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A Randomized Clinical Trial to Compare the Efficacy of Dexmedetomedine and Magnesium Sulphate for Attenuation of Pressor Response in Abdominal Laproscopic Surgeries

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Abstract

Objectives: To evaluate the response of dexmedetomidine and magnesium sulphate for attenuating stress response in laparoscopic abdominal surgeries. *Material and methods:* Patients of ASA grade I and II aged between 20 and 60 years, either gender and who underwent elective laparoscopic abdominal surgeries were included in the study and divided into two groups, group D (n=52) and group M (n=52). Group D patients received Inj dexmedetomidine 1 µg/kg bolus for 15 min followed by 0.2-0.4 µg/kg /hr infusion and group M patients received inj magnesium sulphate 2g bolus for 15 min followed by 12-15 mg/kg/hr infusion. Intraoperative hemodynamic parameters like Heart rate, mean arterial pressure were recorded and emergence time, extubation time and sedation scores were assessed. *Results:* Heart rate and Mean arterial pressure were significantly low in group D compared to group M. Recovery time and sedation score was significantly higher in group M compared to group D. Time to reach Aldrete score ≥ 9 was significantly more in group M compared to group D. *Conclusion:* Dexmedetomidine and Magnesium sulphate attenuated stress response to surgery and pneumoperitoneum. Dexmedetomidine had better hemodynamic stability compared to Magnesium sulphate. Early post operative recovery was found in dexmedetomidine group.

Keywords: Stress response; laparoscopic surgery; dexmedetomidine; magnesium sulphate.

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Introduction

Laparoscopy is the gold standard for several surgical procedures. Laparoscopic surgical procedures are cost effective, have minimal blood loss due to small incision and less postoperative pulmonary complicationsand reduced metabolic stress compared to conventional open procedures leading to early recovery [1,2].

In general anesthesia there is marked sympatho-adrenal response which results in increased heart rate and blood pressure during intubation and

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extubation. Pneumoperitoneum is produced by administration of carbon dioxide (CO_2) into the peritoneal cavity during laparoscopic procedures. Which affects homeostasis and leads to alterations in cardiovascular, pulmonary physiology and stress response. Hemodynamic stability during peri-operative period is of paramount importance as there are many patients who have a compromised cardiovascular status thereby avoiding hypertension, hypotension and tachycardia. Attenuation of circulatory response to Pneumoperitoneum is usually done by opioids, vasodilators, beta blocking agents, and alpha-2 adrenergic agonists [3,4].

Dexmedetomidine, a highly selective alpha-2 adrenergic agonist has several beneficial actions during the peri-operative period. The intravenous administration of dexmedetomidine before induction of anesthesia attenuates sympatho-adrenal responses to laryngoscopy, endotracheal intubation, pneumoperitoneum and extubation. Magnesium has the ability to block the release of catecholamines from both the adrenal gland and the adrenergic nerve terminals. Magnesium sulphate acts as a physiological calcium antangonist as it competes with calcium for membrane channels and modifies calcium mediated responses. The purpose of this study is to compare the effectiveness of Magnesium sulphate in comparison to Dexmedetomidine for attenuation of stress response in laparoscopic abdominal surgeries.

Material and methods

After approval by Institutional Ethical Committee, this randomized clinical trial was done at a tertiary care teaching hospital and written informed consent was taken from all patients.

A total of 104 patients were randomly allocated into twogroups (n=52) using a computerized random number table, Patients with American Society of Anesthesiologists (ASA) grades I and II, aged between 20 and 60 years, either gender and who underwent elective laparoscopic abdominal surgeries were included in the study.

Patients with hypertension, severe hepatic, renal, endocrine, cardiac dysfunction, conduction defects, on beta blockers, pregnancy, morbidly obese, hypomagnesaemia and any contraindication to magnesium sulphate or dexmedetomidine were excluded from the study.

Patients in group D received 1 µg/kg dexmedetomidine infusion and group M received 2 gm of magnesium sulphate infusion.

Preoperative assessment included detailed history, general physical examination, systemic examination, airway assessment and routine investigations, such as complete blood count, bleeding time, clotting time, platelet count, blood glucose, blood urea and serum creatinine. Electrocardiography and chest X-ray were done if required. All patients received tab alprazolam 0.5 mg orally the night before surgery, and a preoperative fasting status of 8 hrs was ensured.

Preoperative baseline vital parameters like Heart rate, blood pressure and oxygen saturation was recorded. Intravenous line was secured with 20 G cannula and premedication i.e Inj. Glycopyrrolate 0.02 mg/ kg, Inj. Ondansetron 0.15 mg/kg, Inj. Midazolam 1 mg, Inj fentanyl 2 µg/kg were given and pre-oxygenated for 3 minutes. Patients in group D Inj. Dexmedetomidine 1 mcg/kg loading dose in 100 ml Normal saline over 15 minutes and in Group M, Inj. Magnesium sulphate 2g loading dose in 100 ml Normal saline over 15 minutes were given. Induction was done with Inj. Propofol 1.5-2 mg/kg, followed by Inj. Atracurium 0.4-0.5 mg/kg to facilitate tracheal intubation, ventilation was confirmed and end tidal carbondioxide recorded. Patients in group D were administered Inj. Dexmedetomidine infusion at the rate of 0.2-0.4 µg/kg/hr as maintenance and patients in group M were administered Inj. Magnesium sulphate at rate of 12-15 mg/kg/hr. Oxygen saturation and end tidal carbondioxide was maintained by controlled ventilation. Ringers lactate was given as a maintenance fluid. Anesthesia was maintained in both groups with isoflurane oxygen, nitrous oxide and maintainence doses of Inj. Atracurium 0.1 mg/kg for muscle relaxation. Inj Paracetamol 1 g IV was given at the end of surgery. Isoflurane and infusion of drugs were stopped at the end of surgery. Neuromuscular blockade was reversed with Inj. Giycopyrrolate 0.02 mg/kg and Inj Neostigmine 0.04 mg/kg and extubated when patients were awake, later shifted to PACU. Recovery time was observed in both groups as time elapsed since stoppage of isoflurane and study drug infusion till patient achieved a modified Aldrete's score of ≥ 9. Sedation score was assessed at the end of surgery, at 15 mins and 30 minutes using Ramsay Sedation Score .

Intraoperative hemodynamic parameters like Heart rate, and Mean arterial pressures was recorded before intubation (P_1), after intubation (P_2), before peritoneal insufflation (P_3), 5 mins after peritoneal insufflations (P_4), 15 min after peritoneal

insufflation (P_5), 30 mins after insufflation (P_6), 60 mins after peritoneal insufflations (P_7), 5 mins after peritoneal deflation (P_8), after extubation (P_9) and after patient was shifted to PACU (P_{10}). Mean valuesof Heart rate, Mean arterial pressures was calculated. Rescue analgesia (Inj Diclofenac 75 mg iv) was given when patient had pain in the postoperative period.

Statistical analysis

According to pierre et al. the anticipated average mean ± SD of HR determined in two groups, group D and group M during operative time was (64.8 ± 3.4 and 66.8 ± 3.9), at 95% level of significance and at 80% power. The calculated sample size in each group was 52, using the statistical formula:

$$N=\frac{(Z_\alpha+Z_\beta)^2*2*SD^2}{MD^2}$$

Where Zα - Z value at α level.

Z_β-Z value at β level.

SD – Standard Deviation

MD – Difference between two parameters.

Data were expressed using Mean ± SD, and percentages. Continues variables like age, weight and duration of surgery were compared using Student t test / Mann Whitney U test. Categorical variables (gender, ASA grade, bradycardia, hypotension, nausea/vomiting and shivering) were compared by chi square/ Fishers Exact test. The level significance used was $p < 0.05$.

Results

A total of 102 patients were included in the study and demographic variables such as age, gender, weight, ASA grading, duration of surgery were comparable. There was no statistical significant difference among the two groups (Table 1).

Mean pulse rate was decreased more in group D compared to group M, which was not statistically significant except at P_7 (60 mins after peritoneal insufflations) and at P_{10} (PACU) (Table 2).

MAP in group D significantly low compared to group M from P_1–P_5 and at P_8. P_7 i.e, MAP 60 min after pertonieal insufflation, P_9 after extubation and $P_{10,}$ at the time of shifting to PACU, group D patients

Table 1: Demographic Data

	Group-D (n=52)	Group-M (n=52)	p- value
Age (Yrs)	42.10 ± 8.566	39.54 ± 10.35	p= 0.173* NS
Gender (M/F)	12/40	15/37	p= 0.502* NS
Weight (KGS)	62.48 ± 5693	61.13 ± 5.570	p= 0.224* NS
Asa Grading –			
I	40	43	p= 0.625* NS
II	12	9	
Duration of Surgery (Min)	72.55 ± 15.02	69.25 ± 17.56	p= 0.550* NS

*Not significant –p> 0.05

Table 2: Mean Pulse Rate in both Groups

Heart Rate Mean (SD)	Group-D n= 52	Group-M n= 52	p Value
Baseline (P_0)	82.326 ± 5.396	82.307 ± 4.832	p- 0.984
Before Intubation (P_1)	62.865 ± 3.118	63.384 ± 3.326	p- 0.413
After Intubation (P_2)	65.826 ± 4.133	66.942 ± 3.500	p- 0.140
Before Peritoneal Insufflation (P_3)	63.865 ± 3.925	64.557 ± 3.420	p- 0.340
5 Mins After Peritoneal Insufflation (P_4)	66.865 ± 4.528	67.884 ± 4.175	p- 0.235
15 Mins After Peritoneal Insufflation (P_5)	64.884 ± 4.236	65.961 ± 4.432	p- 0.208
30 Mins After Peritoneal Insufflation (P_6)	65.826 ± 4.466	66.980 ± 3.567	p- 0.148
60 Mins After Peritoneal Insufflation (P_7)	66.038 ± 3.704	67.673 ± 3.909	p- 0.030
5 Mins After Peritoneal Defflation (P_8)	65.596 ± 4.126	66.846 ± 3.304	p- 0.091
After Extubation (P_9)	67.961 ± 4.029	69.230 ± 3.227	p- 0.07
PACU (P_{10})	71.326 ± 3.341	72.807±4.073	p- 0.045

Table 3: Mean Arterial Pressure in both Groups

Mean Arterial Pressure	Group-D n= 52	Group-M n= 52	p-Value
Baseline (P_0)	93.576 ± 6.948	94.288 ± 5.263	p- 0.557
Before Intubation (P_1)	67.019 ± 3.31	69.903 ± 3.315	p- 0.001
After Intubation (P_2)	71.076 ± 3.92	73.750 ± 3.092	p- 0.0002
Before Peritoneal Insufflation (P_3)	68.799 ± 3.39	71.846 ± 3.816	P- 0.0001
5 Mins After Peritoneal Insufflation (P_4)	72.326 ± 3.148	74.230 ± 3.523	p- 0.004
15 Mins After Peritoneal Insufflation (P_5)	69.566 ± 3.369	72.865 ± 3.217	p- 0.0001
30 Mins After Peritoneal Insufflation (P_6)	73.288 ± 3.771	74.096 ± 3.373	p- 0.252
60 Mins After Peritoneal Insufflation (P_7)	74.038 ± 4.396	74.530 ± 4.135	p- 0.557
5 Mins After Peritoneal Defflation (P_8)	73.211 ± 3.560	73.634 ± 4.039	p- 0.057
After Extubation (P_9)	76.884 ± 4.180	77.313 ± 4.039	p- 0.595
PACU (P_{10})	85.423 ± 4.030	86.548 ± 4.053	p- 0.158

Table 4: Adverse Effects

	Group-D	Group-M	p-value
Bradycardia	7	2	0.1603
Hypotension	6	2	0.269
Vomiting	4	6	0.741
Shivering	2	5	0.436

Table 5: Sedation Score

Score	Group- D	Group- M	p-value
End of Surgery (4-6)	4.86 ± 0.88	4.96 ± 0.625	0.5056
At 15 Mins (2-5)	2.71 ± 0.710	2.98 ± 0.779	0.0659
At 30 Mins (2-3)	2.25 ± 0.487	2.403 ± 0.569	0.1274

showed better blood pressure control over group M patients, but the difference was statistically not significant (Table 3).

Adverse effects like bradycardia and hypotension were more in group D compared to group M but was not statistically significant (p>0.05) responded to inj atropine and vasopressors (Table 4).

The incidence of nausea, vomiting was seen in 4 patients in group D compared to 6 patients in group M (p= 0.741) and patients responded to intravenous ondansetron.

Shivering was seen more in 5 patients in group M compared to 2 patientsin group D which was statistically not significant which did not require any intervention.

Emergence time(time from the end of anaesthesia to the response to verbal commands.) and Extubation time (time from the end of anaesthesia till patient became awake) were comparable in both groups and found to be more in group M which was statistically significant (Table 5).

Time to achieve Aldrete score of ≥ 9 was found more and statistically significant in group M compared to group D.

At the end of surgery and 15 mins after surgery sedation scores weremore in group M compared to group D, but statistically not significant. One hour after surgery both the groups maintained Ramsay sedation score of 2-3, no agitated or deeply sedated patient in either group.

Discussion

This study was done on patients undergoing laparoscopic abdominal surgeries. Drugs like opioids, vasodilators and beta blockers have been used in other studies to attenuate hemodynamic stress response during surgery. The outcome of our study about effect of dexmedetomidine and magnesium sulphate on intra operative hemodynamics like mean heart rate, mean blood pressure were decreased in group D when compared to group M.

Dexmedetomidine, an highly selective, alpha-2 adrenergic agonist has several beneficial actions during the peri-operative period. It acts through three types of α_2 receptors α_2A, α_2B and α_2C situated in brain and spinal cord. It exerts a central sympatholytic action causing sedation, anxiolysis

and analgesia without any respiratory depression. Sedation produced by α_2 agonist is unique as patients can be easily aroused and sleep like state when not stimulated. Dexmedetomidine acts by activating G- proteins in the brain stem which results in inhibition of norepinephrine release [5,6]. The intravenous administration of dexmedetomidine before induction of anesthesia attenuates sympatho-adrenal responses to laryngoscopy, endotracheal intubation, pneumoperitoneum and extubation. Dexmedetomidine reduces narcotic and volatile agent requirements intraoperatively. Surgical stress includes changes like endocrinological, immunological and hematological effects. Activation of sympathetic nervous system and increased secretions of pituitary hormones are seen during surgery, and also increased release of cortisol levels due to increased secretion of ACTH by stimulation of hypothalamus. Our above results correlate with pierre zarif et al. who found that intravenous administration of dexmedetomidine and magnesium sulphate could ameliorate the pressor response to intubation, pneumoperitoneum and extubation in laproscopic colectomies.

In our study we administered dexmedetomidine 1 µg/kg bolus for 15 mins followed by infusion of 0.2-0.4µg/kg/hr. Infusion rates of dexmedetomidine varying from 0.1 to 10 µg/kg/hr have been studied, higher dose of infusion was associated with high incidences of cardiac effects [7]. In some young patients biphasic response is found with bolus dose of dexmedetomidine which is initial hypertension followed by hypotension. In vascular smooth muscles there is stimulation of $\alpha_2\beta$ receptors which are responsible for this effect. In our study we have not observed biphasic response or any untoward cardiac effects.

Magnesium has the ability to block the release of catecholamines from both the adrenal gland and the adrenergic nerve terminals. Magnesium sulphate acts as a physiological calcium antangonist as it competes with calcium for membrane channelsand modifies calcium mediated responses. Apart from that, magnesium can produce vasodilatation by acting directly on blood vessels and also capable of attenuating vasopressin release. Vasopressin concentrations raise in pneumoperitoneum due to increased compression of abdominal capacitance vessels with a consequent reduction in venous return to the heart. In our study Inj Magnesium sulphate 2g loading dose in 100 ml Normal saline over 15 minutes followed by 12-15 mg/kg/hr infusion was used.

Showket Ahmed Dar et al. [8] found that intravenous magnesium sulphate 5 mins before pneumoperitoneum attenuates stress response and significantly lower the heart rate and arterial pressures during laproscopic abdominal surgeries and this attenuation is related to the effect of magnesium sulphate as a physiological calcium anatagonist as it competes with calcium for membrane channels and modifies many calcium mediated responses. Another study by Rania M Ali [9] found that intraperitoneal insufflations of magnesium sulphate attenuated hemodynamic stress response to pneumoperitoneum which reduced postoperative pain, nausea, vomiting in patients undergoing laproscopic cholecystectomy when compared to placebo. Ray et al. in their study concluded that magnesium sulphate and clonidine were effective in attenuating stress response and also observed delayed recovery in magnesium sulphate group.

Rebie Soliman [10] showed that dexmedetomidine has better control of heart rate and blood pressure, provides better exposure of surgical field with minimal blood loss compared to magnesium sulphate. The incidence of hypotension and bradycardia was higher with dexmedetomidine than magnesium sulphate, they also found emergence and extubation time was shorter with dexmedetomidine than magnesium sulphate. In our study Bradycardia was found in 7 patients in group D and 2 patients in group M whereas in group D hypotension was seen in 6 patients as compared to 2 patients in group M. bradycardia responded to inj atropine 0.02 mg/ kg and hypotension was treated with IV fluids and ephedrine. According to studies by Mohamed F Mostafa et al. [11] and Rafat Shamim et al. [12] observed that dexmedetomidine group patients maintained better hemodynamic stability compared to placebo. Mean pulse rate was decreased more in group D compared to group M, from P_1-P_{10} which was not statistically significant except at P_7 (60 mins after peritoneal insufflations) and at P_{10} (PACU). Mean arterial pressure was found statistically significant difference in group D when compared to group M from P_1–P_5 and at P8. Sedation was higher in group M compared to group D which resulted in delayed emergence and extubation time. Vomiting and shivering was found to be more in group M. Patients in group M required more time to reach an aldrete score of ≥ 9 and to be discharged from PACU.

Conclusion

Dexmedetomidine and Magnesium sulphate

attenuated stress response to surgery and pneumoperitoneum. Dexmedetomidine has better hemodynamic stability compared to Magnesium sulphate. Early post operative recovery was found in dexmedetomidine group.

Limitations of the study

1. Both upper abdominal and lower abdominal cases included in the study, positioning of patient which is different may affect hemodynamic parameters.
2. ASA grade I and II only included in the study.

References

1. Pither S., Bayonne Manou L.S., Mandji Lawson J.M., Tchantchou T.D., Tchoua R., Ponties J.P. Surgical approaches to hysterectomy. Sante. 2011;21(2):79–81.
2. Hatakeyama T., Nakanishi M., Murayama Y., et al. Laparoscopic resection for colorectal cancer improves short-term outcomes in very elderly colorectal cancer patients. Surgical Laparoscopy, Endoscopy and Percutaneous Techniques. 2013;23(6):532–35.
3. Meftahuzzaman S.M., Islam M.M., Chowdhury K. K., et al. Haemodynamic and end tidal CO_2 changes during laparoscopic cholecystectomy under general anaesthesia. Mymensingh Medical Journal. 2013;22(3):473–77.
4. Herroeder S., Schönherr M.E., De Hert S.G., Hollmann M. W. Magnesium -essentials for anesthesiologists. Anesthesiology. 2011;114(4):971–93.
5. O' leary E, Hubbard K, Tormey W et al. Laparoscopic cholecystectomy: haemodynamic and neuroendocrine responses after pneumoperitonium and changes in position. Br J Anaesth 1996; 76:640-44.
6. Ishizaki Y, Bandae Y, Shimomura K, Abe H, Ohtomo Y, Idezuki Y. Safe intra abdominal pressure of carbon dioxide pneumoperitoneum during laparoscopic surgery. Surgery. 1993;114:549-54.
7. Jean L Joris, Jean-Daniel Chiche, Jean-Luc M. Canivet, Nicolas J. jacquet, jean Jacques Y. Legros, maurice L. Lamy. Hemodynamic changes induced by laparoscopy and their endocrine correlates: effects of clonidine. JACC. 1998;32(5):1389-96.
8. Dar SA, Gupta DD, Deopujari RC, Gomes P. Effect of Magnesium Sulphate on Attenuation of Hemodynamic Stress Responses during Laparoscopic Abdominal Surgeries. J Anesth Clin Res. 2015;6:590.
9. Ali RM, Rabie AH, Elshalakany NA, El Gindy TM. Effect of intraperitoneal magnesium sulfate on hemodynamic changes and its analgesic and antiemetic effect in laparoscopic cholecystectomy. Ain-Shams J Anaesthesiol. 2015;8:153-9.
10. Soliman R, Zohry G: The myocardial protective effect of dexmedetomidine in high-risk patients undergoing aortic vascular surgery. Ann Card Anaesth. 2016 Oct-Dec;19(4):606-613.
11. Mohamed F Mostafa, Ragaa Herdan, Mohammed Yahia Farrag Aly and Azza Abo Elfadle: Effect of Different Doses of Dexmedetomidine on Stress Response and Emergence Agitation after Laparoscopic Cholecystectomy: Randomized Controlled Double-Blind Study: J Anesth Clin Res 2017;8:2.
12. Rafat Shamim, Shashi Srivastava, and Aneesh Srivastava: Effect of Two Different Doses of Dexmedetomidine on Stress Response in Laparoscopic Pyeloplasty: A Randomized Prospective Controlled Study: Anesth Essays Res. 2017 Oct-Dec;11(4):1030–34.