 1: Age-wise distribution of participants within each group

Table 2 presents the distribution of study participants based on their clinical diagnosis. The most common diagnosis among the participants was cholelithiasis, observed in 92 individuals (87.0%), making it the predominant condition in the study population.

DIAGNOSIS	N	%
APPENDICITIS	7	6.6%
CHOLELETHIASIS	92	87.0%
GALL BLADER POLYP	1	0.95%
INGUINAL HERNIA	5	4.8%
Total	105	100.0%

Table 2: Distribution of study participants according to clinical diagnosis

Heart Rate:

The baseline heart rate in this study was recorded at 86.57 ± 7.71 bpm and a notable decrease in heart rate was observed after Clonidine administration (61.57 ± 1.14 bpm) and at the 5-minute mark (62.77 ± 1.19 bpm), indicating pronounced Vagomimetic effects. results of this study indicate that Clonidine significantly lowered heart rate showcasing its sympatholytic effects, particularly prior to intubation and during the initial intraoperative phase.

Marked bradycardia was observed after test drug administration with dexmedetomidine (61.77 ± 1.03 bpm), and HR remained low at 5 min (63.47 ± 1.13 bpm). Magnesium sulphate administration also led to a reduction in heart rate shortly after administration. However, the magnitude and duration of HR suppression with magnesium appeared to be less consistent than with Dexmedetomidine.

Most HR values post drug administration and around the time of intubation did not differ significantly across groups. However, at 20 minutes after intubation, a statistically significant difference was noted with the Clonidine group showing a higher HR compared to the other two.

Systolic Blood Pressure (SBP):

At baseline, all three groups showed comparable Systolic Blood Pressure values. Similarly, no significant difference was noted in SBP immediately after drug administration and at most subsequent time intervals,



indicating a similar hemodynamic response among the three drug groups.

However, at 75 minutes post-intubation, a significant difference in SBP was observed among the groups, with

Group M showing a notably higher mean SBP (159.67 mmHg) compared to Group C (128.33 mmHg) and Group D (140.08 mmHg).

	Drug						p value
	CLONIDINE		DEXMEDETOMIDINE		MAGNESIUM SULPHATE		
	Mean	SD	Mean	SD	Mean	SD	
SBP at BASELINE	129.94	8.95	130.83	8.69	126.60	9.27	0.891
SBP at 5 min	107.94	1.66	108.50	1.73	107.86	1.63	0.156
SBP After giving test drug	114.17	1.25	113.97	1.15	113.94	1.19	0.461
SBP Pre intubation	112.03	1.67	112.17	1.79	111.51	1.76	0.646
SBP Just after intubation (0 min)	104.77	1.46	104.63	1.40	104.91	1.46	0.553
SBP at 1 min after intubation	117.77	3.17	116.66	3.12	118.06	3.22	0.194
SBP at 5 min after intubation	105.77	2.04	105.97	2.20	105.17	2.31	0.726
SBP at 10 min after intubation	103.60	2.14	103.37	2.03	103.23	1.90	0.860
SBP at 15 min after intubation	122.60	17.09	120.85	17.67	122.51	17.22	0.739
SBP at 20 min after intubation	118.40	10.85	118.17	5.72	117.34	9.10	0.103
SBP at 25 min after intubation	131.51	6.21	130.34	6.24	131.14	6.09	0.866
SBP at 30 min after intubation	113.91	11.35	115.09	11.52	121.83	9.75	0.102
SBP at 35 min after intubation	109.86	12.25	116.17	11.86	117.71	11.37	0.053
SBP at 40 min after intubation	118.77	8.20	121.31	6.35	117.80	8.66	0.235
SBP at 45 min after intubation	104.37	18.62	106.77	18.72	109.89	19.10	0.109
SBP at 50 min after intubation	108.49	17.28	103.20	16.07	121.17	14.03	0.053
SBP at 55 min after intubation	113.11	15.75	115.77	16.10	118.06	15.64	0.647
SBP at 60 min after intubation	150.29	40.48	135.91	43.90	154.88	38.08	0.090
SBP at 65 min after intubation	146.77	37.36	131.94	41.95	152.03	35.97	0.193
SBP at 70 min after intubation	130.67	41.34	144.67	38.83	159.00	30.19	0.059
SBP at 75 min after intubation	128.33	43.59	140.08	39.87	159.67	31.09	0.034
SBP at 80 min after intubation	143.14	41.68	143.50	43.87	149.00	39.11	0.688
SBP at 85 min after intubation	157.00	.	90.00	5.66	172.00	.	0.259
SBP at 90 min after intubation	159.00	.	92.00	7.07	174.00	.	0.259
SBP at 95 min after intubation	163.00	.	92.50	3.54	.	.	0.221
SBP at 100 min after intubation	178.00	.	120.00	.	.	.	0.317

Table 3: Comparison of Systolic Blood Pressure (SBP) at various time intervals among drug groups

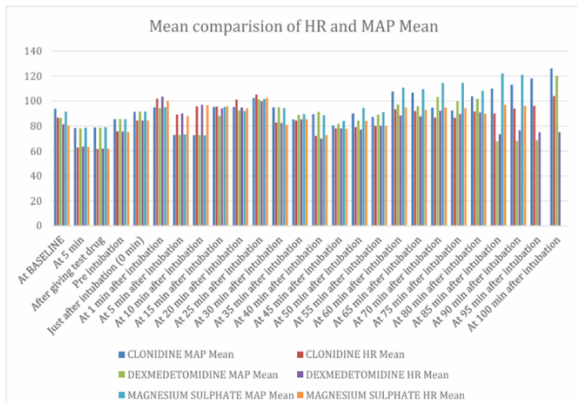
Diastolic Blood Pressure: Most of the subsequent time intervals along with the baseline readings showed no significant variation in DBP between the groups, suggesting a generally comparable diastolic response to the study drugs.

However, at 20 minutes after intubation, Group C exhibited a higher DBP (83.71 mmHg), resulting in a statistically significant difference with p-value 0.014. Similarly, a significant difference was observed at 35 minutes where Group M and Group D showed slightly higher DBP values than Clonidine. The result was consistent at 70 minutes ($p = 0.042$) and 75 minutes ($p = 0.028$), with Magnesium Sulphate showing notably elevated DBP levels compared to the other groups.



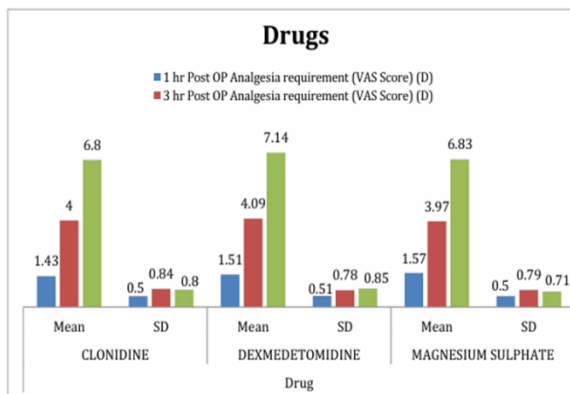
Mean Arterial Pressure:

At baseline, there was no statistically significant difference among the groups ($p = 0.067$), although Dexmedetomidine showed slightly lower MAP values. Throughout the early intervals MAP remained comparable across all three drug groups, indicating similar initial hemodynamic responses to the test drugs.



Graph 2: Comparison of Heart Rate and Mean Arterial Pressure (MAP) at various time intervals among drug groups

However, at 20 minutes post-intubation, a statistically significant difference emerged ($p = 0.018$), with Clonidine showing a higher MAP than the other two groups. Significant differences were also observed at later intervals such as 35 minutes ($p = 0.005$), 50 minutes ($p = 0.032$), 70 minutes ($p = 0.049$), and 75 minutes ($p = 0.007$) where Group M consistently exhibited elevated MAP compared to the other groups.



Graph 3: Comparison of Heart Rate and Mean Arterial Pressure (MAP) at various time intervals among drug groups: Post analgesic requirement (VAS) at 1, 3 and 6 hours

SpO₂:

There was no statistically significant difference in SPO₂ levels among the three groups at most time points, indicating comparable respiratory stability and safety profiles.

A notable exception was at 15 minutes after intubation, where a statistically significant difference ($p = 0.008$) was observed where Group C maintained the highest mean SPO₂ (99.63 ± 0.55), while both Dexmedetomidine and Magnesium Sulphate recorded slightly lower averages (99.31 ± 0.47 and 99.31 ± 0.53 , respectively).

At 30 minutes, higher SPO₂ was observed for Clonidine with p-values approaching 0.053. By 55 minutes post-intubation, all three groups had 100% saturation, indicating optimal oxygenation.

Postoperative analgesia requirement:

The postoperative analgesia requirement was assessed using the Visual Analogue Scale (VAS) at 1, 3, and 6-hours post-surgery revealed no statistically significant differences among the Clonidine, Dexmedetomidine, and Magnesium Sulphate groups.

Maximum requirement for postoperative analgesia was observed at 6 hours for all groups, however, the difference obtained was not statistically significant.

	Drug						p value
	CLONIDINE		DEXMEDETOMIDINE		MAGNESIUM SULPHATE		
	Mean	SD	Mean	SD	Mean	SD	
1 hr Post OP Analgesia requirement (VAS Score) (D)	1.43	.50	1.51	.51	1.57	.50	0.488
3 hr Post OP Analgesia requirement (VAS Score) (D)	4.00	.84	4.09	.78	3.97	.79	0.824
6 hr Post OP Analgesia requirement (VAS Score) (D)	6.80	.80	7.14	.85	6.83	.71	0.146

Table 4: Post analgesia requirement according to Visual Analogue Scale at 1,3,6 hours

DISCUSSION:

Laparoscopic surgeries have established themselves as the preferred approach for numerous abdominal procedures, owing to their minimally invasive nature,



faster recovery time, and lower rates of postoperative complications. [12] The induction of pneumoperitoneum and the positioning of patients during these operations can provoke considerable haemodynamic changes, primarily as a result of sympathetic nervous system activation. [13]

Consequently, there has been increasing interest in the use of adjunctive agents that can help modulate the body's stress response. Agents like dexmedetomidine, clonidine, and magnesium sulphate have been identified as promising drugs which influence both intraoperative haemodynamic and postoperative pain management. [14]

Dexmedetomidine, a highly selective agonist of the α_2 -adrenergic receptor, is recognized for its sedative, analgesic, and sympatholytic effects, which facilitate stable hemodynamic during surgery. Clonidine, while also an α_2 -agonist, is less selective than dexmedetomidine and produces comparable effects, albeit with a different pharmacokinetic profile. In contrast, Magnesium Sulfate functions as a calcium channel blocker and NMDA receptor antagonist, demonstrating anti-nociceptive and sympatholytic effects that may aid in hemodynamic regulation and pain relief. [15]

Thus, the present study was performed to compare the three agents regarding their effectiveness in mitigating hemodynamic responses during surgery, lowering postoperative analgesic needs, and identifying any potential adverse effects.

In this study, the average age of patients within the three intervention groups—Clonidine, Dexmedetomidine, and Magnesium Sulphate—was statistically similar, reflecting a uniform baseline demographic profile.

The mean age recorded in this study aligns with results from prior clinical trials and comparative analyses conducted in analogous surgical and anesthetic environments. Ganesh M et al. (2018) [16] reported a mean age of 36.2 ± 9.8 years in their investigation comparing clonidine and dexmedetomidine. Additionally, Luca E (2023) [17] emphasized the influence of α_2 -agonists on perioperative outcomes, pointing out that age related differences in sympathetic response can modify drug efficacy.

It was found that Clonidine significantly lowered heart rate which was in accordance to a study performed by Giovannitti Jr JA et al. (2015) [18] where it was noted that Clonidine exerts its central effects through α_2 -adrenergic receptors, leading to decreased sympathetic outflow and resulting in bradycardia and hypotension, which aligns with the significant heart rate reduction following drug administration.

Makhni R et al. (2017) [19] conducted a comparison between dexmedetomidine and magnesium Sulfate, where dexmedetomidine significantly lowered HR post-administration and blunted the intubation response more effectively than magnesium sulphate, aligning with the present findings where HR peaked at 1 min but quickly normalized. It was also observed that Clonidine exhibits a similar profile to dexmedetomidine in its ability to lower heart rate which was similar to the results obtained in the present study. According to Ali HSM et al (2022) Clonidine demonstrated superiority in controlling heart rate and enabling a faster recovery when compared to MgSO₄. [20]

Priyamargavi H et al. (2023) [21] demonstrated that oral clonidine premedication effectively reduced SBP during intubation and for 30 minutes post-induction. Current study corroborates this effect, particularly up to 25 min post intubation. Srivastava U et al. (2016) [22] compared Clonidine and Dexmedetomidine and found Clonidine to be less potent and more variable in maintaining stable SBP beyond 45 minutes, again consistent with the findings of this study.

Group M demonstrated markedly elevated DBP (92.38 mmHg at 70 min, 91.83 mmHg at 75 min), significantly higher than Group C and Group D ($p = 0.042$ and 0.028 respectively). This late rebound hypertension with Group M(Magnesium Sulfate) may be due to the shorter duration of action, stress accumulation from prolonged surgery, and inadequate analgesic supplementation. These findings were in line with the biphasic response reported by Morel V et al. (2021). [23]

All groups showed comparable MAP values at baseline with no statistically significant difference ($p = 0.067$), indicating similar hemodynamic states pre-intervention. This was similar to a study by Singh S et al. (2011) [24], who found that both dexmedetomidine and clonidine maintain stable pre-induction MAP values due to their central sympatholytic effect.



ROY I et al. (2024) [25] noted that dexmedetomidine maintained a more consistent MAP throughout intraoperative monitoring compared to magnesium, which showed MAP elevation after 60 minutes. The results were consistent with the values obtained in the present study.

Magnesium showed a progressively higher MAP ($p = 0.049$ and 0.007 , respectively), indicating a rebound sympathetic activity or waning of its initial effect. These trends were comparable to findings of Melvin K Ninan et al. (2023) [26] who reported that Magnesium has a shorter duration of hemodynamic attenuation than dexmedetomidine and clonidine.

Oxygen saturation (SpO_2) remained stable and comparable across all three groups. The p -values across all time points were >0.05 except at the 15-minute mark, where a statistically significant difference was noted. These findings are consistent with existing literature that reports stable SpO_2 maintenance with all three drugs when used in appropriate doses. Naaz S et al. (2014) [27] concluded that despite Dexmedetomidine's sedative and sympatholytic effects, SpO_2 remains unaffected in patients undergoing general anaesthesia. Clonidine is known for hemodynamic modulation with minimal respiratory depression. Kulkarni K et al (2016) [28] demonstrated that premedication with Clonidine did not adversely affect SpO_2 levels during laparoscopic surgeries.

At 1-hour post-op, VAS scores were low in all groups. Kweon DE et al. (2018) [29] reported lower VAS scores and longer time to first analgesic request in patients receiving dexmedetomidine compared to control or placebo. However, in this study, Dexmedetomidine (Group D) did not show significant superiority in VAS scores over Clonidine (Group C) or Magnesium Sulfate (Group M), possibly due to similar systemic effects of the agents used or timing and dosing differences.

Hatti P et al (2021) conducted a study where, both clonidine and dexmedetomidine effectively reduced hemodynamic responses in laparoscopic lower abdominal surgeries when administered as intravenous bolus doses. However, Dexmedetomidine demonstrated superior attenuation of these responses compared to clonidine. [30]

CONCLUSION:

This prospective, randomized, comparative study investigated the effectiveness of three pharmacological agents—Dexmedetomidine, Clonidine, and Magnesium Sulphate, in reducing intraoperative haemodynamic responses and enhancing postoperative analgesia in patients undergoing abdominal laparoscopic surgeries under general anaesthesia. All three agents contributed to intraoperative haemodynamic stability by mitigating the sympathetic response associated with laryngoscopy and intubation. Notably, Dexmedetomidine and Clonidine demonstrated more consistent and significant reductions in heart rate and blood pressure variations, particularly during the early intraoperative phase. However, it was observed that dexmedetomidine emerged as the most effective agent in providing hemodynamic stability and superior postoperative analgesia, followed closely by clonidine, with magnesium Sulfate also offering significant benefits, particularly in BP control.

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