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# "COMPARISON OF EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE AND DEXMEDETOMIDINE ON NEUROMUSCULAR BLOCKADE AND POST-OPERATIVE ANALGESIC REQUIREMENT IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY."

Anaesthesiology

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## ABSTRACT

**Background and aims:** This prospective observational study was designed to evaluate the effect of intravenous magnesium sulphate and dexmedetomidine on onset, duration, time of recovery from neuromuscular blockade as well as duration of postoperative analgesia and total analgesic requirement in 24 hours. **Method:** 60 patients of ASA grade 1,2,3 of either sex in the age group of 18-60 years formed 2 groups : Group M (n=30):- patients who received magnesium sulphate 40mg/kg intravenously as a bolus in 100ml of normal saline preoperatively over 10 minutes before induction of anesthesia and 10mg/kg/hour continuous infusion intraoperatively and Group D (n=30):- patients who received dexmedetomidine 1µgm/kg loading dose in 100ml normal saline preoperatively over 10 minutes and 0.5µgm/kg/hour continuous infusion intraoperatively. All patients received propofol for induction and maintenance of anesthesia with bispectral index monitoring. Atracurium 0.5-0.6mg/kg was administered before intubation, followed by 0.1-0.2mg/kg was given when TOF was ≥2 intraoperatively. Total requirement of atracurium was compared in both groups. Post-operatively, pain was measured using visual analogue scale (VAS) at various time intervals up to 24 hours and time of rescue analgesia with tramadol 1-2mg/kg intravenously was given when VAS score ≥4 & total analgesic requirement in 24 hours was compared in both groups. **Results:** Patients in group M required less atracurium than in group D (P<0.05). Onset of neuromuscular blockade and recovery index were comparable in both groups. Postoperative VAS score and total analgesic requirement was significantly lower in group D than in group M (P<0.05). **Conclusion:** Magnesium sulphate decreases the atracurium requirement with similar effect on onset and recovery from neuromuscular blockage when compared with dexmedetomidine; while Dexmedetomidine prolongs postoperative analgesia and decreases postoperative analgesic requirement compared to magnesium sulphate.

## KEYWORDS

Magnesium Sulphate, Dexmedetomidine, Neuromuscular blockade, Post operative Analgesia, Laparoscopic cholecystectomy.

## INTRODUCTION:

Laparoscopic cholecystectomy has become popular due to advantages like lesser tissue trauma, reduced postoperative pain, shorter hospital stays, rapid return to normal activities with significant cost savings.[1] Postoperative pain is still an important concern after laparoscopic cholecystectomy.[2]

Muscle relaxation is an integral part of balanced anaesthesia technique, involving various drug administration to achieve desired effect, reducing dosage of various anaesthetic agents, increasing the safety and decreasing the side effects with adequate muscle relaxation.[3]

Magnesium sulphate, a N-methyl-D-aspartate (NMDA) non-competitive receptor antagonist is an useful adjunct to anaesthesia and has been found to reduce intraoperative anaesthetic and analgesic requirement. [4] It blocks the release of catecholamine from both adrenergic nerve terminals and the adrenal gland. [5] At the motor end plate, it reduces the release of prejunctional acetylcholine, thereby decreasing the muscle membrane excitability. Pretreatment with magnesium sulphate increases clinical duration and recovery index of neuromuscular blocking agents. [6]

Dexmedetomidine is a selective alpha-2 receptor agonist acting in the dorsal horn of the spinal cord decreasing intra-operative anaesthetic requirement and postoperative analgesic requirement.[2] It decreases catecholamine release by 90% and causes decrease in heart rate and decrease in blood pressure along with decrease in systemic vascular resistance and cardiac output. [5]

This study was carried out to compare the effect of magnesium sulphate and dexmedetomidine pretreatment, on the onset, duration and recovery from neuromuscular blockade and postoperative analgesia in adult patients undergoing laparoscopic cholecystectomy under general anaesthesia using propofol and atracurium for induction and maintenance of anaesthesia.

## MATERIAL AND METHOD: -

After obtaining approval from the **ethical committee of the institution** and **CTRI registration** (CTRI/2021/09/036431), this prospective observational comparative study was conducted in 60 patients, in the age group of 18-60 years of either sex, belonging to ASA grade I, II or III receiving general anaesthesia. Patients with BMI (body mass index) ≥ 30 kg/m$^2$, having major cardiorespiratory, neuromuscular, hepatic or renal disorders, allergy to any of the study drugs, with anticipated difficult airway, at risk of aspiration – pregnant patient and patients with full stomach were excluded from the study.

- The sample size was calculated with convenient sampling technique on the basis of previous year data.
- In the preoperative room, intravenous infusion was started after measuring the baseline vital paremeters. All patients were premedicated with Glycopyrrolate 0.004 mg/kg, Midazolam 0.02mg/kg and Tramadol 2 mg/kg intravenously half an hour before surgery.
- In the operation theater, non-invasive blood pressure, oxygen saturation, ECG and EtCO2 (capnography) monitoring was done. Neuromuscular monitoring was done with INMED nerve stimulator NS100 at the ulnar nerve with the help of two surface electrodes. Patients received pretreatment as per the choice of consultant anesthesiologist. Those who received pre-treatment with inj. Magnesium sulphate 40mg/kg in 100 ml normal saline intravenously over 10-15 min before anaesthesia followed by intravenous infusion of Magnesium sulphate 10mg/kg/hour intraoperatively were included in **group M** and those who received pre-treatment with inj. Dexmedetomidine 1µgm/kg in 100ml normal saline intravenously over 10-15 min before anaesthesia followed by intravenous infusion of Dexmedetomidine 0.5µgm/kg/hour intraoperatively were included in **group D**.
- After preoxygenation with 100% O2 for 3 minutes, induction of anaesthesia was done with intravenous xylocard 2% 1mg/kg followed by propofol 2-2.5 mg/kg intravenous bolus continued as propofol 4-6 mg/kg/hour intravenous infusion. Ulnar nerve was stimulated and baseline TOF response was noted. Atracurium 0.6 mg/kg was given intravenously and patients were ventilated with 100% O2. TOF response was observed every 30 seconds till there was no response and the time of onset of neuromuscular block was noted. Laryngoscopy and intubation was done with proper sized cuffed endotracheal tube.
- Maintenance of anaesthesia was done with O2(50%) + N2O (50%), either magnesium sulphate 10mg/kg/hour intravenous infusion or dexmedetomidine 0.5µgm/kg/hour intravenous infusion, infusion of propofol 4-6 mg/kg/hour intravenously, atracurium 0.2mg/kg intermittently given intravenously when TOF response ≥2 or when there was presence of respiration or sudden movement of patient or notches on EtCO2 waveforms.

Last dose of Atracurium was given approximately 30 minutes before completion of surgery. Magnesium sulphate or Dexmedetomidine infusion was stopped after removal of gall bladder. Propofol infusion was stopped at the time of skin closure or 10 minutes before completion of surgery. After completion of surgery when TOF ≥2 responses, time was noted and the neuromuscular block was reversed with Neostigmine 0.05mg/kg intravenously and Glycopyrrolate 0.008 mg/kg given intravenously. Extubation was done after appearance of 4 responses of TOF and after achievement of regular smooth respiration with adequate tidal volume and spontaneous eye opening, sustained head lift >5 seconds and sustained hand grip.

- Post operatively patients were monitored at every 30 minutes interval up to 4 hours then at 6, 12 ,18 and 24 hours for postoperative pain. When VAS ≥4, rescue analgesia with Tramadol 2mg/kg intravenously was given. Time of 1st analgesic requirement and total number of analgesic doses required in 24 hours was noted.

## OBSERVATION AND RESULTS:

Onset and recovery from neuromuscular blockade, intraoperative atracurium requirement and postoperative analgesia were observed and statistical analysis was done.

The data collected was entered into a database Microsoft excel sheet. The results were expressed as a mean ± standard deviation. The statistical analysis was done using unpaired t-test for quantitative data comparison of both groups and chi-square test was used for qualitative data comparison using EPI software. The difference was considered to be statistically significant when P<0.05.

**Table 1: Demographic data**

| Parameters | Group M (Mean ± SD) | Group D (Mean ± SD) | P – value |
|---|---|---|---|
| Age (years) | 38.83 ± 11.48 | 39.9 ± 10.96 | 0.71 |
| Weight (kilogram) | 55 ± 8.35 | 54.33 ± 8.46 | 0.75 |
| Height (centimetres) | 154.66 ± 5.69 | 155.06 ± 7.08 | 0.81 |

The demographic data were comparable in both the groups (p>0.05).

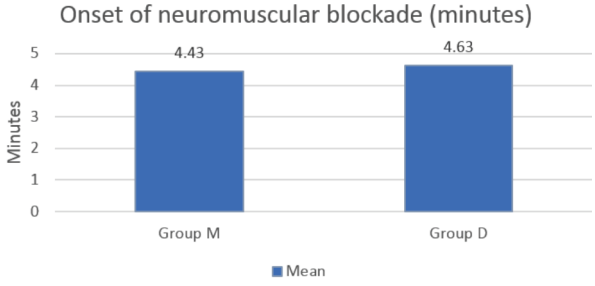


**Chart 1: Onset of neuromuscular blockade (minutes)**

The onset of neuromuscular blockade was comparable in both the groups (P>0.05).

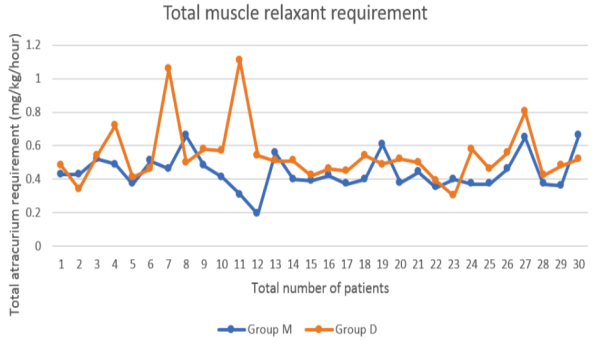


**Chart 2. Total Atracurium requirement (mg/kg/hour)**

Total atracurium required for both loading and maintenance doses in group M was 0.44 ± 0.10 mg/kg/hour and in group D was 0.54 ± 0.17 mg/kg/hour, which was significantly less in group M compared to group D (P<0.05).

**Table -2 Recovery from neuromuscular blockade (minutes)**

| Recovery (minutes) | Group M | Group D | P-value |
|---|---|---|---|
| Mean | 10.6 | 10.53 | 0.973462 |
| SD | 5.401 | 9.276 | |

Recovery from neuromuscular blockade was comparable in both the groups (P>0.05).

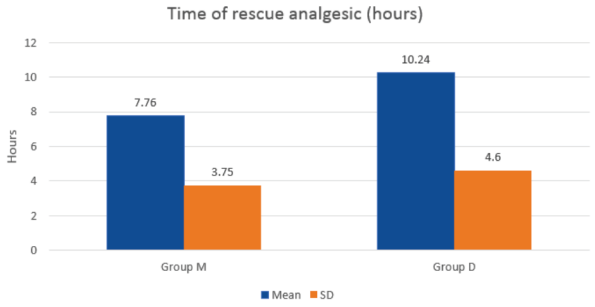


**Chart 3: Duration of postoperative analgesia (hours)**

Duration of postoperative analgesia was significantly prolonged in group D compared to group M (P<0.05).

**Table -3 Total analgesic requirements in 24 hours (mg)**

| Total analgesic requirements in 24 hours | Group M | Group D | P-value |
|---|---|---|---|
| Mean | 243.33 | 150 | 0.028 |
| SD | 56.83 | 86.1 | |

Total tramadol requirement in 24 hours was significantly less in group D than in group M (P<0.05)

## DISCUSSION:

Magnesium sulphate acts as a calcium channel blocker at presynaptic nerve terminal, thus it causes decrease in presynaptic acetylcholine release at the motor endplate, diminished depolarizing action of acetylcholine and depressed excitability of muscle fiber membrane.[7,11] Post-synaptically, magnesium ions and calcium ions both compete each other for activation sites on the myosin ATPase necessary for excitation-contraction coupling and results in enhanced response of neuromuscular blocking agents, prolonging its effect and reducing its requirement.[8]

In present study, **mean time of onset of neuromuscular blockade** was comparable in both the groups **(P=0.312).** Kaussman et al (1997) [7] found that the mean onset time in magnesium sulphate group was 71 ± 20 seconds and in normal saline group was 75 ± 23 seconds and the comparison was statistically insignificant. It may be due to the effect of magnesium sulphate on the neuromuscular endplate which was both concentration and time dependent and at least 4-6 minutes were necessary to reach the motor end plate in a concentration high enough to interfere with the neuromuscular blocking agents.[8]

We found that **total atracurium required** for both loading and maintenance doses was **significantly reduced** in magnesium sulphate group as compared to dexmedetomidine group **(P=0.01).** Similar to our study Mohammed Abdelsalam Menshawi (2022) et al [9] found that the total atracurium requirement was significantly reduced in magnesium sulphate group compared to dexmedetomidine and saline group. (P<0.001). Vinit K. Srivastva et al (2016) [10] found that the vecuronium maintenance dose was significantly reduced in group M compared to group D (P<0.05). Aabid Hussain Mir (2019) et al, Essam M. Manaa (2012) et al, J.-H. Ryu (2008) et al, H.S. Na et al (2009) et al found that the amount of rocuronium used during anaesthesia in group M was significantly less than group S (P<0.005).

In present study, **recovery from neuromuscular blockade** was **comparable** in both the groups (P> 0.97). Similar to our study, Aabid Hussain Mir (2019) et al [4] found that the mean time from last dose of atracurium to return of TOF to ≥3 in group M and in group S (normal saline) was comparable, comparison was statistically insignificant (P>0.05). Contrast to our study, Mohammed Abdelsalam Menshawi (2022) et al [9] found that the anaesthesia recovery time(minutes) was significantly prolonged in dexmedetomidine group than magnesium sulphate group (P<0.001).

We didn't have saline group in our study, so we didn't find significant difference in onset and recovery of magnesium sulphate and

dexmedetomidine with saline group. However, it was comparable in both the groups.

In our study we found that, **duration of postoperative analgesia** was **significantly prolonged** in dexmedetomidine group compared to magnesium sulphate group (P=0.031). **Total Tramadol requirement (mg)** for 24 hours was **significantly less** in group D than group M (P=0.028). Similar to our study, Mohammed Abdelsalam Menshawi (2022) et al [7] found that intraoperative fentanyl requirement was significantly reduced in group D than group M and group C (P=0.001). VAS score was significantly lower in group D < group M < group C (P<0.05). Total dose of postoperative PCA nalbuphine consumption (mg) was significantly reduced in group D than group M (P<0.001). Passaint Fahim Hassan et al (2022)[13] and Vinit K. Srivastava (2016) et al [10] found that intraoperative fentanyl requirement was significantly less in group D compared to group M (P<0.01). Walid Hamed Nofal (2012) et al found that fentanyl consumption was significantly lower in dexmedetomidine group than saline group. Time to the first analgesic dose request(min) was significantly longer in group D than group C (P<0.001). The VAS score was significantly lower in group D at 0, 1 and 2 hours as compared to group C (P<0.001). Kateryna Bielka (2017) et al found that postoperative morphine consumption in 24 hours was significantly less in dexmedetomidine group than control group (p=0.001). Time to first use of rescue analgesia was significantly lower in group D than in group C (p<0.001).

Dexmedetomidine has a perioperative analgesic activity by stimulation of alpha-2 adrenergic receptors at this site reduces central sympathetic outflow, which results in increased firing of inhibitory neurons.[5]It inhibits pain signals to the brain by inhibiting the release of norepinephrine, which in turn induces hyperpolarization at the central pre and post synaptic alpha-2 receptors. Dexmedetomidine helps to modulate the release of nitric oxide by initially releasing of acetylcholine from spinal interneurons, thus it is an analgesic adjuvant.[14]

Magnesium sulphate produces analgesic action as a non-competitive NMDA receptor antagonis. It abolishes hypersensitization by blocking NMDA receptor activation in the dorsal horn by excitatory amino acid transmitter(glutamate).[5]

Limitations of our study was that we have not measured the serum magnesium level. Previous studies by Aabid Hussain Mir et al (2019) observed that toxic level of serum magnesium was not reached even after using magnesium sulphate in the bolus dose of 50 mg/kg followed by continuous infusion of 15mg/kg/hour, which is higher than the dose used in our study for both bolus and maintenance infusion. We didn't have saline group for comparison, so individual effect on onset and recovery with saline group was not possible. Randomization and blinding were not done, so selection and observer bias cannot be totally eliminated as this was an observational study.

## CONCLUSION:

We have concluded that magnesium sulphate decreases the atracurium requirement without affecting onset and recovery of neuromuscular blockage compared to dexmedetomidine. Dexmedetomidine has better analgesic effect and decreases postoperative analgesic requirement more than magnesium sulphate. **Thus, both these drugs are useful adjunct to balanced general anaesthesia technique.**

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