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Effect of magnesium sulphate and dexmedetomidine in attenuating hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy

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I. Introduction And Background

Cholecystectomy is one of the most popular laparoscopic procedures performed in the world. The first laparoscopic cholecystectomy was performed by Prof Dr Med Erich Mühe of Böblingen in Germany on September 12, 1985.

Dr. Jyotsna Kulkarni performed the first laparoscopic cholecystectomy in India in 1990 at the JJ Hospital in Mumbai.

It's done in a reverse Trendelenburg posture, which means the table is tilted with the feet facing down and the head raised 15 to 30 degrees.[3]The surgical field is raised above the level of the heart to enhance drainage of body fluids away from the surgical site, lowering intracranial pressure and reducing haemorrhage.

Pneumoperitoneum is essential for laparoscopic surgery, as it enables visibility and mobility in the working site. Nevertheless, the pneumoperitoneum modifies abdominal-cavity homeostasis and might promote metabolic changes through mechanical and biochemical effects.

Georg Kelling was the first to describe a methodology known as pneumoperitoneum in 1901, and the first to undertake a review of the abdominal procedure, which was later named after him as celioscopy and now the procedure is known as laparoscopy.

In 1924 Zollikofer, was the first who described the use of CO2 in the establishment of pneumoperitoneum. In clinical practice, pneumoperitoneum with CO2 has been employed since the invention of laparoscopic cholecystectomy.

Earlier, several other gases were used to create a pneumoperitoneum like inert gases helium and argon, nitrous oxide with the aim of reducing the incidence of local and systemic adverse effects but because of higher risk of embolism and due to combustible properties all three gases are stopped to create pneumoperitoneum.

The advantage of using carbon dioxide is that it is non-combustible, it is cost effective, it is highly soluble and most importantly it is excreted rapidly through respiration.

During pneumoperitoneum hypercarbia occurs due to direct absorption of CO2 from peritoneal vessels. With increasing intra-abdominal pressure, hypercarbia accentuates due to reduced functional residual capacity and and exacerbated by V/Q mismatch.

Also An elevated IAP causes an increase in intra-cerebral pressure (ICP) by limiting cerebral venous drainage as a consequence of raised intra-thoracic pressure.

Inflammation, acidosis, oxidative stress, mesothelial injury and adhesion development are some of the common adverse effects of pneumoperitoneum which can be seen in peritoneal cavity.[7]

To reduce the responses of pneumoperitoneum and to stabilize the hemodynamics of the patient intraoperatively many drugs have been used like clonidine, lignocaine, magnesium sulphate, dexemedetomidine. In this study we will be comparing magnesium sulphate and dexemedetomidine as an adjuvant drug to attenuate the hemodynamic response to pneumoperitonium and to minimize perioperative critical events.

Magnesium is a vasodilator in both systemic and pulmonary circulations. It is a physiological antagonist of calcium and it has the ability to block the release of catecholemines from both the adrenal gland and the adrenergic nerve terminals, the mechanism of action of magnesium is that it acts on membrane channels

involved in calcium flux and through its action in the synthesis of cAMP and it produces vasodilatation by acting directly on blood vessels and attenuate vasopressin stimulated vasoconstriction.

Dexmedetomidine is an alpha-2 adrenergic agonist that has analgesic, sympatholytic, and sedative characteristics without causing respiratory depression. It reduces the need for opioids and the stress response intraoperatively, resulting in a more stable hemodynamic condition. Because its half-life of distribution is around 6 minutes, it can be utilized to reduce the stress response caused by laryngoscopy.

We designed a randomized double blind comparative study to investigate whether magnesium sulphate or dexmedetomidine is more useful for achieving a better intraoperative hemodynamic status and decrease incidence of adverse events like hypertension tachycardia hypercarbia.

thereby we plan to study the difference between the intra operative hemodynamic profile attained with the use of magnesium sulphate and dexmedetomidine in laparoscopic cholecystectomy.

II. Methodology

After getting approval from Institute Ethics Committee and written informed consent, 90 patients were taken and planned for elective laparoscopic cholecystectomy, well optimized according to inclusion and exclusion criteria was included in this randomized double blinded Hospital based, observational, experimental comparative study. Patients were assigned randomly via computerderived random number sequence into 3 groups. They were divided into 3 groups (group D, Group M and group (NS)

Where,

Group D (dexmedetomidine) was given in dose of 1µg/kg diluted in 10ml normal saline as i/v bolus.

Group M (Magnesium sulphate) was given in dose of 50mg/kg diluted in 10 ml normal saline as i/v bolus.

Group NS (0.9%normal saline) was given 10 ml i/v bolus.

Inclusion criteria:

Patient with ASA CLASS I/ II.

Adult Patient with 18-55years and weight 50 to 70 kg.

Patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia

Patients with written and informed consent**.**

Exclusion criteria:

Patients with predicted difficult airway, mouth opening less than 2.5 cm, intra oral pathology.

Patients with known allergy to either of drugs.

Patients with complications like haematological disorders,

Patients with chronic hypertension,

Patients with AV block,

Patients with morbid obesity (>50% above ideal body weight)

Patients with acute cholecystitis,

Patients chronically using opioid analgesics or β-blockersAll patients were visited on the day before surgery and explained about the study procedure, anaesthetic technique and perioperative course.

Each patient had a precheckup which included:

1. Vital parameters like NIBP, pulse, temperature and respiratory rate.
2. Routine/ general physical/ systemic examination.
3. Any significant present and past medical/ surgical history.

All routine and specific investigations required for the surgery as per hospital protocol were obtained. Informed written consent of the patients for the study, anaesthetic technique, and surgical procedure were taken.

Standard 5 leads electrocardiogram (ECG), pulse oximeter (SpO2), non-invasive blood pressure (NIBP), and capnostat for end-tidal carbon dioxide (EtCO2) measurement were attached and baseline parameters were noted when patients arrived in the OT on the day of surgery.

Intravenous line was secured using 18 G or 20 G bore cannula on the dorsum of the non-dominant hand preferably. The drugs were prepared and administered by an anaesthesiologist who was not involved with data collection or patient management. In operation theatre routine monitoring including NIBP, Spo2, ECG

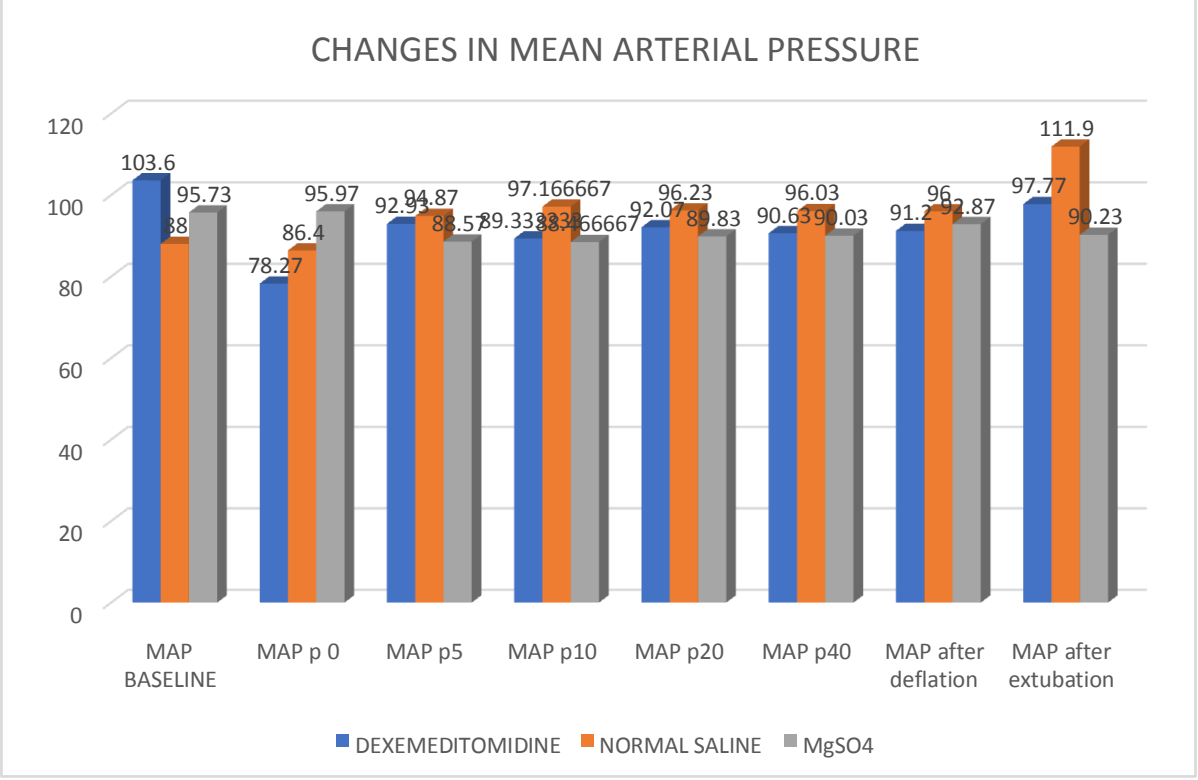
was done for all the patients and all the patients were preoxygenated with 100% O2 for 3 mins, and an intravenous line secured, Premedication started with Inj. glycopyrrolate 0.2 mg and inj midazolam 1 mg, 1µg/ kg of fentanyl, induction through 2mg/kg of propofol ,0.1 mg/Kg vecuronium, After given of IV drugs all patients were intubated with appropriate size of endotracheal tube, patients then ventilated with 50% O2, 50% air for next 5 min, then The test drug was given over a period of 10 min in both the groups before creating pneumoperitoneum.In our clinical study pneumoperitoneum was created with the

insufflation of CO2 with a pressure of around 12-14 mm hg.6 Vitals like systolic BP, diastolic BP, mean arterial pressure and heart rate were be recorded at the end of test drug administration but before creation of pneumoperitoneum(p0), and thereafter80

5min after pneumoperitoneum (p5)
10min after pneumoperitoneum (p10)
20min after pneumoperitoneum (p20)
30min after pneumoperitoneum (p30)
40min after pneumoperitoneum (p40)
Before deflation of pneumoperitoneum
After extubation
Maintenance of anaesthesia was done with nitrous oxide 50%, oxygen 50% and Isoflurane.
Intravenous Fentanyl was given at the dose of 0.5µg/kg to maintain analgesic effect and Vecuronium 0.02mg/kg was used for maintenance of muscle relaxation.
At the end of surgery reversal of muscle paralysis was done patients using a combination of injection neostigmine 0.05 mg/kg iv and injection glycopyrrolate 0.008 mg/kg Iv and extubated after achieving adequate respiratory efforts and adequate muscle power. After extubation patients were shifted to Post Anaesthesia Care Unit for Post operative monitoring. Following time duration were noted down after tracheal extubation:
(i)Time to tracheal extubation after the completion of surgery.
(ii) time to response to verbal commands.
Entire data was entered into a microsoft office excel sheet and Chi square statistical test was used for categorical variables and One Way ANOVA and POSTHOC TUKEY test were applied for continuous variables.

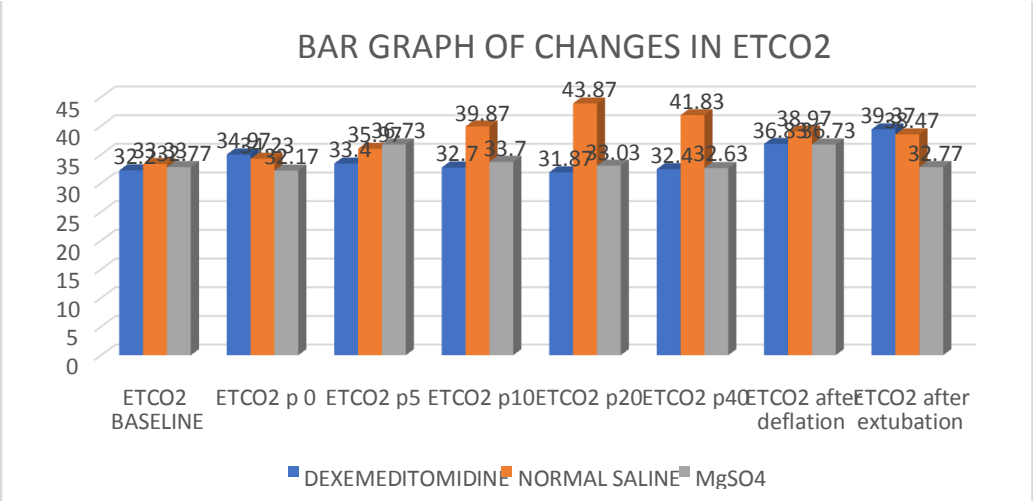
III. Results And Observation

FIGURE 1



- After we run ONE WAY ANOVA test we observed that MGSO4 lowered the mean arterial pressure (MAP) at maximum time intervals intraoperatively as compared to other 2 groups with significant p value =<0.001, whereas at time interval p0 dexmedetomidine lowered the MAP maximum which is statistically significant with p value <0.001. According the POSTHOC TUKEY TEST group dexmedetomidine and group MGSO4 shows no significant difference while measuring MAP except at time interval of baseline, p0 and after extubation where MGSO4 lower the MAP at baseline and after extubation with significant p value 0.003 and group dexmedetomidine has the lower value of MAP at time interval p0 with the significant p value<0.001

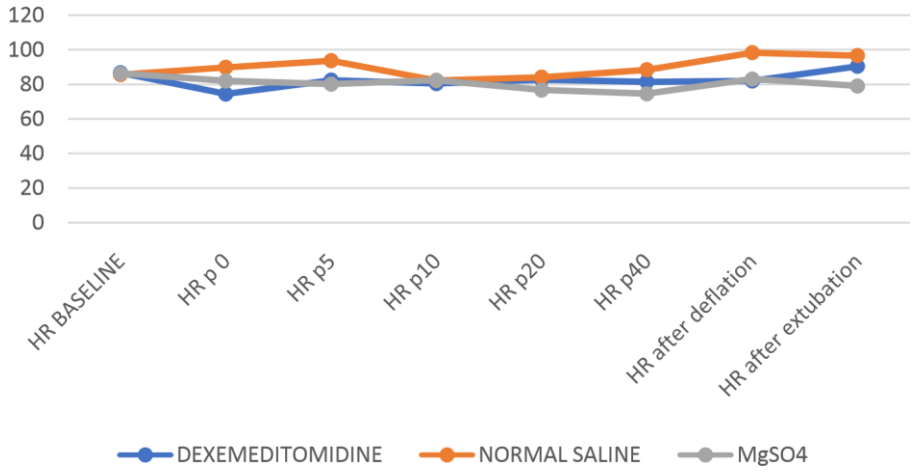
FIGURE 2



Comparison of ETCO2 p20 between the three groups shows that NORMAL SALINE group has the highest value of 43.87 and DEXEMEDITOMIDINE has the least value of 31.87. This difference is statistically Significant with a test value of 297.693 and p value of <0.001.Posthoc Tukey tests comparing DEXEMEDITOMIDINE and NORMAL SALINE groups shows a mean difference of -12 and is statistically significant with a p value of <0.001. Comparing DEXEMEDITOMIDINE and MgSO4 groups shows a mean difference of -1.167 and is NOT statistically significant with a p value of 0.086. Comparing NORMAL SALINE and MgSO4 groups shows a mean difference of 10.833 and is statistically significant with a p value of <0.001 and Comparison of ETCO2 p40 between the three groups shows that NORMAL SALINE group has the highest value of 41.83 and DEXEMEDITOMIDINE has the least value of 32.4. This difference is statistically Significant with a test value of 159.28 and p value of <0.001.Posthoc Tukey tests comparing DEXEMEDITOMIDINE and NORMAL SALINE groups shows a mean difference of -9.433 and is statistically significant with a p value of <0.001. Comparing DEXEMEDITOMIDINE and MgSO4 groups shows a mean difference of -0.233 and is NOT statistically significant with a p value of 0.921. Comparing NORMAL SALINE and MgSO4 groups shows a mean difference of 9.2 and is statistically significant with a p value of <0.001.

FIGURE 3

CHANGES IN HEART RATE



We observed that according to ONE WAY ANOVA TEST heart rate was lower in both the groups od dexmedetomidine and MGSO4 as compared to the group NS at all the time intervals which was stastistically significant with p value <0.001showing that both the drugs attenuate the hemodynamic response of pneumoperitoneum except time interval of p10 min. According to the POSTHOC TUKEY TEST dexmedetomidine showed the lowest heart rate at time interval of p0 min, p10 min and after the deflation as compared to group NS with the significant p value <0.001. Also, no significant changes in heart rate seen in between both the groups dexmedetomidine and MGSO4 except the time interval of after extubation where MGSO4 lowered the heart rate more than dexmedetomidine with the significant p value <0.001. In comparison

to group NS, MGSO4 lowered the heart rate more at various intervals intraoperatively with significant p value<0.001 except baseline value, heart rate at p0 min and heart rate at p10 min.

In our study, we observed that out of 30 patients of group D who received dexmedetomidine 3 patients got affected with bradycardia(<50 beats/min) and 2 patients had an incidence of hypotension (MAP<60 mm of Hg). Bradycardia in patients were treated with and hypotension responded to fluid administration, rest all patients were hemodynamically stable intraoperatively.

IV. Conclusion:

Both dexmedetomidine and magnesium sulphate are useful in combatting pressor reponse to pneumoperitoneum in laparoscopic cholecystectomy. This also results in less consumption of anaesthetic drugs intraoperatively and better pain control in post operative period.However, in our study magnesium sulphate at the dose of 50 mg/kg was found to be superior than dexmedetomidine at the dose of 1mcg/kg for hemodynamic stability intraoperatively and early extubation after completion of surgery.

KEYWORDS: Dexemedetomidine, magnesium sulphate, pneumoperitoneum, laparoscopic cholecystectomy

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