Original Research Article

Hemodynamic stability after epidural fentanyl alone and with magnesium sulphate for post-operative analgesia: A comparative study

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Abstract

Background: Postoperative pain management is a major concern for the treating physicians. Epidural opioids are proven to be very effective for postoperative analgesia. Magnesium, the non-competitive NMDA antagonist, administered intrathecally, is proved to prolong the duration of spinal opioid analgesia in humans. **Aim:** To compare the effects of epidural fentanyl and fentanyl with magnesium sulphate on hemodynamic stability in patients undergoing elective lower limb and lower abdominal surgeries. **Material and Methods:** A total of 50 ASA I/II patients scheduled to undergo elective lower limb and lower abdominal surgeries were selected for the study and allocated into one of the two groups: Group F (25 patients): received Epidural Fentanyl 50 µg (1cc) diluted and made up to 6cc with normal saline and Group FM (25 patients): received Epidural Fentanyl 50 µg(1cc)+ Magnesium sulphate 50mg (4 units in insulin syringe of 50% solution) diluted and made up to 6cc with normal saline. Duration of analgesia (min) and effects on pulse rate and blood pressure were assessed. **Results:** There was significant increase in pulse rate in Group F compared to Group FM from 1 hour 15 minutes. Similarly, there was significant increase in SBP in Group F compared to Group FM from 1 hr 30 minutes. These parameters remained stable in Group FM. The DBP and MAP between the two groups were comparable throughout the study period, and they were stable. **Conclusion:** addition of Magnesium Sulphate to Fentanyl in Epidural analgesia prolonged the duration of analgesia with hemodynamic stability.

Key Word: Epidural anaesthesia, Fentanyl, Magnesium sulphate, Post-operative analgesia, Hemodynamics

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INTRODUCTION

Postoperative pain management is a major concern for the treating physicians.[1]Poorly managed acute pain that might occur following surgery can produce pathophysiologic processes in both the peripheral and central nervous systems that have the potential to produce chronicity.[2]

Continuous spinal epidural (CSE) block combines the rapidity, density and reliability of the subarachnoid block with the flexibility of continuous epidural block to extend the duration of analgesia. The CSE technique has become popular for major orthopedic surgery and in obstetrics.[3] Epidural opioids are proven to be very effective for postoperative analgesia. Because of its greater lipophilic nature, fentanyl offers some advantages for epidural analgesia. Fentanyl undergoes rapid vascular absorption from the Epidural space, and it spreads less rostrally than other commonly used opioids.[4] It may also undergo uptake into Epidural fat or diffusion across the dura into the cerebrospinal fluid (CSF). The rapidity of analgesic effect of Epidural Fentanyl administration and the relatively short duration of action makes it the drug of choice for postoperative acute pain.[4] Magnesium, the non-competitive NMDA antagonist, administered intrathecally, is proved to prolong the duration of spinal

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opioid analgesia in humans.[5] Co-administration of epidural magnesium sulphate for postoperative epidural analgesia has provided a pronounced reduction in patient-controlled epidural fentanyl consumption without any side-effects.[6] On the basis of these evidences, the present study was undertaken to compare the effects of epidural fentanyl and fentanyl with magnesium sulphate on hemodynamic stability in patients undergoing elective lower limb and lower abdominal surgeries.

MATERIAL AND METHODS

The present prospective comparative clinical study was conducted in patients scheduled to undergo elective lower-limb and lower abdominal surgeries. Ethical clearance was obtained from Institutional Ethical Committee. Informed/written valid consent was obtained from each patient before starting the study. A total of 50 ASA I/II patients scheduled to undergo elective lower limb and lower abdominal surgeries were selected for the study and allocated into one of the two groups:

- **Group F (25 patients):** received Epidural Fentanyl 50 µg (1cc) diluted and made up to 6cc with normal saline.
- **Group FM (25 patients):** received Epidural Fentanyl 50 µg (1cc)+ Magnesium sulphate 50mg (4 units in insulin syringe of 50% solution) diluted and made up to 6cc with normal saline.

Inclusion criteria

- Patients aged between 35 to 45 years of age of either sex.
- Posted for elective lower limb and lower abdominal surgeries
- ASA grade I/II

Exclusion criteria

- Patient's refusal
- Morbidly obese patients and patients with coagulopathies.
- Patients with vertebral column defects, local sepsis or significant neurological deficits
- ASA grade III/IV/V

Preoperatively routine investigations were done in all patients. The Epidural space was identified at L2-L3 or L3-L4 by midline approach using 16 gauge Tuohy's needle by loss of resistance technique. Dural puncture was performed by a needle-through-needle technique with a 25G spinal needle and 3 ml of 0.5% Bupivacaine heavy injected into the intrathecal space. 18 G Epidural catheter was then inserted into the Epidural space. Routine intra-operative monitoring of pulse rate, blood pressure, oxygen saturation and respiratory rate was done for all the patients and the following parameters were noted. After regression of sensory block (checked by pin prick) to L1, patients in Group F received 50 µg of Fentanyl and Group FM received 50 µg of Fentanyl plus 50 mg Magnesium sulphate. Patients were monitored for duration of analgesia, haemodynamic changes, respiratory rate, SpO2 and side effects. After 30 minutes of monitoring in PACU patients were transferred to post-operative ward. Patients' first analgesic requirement time were recorded. Adverse events related to drug and Epidural catheter were observed for 24 hrs.

Statistical analysis: Results obtained on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number(%). Significance was assessed at 5% level of significance. SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 softwares were used for the analysis of the data. Student t-test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups Chi-square/ Fisher Exact test were used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

In present study,the mean age of study population in group F was 39.92±4.23years and in Group FM it was 40.6±4.46 years. The association of two groups with age was statistically not significant (P value>0.05). There was no statistically significant difference in the ratio of males to females in both the study groups. Femur fracture cases were more in both the study groups as compared to other fracture types but there was no statistically significant difference between two groups with the type of fractures (P value>0.05).

Table 1: Comparison of Sociodemographic parameters

Parameter	Group F	Group FM
Age (years)		
Mean age	39.92±4.23	40.6±4.46
Sex		
Male	18 (72%)	18 (72%)
Female	07 (28%)	07 (28%)
Types of cases		
Fracture femur	09 (36%)	11(44%)
Hysterectomy	05 (20%)	04 (16%)

Fracture tibia and fibula	09 (36%)	07 (28%)
Inguinal hernia	02 (8%)	03 (12%)

Time taken for highest sensory level (Min) in Group F and Group FM were comparable. And also duration of surgery (min) in Group F was 99.00±13.31 and in Group FM was 92.20±15.21 with a p=0.099 and they were comparable. Time for regression to L1 (min) in Group F was 118.80±13.41 and in Group FM was 119.60±17.85 with p=0.859 and they were comparable. Once the sensory level regressed to L1, test drug was administered. Duration of analgesia (time from administering test drug to patient's first complaint of pain) in Group FM was 143.40±39.57 min and in Group F was 107.00±25.82 min with a p<0.001. It was significantly prolonged in Group FM compared to Group F. Minimum analgesic duration in Group F was 65 min and 80 min in Group FM. Maximum analgesic duration in Group F was 170 min and Group FM was 215 min. Time taken for regression of sensory level to L1 was comparable in both the groups, but duration of analgesia was significantly prolonged in Group FM compared to Group F.

Table 2: Comparison of other parameters between two study groups

Parameter	Group F	Group FM
Highest sensory blockage		
T10	0	3 (12%)
T8	7 (28%)	6 (24%)
T6	15 (60%)	15 (60%)
T4	03 (12%)	01 (4%)
Min. time taken for highestsensory level	13.92±4.50	12.24±3.43
Duration of surgery	99.00±13.31	92.20±15.21
Time for regression to L1(min)	118.80±13.41	119.60±17.85
Duration of analgesia(min)	107.00±25.82	143.40±39.57

There was a significant increase in the pulse rate from 1 hr 15 min in Group F compared to Group FM, but it was stable in Group FM during the study period.

Table 3: Comparison of pulse rate between two groups

Pulse rate	Group F	Group FM	Significance
1 minute	84.16±13.45	81.44±12.07	P=0.455
2 minutes	84.16±14.25	81.40±11.56	P=0.456
3 minutes	83.84±13.99	80.04±10.66	P=0.285
4 minutes	84.76±14.12	80.60±9.10	P=0.222
5 minutes	84.64±14.16	79.64±9.05	P=0.143
10 minutes	84.36±14.15	79.48±8.19	P=0.142
15 minutes	84.16±13.31	78.60±8.49	P=0.085
20 minutes	82.44±12.55	79.60±8.89	P=0.360
25 minutes	83.00±12.43	78.76±9.03	P=0.174
30 minutes	83.64±11.93	79.20±8.66	P=0.139
45 minutes	82.96±10.02	78.92±6.56	P=0.098+
1 hr	84.84±9.41	79.24±6.62	p=0.019*
1 hr 15 min	85.17±10.10	79.48±6.97	P=0.027*
1 hr 30 min	87.95±9.75	82.00±8.50	P=0.032*
1 hr 45 min	89.46±8.92	82.48±7.61	P=0.021*
2 hr	92.33±11.75	85.88±6.77	p=0.104
2 hr 30 min	95.33±12.86	86.10±6.99	p=0.122
3 hr	92.33±11.75	85.88±6.77	p=0.104
3 hr 30 min	95.33±12.86	86.10±6.99	p=0.122
4 hr	92.33±11.75	85.88±6.77	p=0.104

There was significant increase in SBP from 1 hr 30 min in Group F compared to Group FM and it was stable in Group FM.

Table 4: Comparison of systolic BP between two groups

Systolic BP	Group F	Group FM	Significance
1 minute	112.72±11.66	113.60±8.89	P=0.765
2 minutes	111.80±12.03	112.00±7.50	P=0.944
3 minutes	112.00±11.82	112.64±8.21	P=0.825
4 minutes	111.40±12.49	113.64±7.47	P=0.445
5 minutes	112.64±11.01	113.40±8.16	P=0.783
10 minutes	112.88±10.80	112.56±7.26	P=0.903

15 minutes	113.60±11.18	112.92±7.93	P=0.805
20 minutes	113.72±11.48	112.44±5.64	P=0.619
25 minutes	112.68±11.64	113.56±5.86	P=0.737
30 minutes	112.08±10.34	112.44±6.40	P=0.883
45 minutes	114.84±8.28	114.36±5.33	P=0.888
1 hr	116.60±9.79	114.80±5.04	P=0.418
1 hr 15 min	119.26±8.84	115.36±4.91	P=0.062+
1 hr 30 min	121.90±7.03	117.62±5.43	P=0.026*
1 hr 45 min	126.15±10.14	118.85±5.44	P=0.011*
2 hr	130.67±14.97	119.74±6.19	P=0.015*
2 hr 30 min	124.67±5.03	119.10±6.61	P=0.210
3 hr	130.67±14.97	119.74±6.19	P=0.015*
3 hr 30 min	124.67±5.03	130.67±14.97	P=0.210
4 hr	130.67±14.97	119.74±6.19	P=0.015*

There was no significant variation in DBP among the two groups.

Table 5: Comparison of diastolic BP between two groups

Diastolic BP	Group F	Group FM	Significance
1 minute	70.48±7.47	72.92±7.86	P=0.266
2 minutes	71.12±7.48	72.32±5.34	P=0.517
3 minutes	71.08±7.09	71.40±5.32	P=0.857
4 minutes	70.44±7.25	71.76±6.20	P=0.492
5 minutes	70.44±8.05	71.88±5.66	P=0.468
10 minutes	71.36±7.23	73.56±6.44	P=0.262
15 minutes	70.96±6.73	71.44±5.14	P=0.778
20 minutes	71.08±7.53	71.00±4.49	P=0.964
25 minutes	71.68±6.90	72.04±5.65	P=0.841
30 minutes	70.88±6.13	71.40±5.12	P=0.746
45 minutes	72.40±5.62	74.20±4.67	P=0.224
1 hr	72.84±5.67	74.36±5.39	P=0.336
1 hr 15 min	74.91±6.65	75.32±4.83	P=0.807
1 hr 30 min	76.52±6.43	77.04±5.17	P=0.766
1 hr 45 min	77.54±6.27	77.50±5.03	P=0.985
2 hr	78.00±7.04	78.42±5.68	P=0.882
2 hr 30 min	74.67±3.06	76.50±6.52	P=0.654
3 hr	78.00±7.04	78.42±5.68	P=0.882
3 hr 30 min	74.67±3.06	76.50±6.52	P=0.654
4 hr	78.00±7.04	78.42±5.68	P=0.882

MAP was stable throughout in both the groups and it was comparable.

Table 6: Comparison of mean BP between two groups

Mean BP	Group F	Group FM	Significance
1 minute	84.56±7.87	86.48±7.68	P=0.387
2 minutes	84.68±7.98	85.55±5.28	P=0.653
3 minutes	84.72±7.42	85.15±5.30	P=0.238
4 minutes	84.09±8.03	85.72±5.49	P=0.407
5 minutes	84.51±7.73	85.72±5.42	P=0.407
10 minutes	85.20±7.41	86.56±5.42	P=0.407
15 minutes	85.17±7.30	85.27±4.57	P=0.957
20 minutes	85.29±7.56	84.81±4.03	P=0.781
25 minutes	85.35±7.56	85.88±5.06	P=0.387
30 minutes	84.61±7.03	85.08±4.51	P=0.387
45 minutes	86.48±5.93	86.48±7.68	P=0.795
1 hr	87.42±6.48	87.84±4.53	P=0.795
1 hr 15 min	88.04±10.51	88.67±4.21	P=0.784
1 hr 30 min	91.65±5.84	90.56±4.77	P=0.498
1 hr 45 min	93.74±7.06	91.28±4.72	P=0.238
2 hr	95.55±9.42	91.19±5.36	P=0.278

2 hr 30 min	91.33±3.71	90.70±5.72	P=0.862
3 hr	95.55±9.42	92.19±5.36	P=0.278
3 hr 30 min	91.33±3.71	90.70±5.72	P=0.862
4 hr	95.55±9.42	92.19±5.36	P=0.278

One patient from group F had nausea/vomiting, whereas two patients had nausea/vomiting from group FM. One patient from group FM had urinary retention but none of the patient had urinary retention from group F. There was no significant difference in incidence of adverse effects likenausea/vomiting, pruritis, urinary retention and others in the two groups.

DISCUSSION

Postoperative pain may produce a range of detrimental effects and if not treated effectively may lead on to chronic postsurgical pain.[7] Combined Spinal Epidural block, as it combines the rapidity, density, and reliability of the subarachnoid block with the flexibility of continuous Epidural block to extend duration of analgesia, is used for the study purpose.[3] Epidural anaesthesia and analgesia is proven to reduce the incidence and severity of perioperative physiologic derangements, in addition to relieving pain. Adjuvants such as opioids and Magnesium can improve the duration and quality of post-operative analgesia. Epidural Fentanyl because of its rapidity of onset of analgesia and relatively short duration of action has been the drug of choice for acute postoperative pain22. Effective single Epidural dose for Fentanyl is found to be 50- 100 µg 13,70 with rapid onset of analgesia in 5-10 min and shorter duration of action (2-4 hr). In our study, both groups were comparable in terms of baseline characteristics such as age, gender distribution, type of cases taken up for surgery. Since the duration of surgery and time to regression of sensory block to L1 was similar and comparable in both the groups statistically, the time between regression to L1, when test drug was given, and patient's first complaint of pain more correctly represents duration of analgesia due to test drugs with minimal bias associated with spinal block and duration of surgery. In the present study, there was significant prolongation of duration of analgesia in Group FM (143.40 mins) compared to Group F (107.0 mins) with $p<0.001$. Out of 25 patients in Group F, maximum duration of analgesia was 170 min and minimum was 65 min with a Mean of 107±25.82. In Group FM maximum duration of analgesia was 215 min and minimum was 80 min with a Mean of 143.4±39.57.Noxious stimulation leads to the release of neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. NMDA receptor signaling may be important in determining the duration of acute pain[8] Therefore, NMDA receptor antagonists may play a role in the prevention and treatment of post-injury pain. Magnesium blocks calcium influx and noncompetitively antagonizes NMDA receptor channels.[9] Mg can have an effect on pain when used alone, but it has also been shown that it can reveal the analgesic properties of opioids.[10] In this way the co administration of Magnesium with Fentanyl may prolong Fentanyl analgesia. Bilir *et al*,[6] where they used Fentanyl PCEA in Group F and Fentanyl PCEA with 50 mg bolus Mg and continuous Mg infusion Epidurally in Group FM, time to first analgesic requirement (comparable to duration of analgesia in our study) was slightly longer in Group FM (51.6 min) compared to Group F (37.1 min). Compared with patients in Group F, patients in Group FM received smaller doses of Epidurally infused Fentanyl at all time points after 30 min. There was 25% reduction in Fentanyl consumption in Group FM at the end of 24 hr compared to Group F. Thus, addition of Mg allowed lesser requirement of Fentanyl in the post-operative period due to its NMDA receptor antagonist action and potentiation of opioid analgesic effects. This is comparable to the results of the present study wherein adding Mg (50 mg) to Fentanyl (50 µg) Epidurally as a single dose markedly increased duration of Fentanyl analgesia in group FM compared to group F. In the study conducted by Arcioni *et al*[11] using Epidural Mg infusion and morphine for postoperative analgesia, postoperative morphine requirements assessed for 36 hrs were less in Epidural Magnesium group (24.0 mg) compared to control group (38.96 mg). Mean morphine requirement was reduced by 38%. This was attributed to NMDA receptor antagonism of Mg and pain modulation and its potentiation of opioid analgesia. Similar potentiation of Fentanyl analgesia is seen with Epidurally administered Mg as a single dose in the present study. There was significant increase in pulse rate in Group F compared to Group FM from 1 hour 15 minutes. Similarly, there was significant increase in SBP in Group F compared to Group FM from 1 hr 30 minutes. These parameters remained stable in Group FM. The DBP and MAP between the two groups were comparable throughout the study period, and they were stable. Significant increase in the pulse rate and SBP in Group F compared to Group FM in our study from 1 hour 15 minutes could be attributed to onset of patient's pain (coinciding with the wear off of the analgesic effect: mean duration of analgesia in Group F was 107 min, with minimum analgesic duration of 65 min±SD25.8). Oxygen saturation and respiratory rates remained stable, and there was no significant difference between the groups. Thus,

we infer that Mg 50 mg administered Epidurally along with Fentanyl has no significant cardiorespiratory adverse effects. Bilir *et al*[6] in the study of Epidural Magnesium and Fentanyl for postoperative pain, found that SBP, DBP, MAP, pulse rate and oxygen saturations remained stable, and there was no significant difference between the groups. Epidural Mg had no adverse effects on cardiorespiratory systems. No significant differences were found in cardiorespiratory variables like SBP, DBP, MAP, heart rate, respiratory rate or SPO2 between the groups in study, of Epidural Mg to reduce postoperative analgesic requirements, conducted by Arcioni *et al*[11] Magnesium maintained hemodynamic stability. In the above mentioned studies the hemodynamic parameters were stable and comparable between the groups for the obvious reasons that one of the studies had used PCA (using morphine) and the other PCEA (using Fentanyl) for postoperative analgesia. Similarly, in the present study, during the duration of analgesia, hemodynamic parameters were stable and comparable in the two groups. Thus, we conclude that 50 mg of Epidurally administered Mg has no adverse effects on hemodynamics.

CONCLUSION

It can be concluded from the present study that addition of Magnesium Sulphate to Fentanyl in Epidural analgesia prolonged the duration of analgesia with hemodynamic stability.

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