Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Original Research Paper

Studying The Effects of Intravenous Magnesium Sulfate and Fentanyl Citrate on Circulatory Changes During Anaesthesia and Surgery

Medical Science

KEYWORDS : Fentanyl Citrate, magnesium sulfate, anaesthesia , hemodynamic responses, surgery

*** Dr.Dipika Patel**	Anaesthesia, Gujarat Cancer & Research Institute, B.J.Medical college, Ahmedabad, Gujarat, India * Corresponding Author
Dr. Amita Jansari	Anaesthesia, Gujarat Cancer & Research Institute, B.J.Medical college, Ahmedabad, Gujarat, India
Dr. Surekha Shaboo	Anaesthesia, Gujarat Cancer & Research Institute, B.J.Medical college, Ahmedabad, Gujarat, India
Dr. Kuldeep Singh	Anaesthesia, Gujarat Cancer & Research Institute, B.J.Medical college, Ahmedabad, Gujarat, India

ABSTRACT

Introduction: *Magnesium sulphate is a inhibitor of catecholamine from adrenergic nerve endings and adrenal medulla, calcium antagonist and a potent L-type calcium channel inhibitor which plays important role to attenuate the symapthoadrenal responses during anaesthesia and surgery.*

Aim: *To compare the effect of intravenous magnesium sulfate with potent short acting opoid fentanyl citrate on circulatory changes and other effects during perioperative period and surgery.*

Material and method: *50 adult patients ranging from 18-60 years of age, ASA 1 and 2 undergoing modified radical mastectomy were selected and placed in two different groups (25 in each group). Group M received Inj. Magnesium sulfate 30 mg/kg i.v. 5 mins before induction, 20 mg/kg 5 mins before skin incision, 10 mg/kg every 30 mins till the end of surgery. Group F received Inj. Fentanyl Citrate 1.5 mcg/kg i.v. 5 min before induction ,1mcg/kg 5 min before skin incision ,0.5 mcg/kg every 30 min till the end of surgery. Changes in HR, S.B.P., , D.B.P. M.A.P. were recorded at different time interval.*

Result: *All parameters maximum rise is immediately after intubation followed by rise lesser than the previous rise at the time of skin incision which is statistically not significant in both the groups. Rises in MAP and mean HR from pre induction value, immediately after intubation was 5.46% and 5.55% in magnesium sulphate and fentanyl citrate group respectively. Total requirement of Inj. Vecuronium is reduced by 40% in group M compared to group F.*

Conclusion: *Magnesium sulphate and fentanyl citrate both are equally effective for attenuation of hemodynamic response to stress of surgery and anaesthesia.*

Introduction

Laryngoscopy, intubation and surgery are associated with significant increase in sympatho adrenal activity which may result in hypertension, tachycardia and arrhythmias [1,2]. Many methods have been identified to attenuate these responses including opioids, or vasodilators etc[3,4,5]. Magnesium blocks the release of catecholamines from both adrenergic nerve terminals and the adrenal gland[6,7,8] .

Moreover, magnesium produces vasodilatation [7] and high dose magnesium attenuates vasopressin-stimulated vasoconstriction. It is an antagonist of NMDA receptors which shows its adjuvant effect in perioperative analgesia [6,9,10,11].

Fentanyl citrate, an opioid produces effective analgesia and attenuation of hemodynamic responses to stress [11] but has the disadvantage of respiratory depression. So, purpose of our study is to compare the effects of magnesium sulfate with fentanyl on hemodynamic parameters during anaesthesia and surgery.

Material and method

50 adult patients ranging from 18-60 years of age, ASA 1 and 2 undergoing modified radical mastectomy were selected for the study. Patients were assessed pre operatively through history and clinical examination. Investigations were carried out and analysed. Patients with hepatic, renal, cardiac or respiratory problems, Diabetic patients, patient with Haematological disorders and coagulopathies, Morbid Obese, Pregnancy, History of neuropathy, myopathy and neuromuscular diseases, Prior treatment with corticosteroids, calcium channel blockers, Opioids and anticoagulants, MAO inhibitors are excluded from study.

After obtaining institutional Review Committee approval, written informed consent was obtained. Patients were placed in two different groups (25 in each group). Group M received Inj. Magnesium sulfate 30 mg/kg i.v. 5 mins before induction, 20 mg/kg 5 mins before skin incision, 10 mg/kg every 30 mins till the end of surgery. Group F received Inj. Fentanyl Citrate 1.5 mcg/kg i.v. 5 min before induction, 1mcg/kg 5 min before skin incision ,0.5 mcg/kg every 30 min till the end of surgery.

Patients were instructed to remain nil orally for at least eight hours before surgery premedicated with Tab.Lorazepam hydrochloride 1 mg night before surgery and Tab. Diazepam hydrochloride 5 mg in morning at 6:00 am on the day of surgery. Anaesthetic technique was identical in all the patients. On arrival in the operation theatre patients were monitored with routine non-invasive blood pressure measurement, pulse oxymetry and E.C.G. H.R., S.B.P., D.B.P., M.A.P. were recorded as baseline value designated as B. 5mins after giving study drug and before induction H.R., S.B.P., , D.B.P. M.A.P. were recorded and designated as pre induction value designated as P. The trachea was intubated after the induction of anaesthesia with inj.Glycopyrolate 0.2 mg i.v., Inj. Thiopental Sodium 5 mg/ kg i.v.,Inj. Vecuronium Bromide 0.1 mg /kg i.v. Anaesthesia was maintained with 1% sevoflurane and 1:1 O2/N2O at 3litre /min and. Vecuronium requirement is measured by peripheral nerve stimulation and total dose of vecuronium noted in each surgery. No other analgesics except study drugs were used. All patients were mechanically ventilated on volume control mode of ventilator(tidal volume: 8 ml/kg and respiratory rate : 12/min) . Throughout surgery HR, SBP, DBP & MAP were recorded. Timings of recording were Baseline(B), before induction(P),Immediately

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

after intubation(E) ,1 min,3 min,5 min,10 min after intubation(E+1,E+3,E+5,E+10), Every 5 minutes for next 20 minutes followed by every 15 minutes till the end of surgery(15,20,25,30,45,60,75….).

After completion of surgery inj.Glycopyrolate 0.4 mg i.v. and inj.Neostigmine 0.05 mg/kg i.v. were given to reverse neuromuscular blockade followed by extubation in operation there only. Post operatively patients were observed for side effects like sedation, respiratory depression, nausea, vomiting.

We had defined following parameters for study: 1) Hypotension was defined as SBP<25% of baseline value or 90 mm of hg, whichever was lower. 2) Hypertension was defined as SBP>25% of baseline value or 150 mm of hg, whichever was greater. 3)Tachycardia was defined as HR>25% of baseline value. 4) Bradycardia was defined as HR<60 beats per minute. 5) An arrhythmia was defined as any ventricular or supraventricular premature beat or any rhythm other than sinus.

Statistical analysis was done using Graph pad software and mean value was calculated for each parameter. Comparison between two groups was conducted using students t test, analysis of variance (ANOVA). Hemodynamic variables were represented by mean±SD and P value < 0.05 was considered significant.

Results

Table 1 show that both the groups were comparable in patient characteristics with respect to age, gender and ASA physical status. (p>0.05)Fig.1 shows the changes in heart rate during the surgery which increased immediately after intubation beyond the baseline and decreases thereafter and again increases at (E+10=skin incision time) but not beyond the baseline value in both groups. However in both the groups stress response was found to be attenuated significantly throughout the surgery. Fig. 2 shows the changes in systolic blood pressure during study period. We can see that there is effective suppression of stress response throughout surgery and maximum rise in SBP is seen at immediately after intubation followed by at the time of skin incision in both groups. In fig.3 we can see that DBP also peaks at immediately after intubation and during skin incision in both groups. Otherwise both the drugs produces almost parallel & effective attenuation of stress response. Fig 4 shows the changes in mean arterial pressure during study period. We can see that the graph pattern of mean arterial pressures is identical to graph pattern of changes in HR and SBP. Maximum rise is immediately after intubation followed by rise lesser than the previous rise at the time of skin incision in both groups. All vitals were decreased continuously except immediately after intubation,at that time arise of 6.15% & 4.9% in SBP and 6.07% & 5.1% in DBP in magnesium group and fentanyl group respectively. Rises in MAP and mean HR from pre induction value, immediately after intubation was 5.46% and 5.55% in magnesium and fentanyl group respectively. Table 2 shows total requirement of vecuronium in both the groups during surgery. It shows vecuronium requirement is reduced by 40% in group M compared to group F.

Discussion

Laryngoscopy, intubation, surgery and anaesthesia results in increase in stress response which is associated with catecholamine release. Magnesium reduces this release by the adrenal medulla and adrenergic nerve endings [6,7,8].

Fentanyl plays an important role in balanced general anaesthesia by virtue of meeting all aspects of balanced anaesthesia like narcosis, analgesia and attenuation of stress responses but apart from associated bradycardia, respiratory depression, chest rigidity and PONV, its procurement in India is difficult due to rigid narcotic regulation. [6] In circumstances in which these complications may be undesirable, magnesium could be a useful alternative.

Dilip Kothari et al [6] found that both the drugs equivalent in suppressing hemodynamic parameters throughout surgery and anaesthesia. They found both SBP & DBP decreased continuously in both the groups except for a rise of 6.95% & 4.01% in SBP and 5.96% & 4.95% in DBP from pre induction value, immediately after intubation, in magnesium group and fentanyl group respectively which correlate with our study.

Gupta kumkum et al [12] compared the effects of clonidine hydrochloride& fentanyl citrate for hemodynamic stability during surgery and anesthesia and recovery outcome in patients undergoing laparoscopic cholecystectomy under general anaesthesia. Rise in mean HR and mean MAP were 6.7% and 7.4% respectively from preinduction value immediately after intubation.

In our study, we found vitals were well maintained below baseline throughout surgery except rises in mean HR and mean MAP were 5.8% and 5.3% from pre induction value, immediately after intubation.

Weisskopf R B and Daniel M et al [13] studied the effect of fentanyl, esmolol and clonidine for blunting the cardiovascular responses to laryngoscopy and intubation induced by desflurane concentration. They found fentanyl the most clinically useful of these drugs because it blunts the increase heart rate and blood pressure and has minimal cardiovascular depressant effect and little postoperative sedation.

In our study we had given the fentanyl citrate and magnesium sulfate and compared the effects of both in attenuation of haemodynamic responses. We found out that both of them decrease the haemodynamic parameters sufficiently and prevent any rise in parameters if given in sufficient doses and at an optimum time interval.

In our study in Group M vitals were well maintained below baseline throughout surgery except for a rise in hemodynamic parameters immediately after intubation. And these rises in mean MAP and mean HR from pre induction value, immediately after intubation were 5.46% and 5.55% respectively.

Magnesium has cardiovascular effects with the actions of both a calcium antagonist with vasodilator and antiarrhythmic effects and an adrenergic antagonist with principally a-antagonistic actions [15]. As a result of these dual actions, magnesium has a number of potential indications in anesthesia. Magnesium has the potential to treat and prevent pain by acting as an antagonist of NMDA receptors also reduces catecholamine release through sympathetic stimulation by which it might causes peripheral nociceptor sensitization or stress response to surgery and blunt hemodynamic responses to inadequate analgesia. [2] The control of blood pressure in magnesium group is due to combination of vasodilatory effects of the ion and inhibition of catecholamine release.

S.Rajan et al [16] studied effects of magnesium sulphate for hemodynamic stability in TNTS surgery. They found magnesium sulphate effective in attenuating the hemodynamic

responses to stress responses. Vitals were maintained below baseline value throughout surgery except for a rise at immediately after intubation from pre induction value by 5.2% in HR,5.8% in SBP,6.7% in DBP and 4.9% in MAP.

J.H.Rayu et al [17]studied the effects of magnesium sulphate on intraoperative anaesthetic requirements and post operative analgesia in gynecology patients receiving general anaesthesia.. Throughout surgery vitals were well maintained below the baseline value. Increase in vitals from pre induction value noted immediately after intubation. Rise in MAP by 6.66% and rise in HR by 4.76 % from preinduction value immediately after intubation.

It is well known that magnesium inhibits acetylcholine release at motor nerve terminals, thus potentiating the effects of neuro muscular blocking agent. If this combination is to be used, then the dosage of relaxant should be reduced. [18]

Sinatra RS et al [19] studied that Magnesium sulfate potentiates neuromuscular blockade induced by non-depolarizing neuromuscular blocking agents.

Krendal et al [20] showed that magnesium produces dose related inhibition of neuromuscular transmission by competition with calcium for membrane channels on the presynaptic terminals leading to decrease in acetylcholine release. Thus the potential exists for possible interaction between magnesium and muscle relaxants used during anesthesia. We also found the 40% less requirement of vecuronium intraoperatively in group M as compared to fentanyl group.

Magnesium sulfate cheap, easily available, better alternative to costly, not easily available because of narcotic law, potent, opoid fentanyl for attenuation of circulatory changes during surgery and anesthesia.

No adverse outcome like sedation, nausea, vomiting, respiratory depression or any cardiac insult was found during our study. None of these patients had any residual effect of muscle relaxant because they did not require any additional doses of reversal agents nor they require any ventilator support in post operative period.

Conclusion

Hence we conclude that magnesium sulphate and fentanyl citrate both are equally effective for attenuation of hemodynamic response to stress of surgery and anaesthesia. Even though effects of both the drugs are almost same on hemodynamic parameters, magnesium sulfate is a cheap, easily available and good alternative to fentanyl and also reduces the requirement of muscle relaxant than fentanyl.

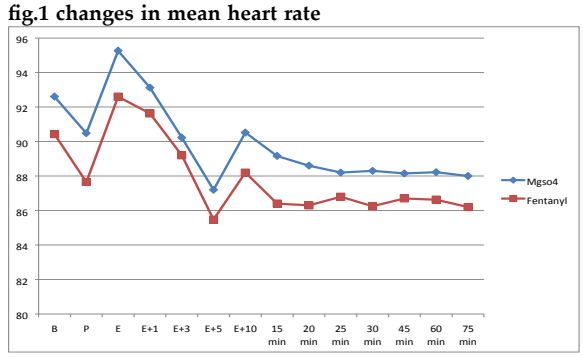
Table 1: Demographic data

Group	Age in years Mean+/-SD	Weight in kg Mean+/-SD
M group(n=20)	43.2 +/-8.6	52.15+/-6.9
F group(n=20)	45.1+/-7.6	55.8+/-5.9

Table 2: Total vecuronium requirement

	Group M	Group F
Total vecuronium requirement (mg)	4.92±0.68 mg	8.16±0.67 mg
Duration of surgery (min.)	110±20min.	115±15min.

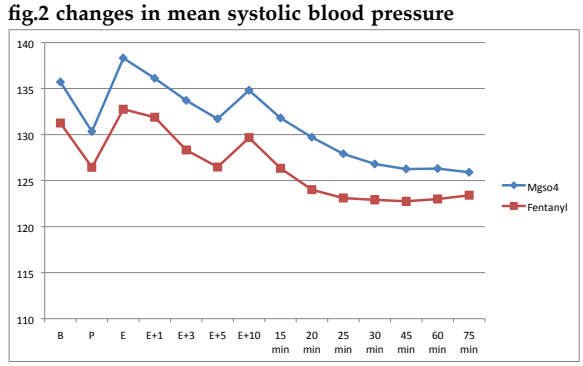
fig.1 changes in mean heart rate



Y axis -Heart Rate Beats per minute

X axis-Time in minute

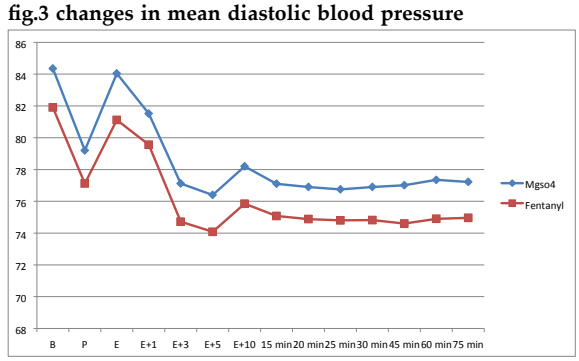
fig.2 changes in mean systolic blood pressure



Y axis -Systolic blood pressure in mm of hg

X axis- Time in minute

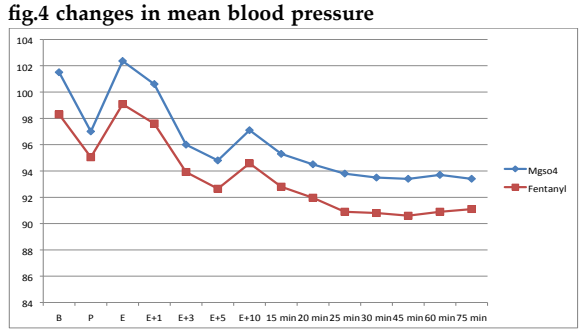
fig.3 changes in mean diastolic blood pressure



Y axis -Diastolic blood pressure in mm of hg

X axis- Time in minute

fig.4 changes in mean blood pressure



Y axis -Mean blood pressure in mm of hg

X axis- Time in minute

Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

References

1. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine response to laryngoscopy with or without tracheal intubation. Br J Aneasth. 1986;59:295-9.
2. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without lidocaine. Anaesthesiology 1977;47:381-84.
3. Helfmann SM, Gold MI, Delisser EA. Which drug prevents tachycardia and hypertension associated with tracheal intubation lignocaine, fentanyl, or esmolol Anaesth Analg 1991; 72:482-86.
4. Sharma J, Sharma V, Ranbushan, Gupta S. Comparative study of magnesium sulphate and esmolol in attenuating the pressor response to endotracheal intubation in controlled hypertensive patients. J Anaesth Clin Pharmacol 2006; 22(3):255-59.
5. Mikawa K, Nishina K, Maekawa N et al. Comparision of nicardipine, diltiazen and verapamil for controlling the cardiovascular response to tracheal intubation. Br J Anaesth 1996;76:221-26.
6. Dilip Kothari, Amrita Mehrotra, Bhanu Choudhary, Alok Mehra. Effect of Intravenous Magnesium Sulfate and Fentanyl Citrate on Circulatory Changes During Anaesthesia and Surgery: A Clinical Study. Indian Journal of Anaesthesia 2008; 52 (6):800-804.
7. G. D. Puri, K. S. Marudhachalam, Pramila Chari, R. K. Suri. The Effect of Magnesium Sulphate on Hemodynamics and Its Efficacy in Attenuating the Response to Endotracheal Intubation in Patients with Coronary Artery Disease. Anesth Analg 1998;87:808-11.
8. Michael F. M. James, R. Eryk Beer, Jan D. Esser. Intravenous Magnesium Sulfate Inhibits Catecholamine Release Associated with Tracheal Intubation. ANESTH ANALG.1989;68:772-6.
9. T. O. Seyhan, M. Tugrul, M. O. Sungur, S. Kayacan, L. Telci, K. Pembeci and K. Akpir. Effects of three different dose regimens of magnesium on propofol requirements, haemodynamic variables and postoperative pain relief in gynaecological surgery. British Journal of Anaesthesia.2006; 96 (2): 247–52.
10. Laurent Dubé, Jean-Claude Granry. The therapeutic use of magnesium in anesthesiology. intensive care and emergency medicine: a review. CAN J ANESTH 2003; 50(7): pp 732–746.
11. L. Telci, F. Esen, D. Akcora, T. Erden, A. T. Canbolat and K. Akpir. Evaluation of effects of magnesium sulphate in reducing intraoperative anaesthetic requirements. British Journal of Anaesthesia.2002; 89 (4): 594-8.
12. Gupta kumkum et al .Anaesthesia : essay and researches .premedication with clonidine versus fentanyl for intraoperative hemodynamic stability and recovery outcome during laparoscopic cholecystectomy under general anaesthesia.
13. Weiskopf RB, Eger EI, Noorani M. Fenatnyl, esmolol and clonidine blunt the transient cardiovascular stimulation induced by desflurane in humans Anaesthesiology, 1994;1350-1355
14. Ko, Seong-Hoon, Kim, Dong-chan, Han, Young-jin, Song, He-sun. small dose fentanyl: optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesthesia & Analgesia. 1998: 86 (3): 658-661.
15. Michael F. M. James. Clinical Use of Magnesium Infusions in Anesthesia. Anesth Analg 1992;74:129-36.
16. S.Rajan,M.Kavita,S.Andrews. Attenuating effect of magnesium on hemodynamic responses during transnasal transsphenoidal surgery.Amrita journal of medicine.vol.8:no.2:july-dec 2012.
17. J.-H.Rayu,M.-H. Kang,K.-S.Park and S.-H. Do.Effects of magnesium sulphate on intraoperative anaethetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. British journal of anaesth.100(3):397-403(2008).
18. Ghonheim MM, Long JP. The interaction between magnesium and other neuromuscular blocking agents. Anesthesiolgy 1970;32;23-8.
19. Sinatra RS, Philip BK, Naulty JS, Ostheimer GW. Prolonged neuromuscular blockade with vecuronium in a patient treated with magnesium sulphate. AnesthAnalg. 1985;64:1220–2.
20. Krendal D.A. Hypermagnesemia and neuromuscular transmission. Semin.Neurol, 1990; 10: 42-45.