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COMPARATIVE STUDY ON EFFECT OF INTRAVENOUS MEGNESIUM SULPHATE AND FENTANYL CITRATE ON THE HEMDYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN ABDOMINAL SURGERIES.

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ABSTRACT

Introduction: Various analgesics available maintain the hemodynamic stability under general anesthesia . Present study was undertaken to compare the efficacy of intravenous Fentanyl and Magnesium for all abdominal surgeries.

Materials and methods: 60 ASA I and II patients of both sexes, posted for various abdominal surgeries were chosen for the study and the patients were divided into two groups of 30 each. Group-M inj. Magnesium sulfate 30mg/kg 5min. before induction. 10mg/kg 5min. prior to skin incision and 10mg/kg every 30min. interval. Group F were given inj. Fentanyl citrate 2mcg/kg, 0.5mcg/kg and 0.5mcg/kg at similar time intervals.HR, SBP, DBP were recorded at 0 min(basal value), after study drug, immediately after intubation, at every 5min interval for next 30min thereafter every 15min till 90min.

Result: Analysis revealed that there was no significant changes in HR, SBP & DBP were observed during the study period in both the groups. But side effects like respiratory depression, sedation, nausea, vomiting and restlessness are more common in group-F as compared to group-M.

Conclusion: From our study we concluded that although the action of Mgso4 is not superior than fentanyl, however, use of Mgso4 has been associated with less side effects like respiratory depression, postop sedation, etc. So after this study we concluded MgSO4 could be a cost effective, easily available and useful alternative to fentanyl.

Keywords: Magnesium sulfate, Fentanyl, General anesthesia.

INTRODUCTION

Magnesium sulfate has been used as anticonvulsant and antiarrhythmic agent in the past. Recently, magnesium has been shown to have antinociceptive effect in animal and human models of chronic pain, mainly due to its antagonist effect on NMDA receptors and calcium ion channels . It also inhibits the catecholamine release from adrenergic nerve terminals and

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adrenal medulla· For these reasons several authors have used magnesium sulfate to attenuate the pressor response to endotracheal intubation and perioperative analgesia. Fentanyl, a widely used narcotic analgesic produces effective analgesia and attenuation of the cardiovascular , hormonal and metabolic responses to stress but has the disadvantage of prolonged respiratory depression . In addition cumbersome narcotic laws in India make it difficult to procure in small hospitals. Hence, based on available literature we decided to compare the effects of magnesium sulfate, a cheap, readily available and widely used drug in obstetric practice with fentanyl, an established anesthetic adjuvant on hemodynamic parameters during anesthesia and surgery.[1,2] The aim of the study is to compare the following factors in two groups i.e., Magnesium sulphate and Fentanyl citrate

MATERIALS AND METHODS

Inpatients posted for major surgeries, below umbilical level, in Osmania General Hospital, Hyderabad were chosen for the study.

Inclusion Criteria: ASA physical status class I and II. Age between 18 – 60 years of either sex IN Patients scheduled to undergo various abdominal surgeries

Exclusion Criteria: patients with major organ dysfunction, patients on calcium channel blockers, hypnotics, narcotic analgesics, allergic to drugs , patients with history of hypertension, ischemic heart disease, A-V Block

After approval from the ethical committee of our Hospital, 60ASAI and II patients scheduled for major surgeries under general anesthesia were chosen for the study. Preanesthetic check-up was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations recorded. The procedure of general anesthesia was explained to the patients and written consent was obtained. Preparation of patients included period of overnight fasting. Patients were premedicated with Tab. Rantac 150mg and Tab. Alprazolam 0.5mg H.S

Boyle‘s anesthesia machine was checked. Appropriate size endotracheal tubes, masks ,working laryngoscope with medium and large size blades, stylet , airways and working suction apparatus were kept ready before the procedure. Difficult airway cart checked and kept on stand by. Emergency drug tray consisting of atropine, adrenaline, nor adrenaline ,dobutamine and dopamine were kept ready.

Patients shifted to Operating table, Baseline vitals were recorded. IV access was obtained on the forearm with No. 18G IV cannula. All the patients received a uniform premedication by glycopyrrolate 0.2mg I.M., 30 min before the start of anesthesia.

Patients were randomly allocated into groups. After securing an intravenous line the study drug was injected slowly over a period of two minutes, then general anesthesia was induced with thiopentone sodium 5 $mg.kg^{-1}$ followed by succinylcholine 2 $mg.kg^{-1}$.

Endotracheal intubation with appropriate size tube was done and lungs were ventilated with O 2 : N 2 O (33% : 66%) and 0.5% sevoflurane using Bain's circuit with a fresh gas flow of 110 $ml.kg^{-1}$. min^{-1} .

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Muscle relaxation was provided by vecuronium 0.08 mg.kg $^{-1}$ (loading dose) and 0.02 mg.kg $^{-1}$ (incremental doses). Study drug was repeated at 5 min before skin incision and at every 30 min interval thereafter. All the patients were reversed with glycopyrrolate 0.4 mg and neostigmine 2.5 mg at the end of procedure. PR, SBP, DBP were recorded at 0 min (basal value), after study drug, immediately after intubation, at every 5 min interval for next 30 min and thereafter every 15 min till 90 min. Observation of those surgeries lasting more than ninety min (three cases) were excluded from analysis, but to complete the study three other cases were included.

In addition sympatho somatic responses were also recorded regarding the presence of lacrimation, sweating, eye movement and any somatic response like swallowing, grimacing, coughing and eye opening through out the study period. Any change in hemodynamic values (±20% of basal values) were recorded and treated accordingly eg. bradycardia by atropine or hypotension by increasing infusion rate or mephentramine 6 mg. I.V. Rise in B.P.& HR was treated by increasing the concentration of sevoflurane. Routine monitoring by E.C.G. recording and pulse oximetry was done by Mindray MEC-509B Multiparameter Patient Monitor. Observations recorded in both the groups of study were tabulated and statistical analysis was carried out by using "percent changes for intragroup(within group) and by using analysis of variance (ANOVA) test student unpaired test for intergroup comparison(Group M and F). Values >0.05 were considered as nonsignificant (NS) and <0.05 as significant(S)..

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.
The following assumptions on data is made, Assumption: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent. Student test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Statistical analysis was done by applying Chi-square test, Anova test and students t‘ test to analyze the data, p value was determined. P>0.05 is not significant; P<0.05 is significant ;P<0.001 is highly significant.

RESULTS

Table 1: Age and Weight distribution of Patients studied

	Magnesium Mean ±SD	Fentanyl Mean ±SD	P value
Age in years	32.36±9.45	35.1±8.67	0.22 (NS)
Weight in Kgs	54.32 ±3.09	57.83 ±9.62	0.062(NS)
Sex ratio	22 : 13	20 : 15	

Table-2: Systolic blood pressure in present study

Systolic blood pressure in mm of Hg	Magnesium Mean ± SD	Fentanyl Mean ± SD	P value
Pre Op	117.87 ±	119.1 ± 10.16	0.632 (NS)
At 0 mins	120.9 ± 7.45	121.5± 9.12	0.781 (NS)

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At 5 mins	118.07 ± 10.31	119.07 ± 11.06	0.718 (NS)
At 10 mins	118.47± 9.49	118.93 ±9.62	0.852 (NS)
At 15 mins	117.33± 10.02	117.76 ±10.10	0.869 (NS)
At 30 mins	118± 9.18	119± 9.01	0.671 (NS)
At 45 mins	116.5± 9.74	116.9 ± 9.4	0.872 (NS)
At 60 mins	116.6± 9.85	117.1±9.78	0.844 (NS)
At 90 mins	116.9±8.92	117.7±9.13	0.732 (NS)

Comparison of the SBP all periods between the two groups shows higher in GROUP F group and is statistically non significant.

Table-3: Diastolic blood pressure in present study

Diastolic blood pressure in mm of Hg	Magnesium Mean ± SD	Fentanyl Mean ± SD	P value
Pre Op	75.83±7.13	76.83 ±7.82	0.606 (NS)
At 0 mins	76.27 ±8.34	76.37 ±7.79	0.96 (NS)
At 5 mins	76.4 ±7.37	76.6 ±7.19	0.91 (NS)
At 10 mins	76.76 ±7.40	75.86 ±5.96	0.605 (NS)
At 15 mins	76.53 ±6.22	76.86 ±6.65	0.84 (NS)
At 30 mins	76.3 ±6.92	76.9 ±7.23	0.74 (NS)
At 45 mins	76.3 ±6.72	76.5 ±7.33	0.91 (NS)
At 60 mins	75.93 ±6.61	76.33 ±7.37	0.82 (NS)
At 90 mins	76.5 ±7.02	76.73 ±6.65	0.89 (NS)

Comparison of the DBP all periods between the two groups shows higher in Group F group and is statistically non significant .

Table-4: Pulse rate per minute in present study

Pulse rate per minute	**Magnesium Mean ± SD**	**Fentanyl Mean ± SD**	**P value**
At 0 mins	122.0±11.6	121.4±9.40	0.86
At 5 mins	121.8±10.87	121.16±11.6	0.82
At 10 mins	121.84±10.7	122.6±10.6	0.78
At 15 mins	121.6 ± 9.87	122.34±11.2	0.78
At 30 mins	121.46±10.8	122.65±10.5	0.66
At 45 mins	121.34±10.7	121.8±9.78	0.86
At 60 mins	122.6±11.2	120.68±9.84	0.49
At 90 mins	122.66±11.3	120.5±10.6	0.44
AE	123.12±11.85	122.8±9.87	0.90

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Comparison of the pulse rate per minute all periods between the two groups shows higher in Group F group and is statistically non significant.

Table-5: Saturation and respiratory rate in both groups

	Magnesium Mean ± SD	**Fentanyl Mean ± SD**	**P value**
Saturation %	99.7 ±0.59	99.7 ± 0.59	**1.000(NS**
Respiratory rate	16.1 ± 1.61	16.1 ±1.61	**1.000(NS**

Comparison of the saturation % and respiratory rate all periods between the two groups shows higher in Group F group and is statistically non significant.

Table-6: ASA grade comparision between 2 groups

		GROUP		
		FENTANYL	MAGNESIUM	Total
	Count	26	33	59
I	Percent	44.06%	55.94%	100.0%
	Count	24	17	41
II	Percent	58.5%	41.5%	100.0%
	Count	50	50	100
Total	Percent	50.0%	50.0%	100.0%

Comparison of ASA grade between the two groups shows higher in Group F group and is statistically non significant.

Table-7: Side Effects in present study

	Magnesium		Fentanyl	
Observation	n	%	n	%
1) nausea	3	10	2	6.66
2) vomiting	2	6.66	1	3.33
3) Respiratory depression	-	-	1	3.33
4) sedation	-	-	3	10
5) restlessness	2	6.66	2	6.66

Comparison of the **side effects** between the two groups shows higher in Group F group and is statistically non significant.

DISCUSSION

General Anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function

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may be impaired. The requirements of balanced general anesthesia hypnosis analgesia, muscle relaxation, adequate oxygenation, control of undesirable reflex activity maintenance of circulatory, acid base and electrolyte equilibrium removal of waste products particularly heat & co2 the requirements enable prompt working conditions and prompt return of physiological status quo . [3,4]

Analgesia a component of balanced general anesthesia and the effect of analgesia is on the hemodynamic changes is the aim of the study. Fentanyl, a lipophilic μ-receptor opioid agonist, as a analgesic component of balanced anesthesia can reduce pre operative pain and anxiety ,decrease somatic and autonomic responses to airway manipulations , improve hemodynamic stability , lower requirements of inhaled anesthetics and immediate post operative analgesia.

In our study design Group-F received Fentanyl 1.5mcg/kg initial dose and subsequent dose of 0.5mcg/kg and Group-M received magnesium sulphate of 20mg/kg initial dose and subsequent dose of 10mg/kg to the patients undergoing abdominal surgeries . In the present study, we evaluated the circulatory changes during anesthesia and surgery ; the results are as Recorded at preoperative (baseline) at 0 mins, at 5mins (after study drug), at 10mins, at 15mins , at 30mins , at 45min, at 60mins , at 90 mins , AE (after extubation). Comparison of the SBP 0 between the two groups shows that SBP 0 is higher in group F group and is statistically non significant with a p value of 0.632 In this comparative study we evaluated the circulatory changes after iv magnesium sulfate and iv fentanyl citrate during general anesthesia and surgery. A clinically significant rise (8.4%) in HR was observed after iv magnesium sulfate, which further decline to baseline values towards the end of study. Ability of magnesium sulfate to inhibit acetylcholine release from vagus nerve in intact animal has been attributed to this effect.

Both the drugs produced statistically insignificant (P>0.05) fall in blood pressure immediately after initial injection but later in the course of study insignificant rise was observed up to 5 minutes after intubation.

No significant changes were observed during rest of the study period in both the groups. Our results are in accordance with Puri et al[10] who also observed increase in pulse rate after magnesium sulfate which further increased after intubation. Nooraei N, Dehkordi concluded that magnesium sulfate is more effective in controlling hemodynamics, although it may increase the heart rate.

They noted a significant fall in MAP after MgSO4 at pre-induction stage with a sudden rise in post intubation period. Shin YH et al [7]also observed a rise in blood pressure after intubation in patient pretreated with i.v. magnesium sulfate

Kothari D, Mehrotra A, Choudhary B, Mehra A et al [8] conducted to compare the effects of magnesium sulfate and fentanyl citrate on circulatory variables during anesthesia and surgery. Sixty patients (ASA-I& II) of either sex, between the age of 25-45 years were given either magnesium sulfate (Group M, n=30) 20mg.kg -1 5 min before induction, 10 mg.kg -1 5 min before skin incision and 10 mg.kg -1 every 30 min interval or fentanyl citrate (Group F, n=30) 1.25 mcg.kg -1 , 0.5 mcg.kg -1 and 0.5 mcg.kg -1 at similar time intervals. A clinically significant rise in pulse rate (±11.3%) was recorded in Group M after initial

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injection. Statistically insignificant rise in all hemodynamic variables from baseline values were recorded immediately after intubation in both the groups, after which they returned and maintained, nearer to baseline values. No sympatho-somatic responses like tearing, sweating, eye movement etc. were observed during the course of study. In conclusion, the clinical results suggest that magnesium sulfate could be a safe and cheaper alternative analgesic to fentanyl citrate during general anesthesia.

Ravi Shankar Goarya , Ashish Mathur et al [9]study was to compare the effects of magnesium sulfate and fentanyl citrate on hemodynamic variables during anesthesia and surgery. Side effects like respiratory depression, sedation, nausea, vomiting and restlessness are more common in group B as compared to group A. Study concluded that although the action of Mgso4 is not superior than fentanyl, however, use of Mgso4 has been associated with less side effects like respiratory depression, postop sedation, etc. So after his study concluded MgSO4 could be a cost effective, easily available and useful alternative to fentanyl. Magnesium caused a significant delay in the onset of both sensory and motor blockade compared with the fentanyl and control groups. The duration of spinal analgesia in group F (fentanyl) was significantly greater than in group C (control) and group M (magnesium) Addition of intrathecal magnesium sulfate to spinal anesthesia induced by bupivacaine significantly prolonged the onset of both sensory and motor blockade compared with fentanyl. They concluded, (100 mg) magnesium sulphate or (25 μg) fentanyl as adjuvants with bupivacaine to spinal anaesthesia. With magnesium, in Group BM there was slower ascent of the drug, probably due to change in baricity of the drug. Analysis of intra-operative haemodynamics showed that the incidence of hypotension and bradycardia was more in fentanyl group as compared to magnesium group. The haemodynamic variables were comparable between groups B and C, similar to the study by Nath *et al.*[10]

According to Rout CC et al[11] the patients receiving intrathecal opioids should be under close surveillance for adequacy of breathing but suggests that low dose neuraxial administration of narcotics as in our study does not obligate observation in an intensive care environment.

CONCLUSION

The stability with magnesium sulfate could be attributed to its antagonistic activity on Ca^{++} and NMDA receptor or inhibition of catecholamine release or vasodilatory effect of the ion or a combination of all these. Fentanyl suppresses the nociceptive stimulation or centrally decreases the sympathetic tone . MgSO4 in several studies is shown to reduce the requirement of narcotics for postoperative pain due to analgesic and co-analgesic effects. In the practice of anesthesia, any increase in hemodynamic values in ASA status I& II patients is usually considered to be due to inadequate analgesia. Therefore we think that near stable hemodynamic variables and absence of any sympatho-somatic response with both the drugs in this study should be an indication of adequate analgesia. Hence, we conclude that although the action of magnesium sulfate is not superior to the actions of po-tent short acting opiate fentanyl, however, use of opi-ate has been associated with some side effects like res-piratory depression, PONV etc. In circumstances, where these complications are undesirable, magnesium sulfate could be a cheap, easily available and useful alternative.

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