Original Research Article

A comparative study of dexmedetomidine HCL infusion and fentanyl citrate infusion as an anaesthetic adjuvant in patients for supratentorial craniotomy

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Abstract

Background: The present study compares the efficacy of Dexmedetomidine Hcl and Fentanyl Citrate as an anaesthetic adjuvant in patients of supra tentorial craniotomy. This prospective, randomised study, was carried out in out in our institute, 100 cases of ASA grade I and II patients, aged 18-65 years of either sex. the patients were divided in two groups. Group D received inj. Dexmedetomidine HCL in a loading dose of 1µg/kg in 100ml NS 0.9% over 10 min. before induction and maintenance and infusion in a dose of 0.4-0.5µg/kg/hr. group F received inj. fentanyl citrate at loading dose 4µg/kg/hr. and in an infusion dose of 0.02-0.03µg/kg/hr. inj. Dexmedetomidine and inj. Fentanyl infusion were continued until the skin sutures initiated. Extubation time recovery time and time to reach aldret score 8 was noted. Post operative nausea, vomiting, bradycardia, tachycardia, hypotension, shivering was observed. **Observations:** all the parameters like age,sex, heart rate, SBP, DBP, MAP were compared in both the groups. P value is statistically significant in group D. Extubation time in group D is less as compared to group F. time to reach aldret score 8 is less with Dexmedetomidine Hcl as compared to Fentanyl Citrate. **Conclusion:** we can conclude that inj. Dexmedetomidine HCL is better than inj. Fentanyl Citrate for perioperative hemodynamic stability in a loading dose of 1µg/kg followed by maintenance dose of 0.4µg/kg/hr in patients undergoing supratentorial craniotomy.

Keywords: Dexmedetomidine HCL, Fentanyl Citrate

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INTRODUCTION

The aims of Neuroanaesthesia are to provide good operating conditions and to ensure stable cerebral hemodynamic without a sudden increase in intracranial pressure or acute brain swelling. Early recovery from anaesthesia is often preferred to allow immediate neurological evaluation.[2]During recovery, abrupt increase in arterial blood pressure can pose a risk for postoperative hematoma, haemorrhage.

Opioids like Fentanyl with a quick onset and short duration of action upon µ receptors prevents hemodynamic responses to awakening and extubation, but it may result in respiratory depression and high CO_2 tension with the subsequent increase in intracranial pressure.[2] α-2 adrenergic agonists have been introduced to clinical anaesthesia for their sympatholytic, sedative, anaesthesia-sparing and hemodynamic stabilizing properties. Dexmedetomidine has shown analgesic effects without respiratory depression. It provides good perioperative hemodynamic stability. This study seeks to compare

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Fentanyl, one of the standard drugs used in neuroanaesthesia with dexmedetomidine, with regard to hemodynamic responses to stimulants, recovery criteria and side-effects. fentanyl undergoes hepatic metabolism with no active metabolites. approx. 7% is excreted unchanged in urine. however, clearance is decrease in uraemia.

MATERIALS AND METHODOLOGY

After obtaining approval from the ethical committee of Gujarat cancer and research institute, Ahmedabad and after taking written consent from each and every patient the following study was concluded. 100 cases of ASA grade I and II aged 18-65years of either sex who were scheduled to undergo an elective supra tentorial craniotomy were included in this study. The following patients were excluded from the study – women who were pregnant and lactating, patients with hepatic or renal disorders, patients having sensitivity to opioids or any of the drugs used, patients on opioids, benzodiazepines or Tricyclic Antidepressants 48 hours prior to the study, patients with neurological diseases like Parkinsons, Alzheimer's, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Gullies-Barre Syndrome, alcohol and drug addicts, patients suffering from any psychiatric illness and patients with any active infections and patients in whom the duration of laryngoscopy is >30 sec. The patients were randomized into two groups. First group – Group D, received inj. Dexmedetomidine HCL in a loading dose of 1 µg/kg in 100 ml NS over 10 minutes before induction and maintenance infusion in a dose of 0.4-0.5 µg/kg/hr throughout the surgery. The second group – Group F, received inj. Fentanyl Citrate at a loading dose of 4 µg/kg and maintenance infusion in a dose of 0.02-0.03 µg/kg/hr throughout the surgery. Patients were kept NBM for 8 hours before surgery and instructed to take all the drugs which he/she was taking as a part of treatment as scheduled with sips of water on the day of the surgery. On the arrival of the operation theatre baseline vital parameters were recorded – ECG, HR, SBP, DBP, MAP, SpO_2. The gender, age, body weight and duration of operation for each case were recorded. HR, BP, SpO_2 were recorded at baseline, after infusion of study drug, after induction, after intubation, before and after skull pin insertion, intra-operatively every 30 minutes, at the time of extubation and in the post-operative period at 2,4 and 8 hours. Patients were premedicated with IV Inj.Glycopyrrolate 0.004 mg/kg, Inj. Ondansetron 0.08 mg/kg and Inj. Ranitidine 1 mg/kg. In Group D patients, dexmedetomidine 1 µg/kg was started 10 minutes before induction. After preoxygenation with 100% O_2 Patients were induced with I.V. Inj. Thiopentone Sodium 5mg/kg, Inj.Vecuronium Bromide 0.1 mg /kg and Inj.fentanyl citrate 2 µg/kg. IV Lignocaine 2% 1.5mg/kg was given to prevent the stress response to intubation. intubated with the proper sized flexometalic endotracheal tube. Proper placement of endotracheal tube was confirmed by air entry in lungs and $etCO_2$. Maintenance of anaesthesia was achieved with N_2O and O_2, inhalational agent like Sevoflurane or isoflurane and Infusion of vecuronium bromide 0.001mg/kg/hr. Dexmedetomidine infusion at a rate of 0.4-0.5 µg/kg/hr. In Group F induction was achieved by Inj. fentanyl citrate 4 µg/kg and the same dose of thiopentone and vecuronium. Maintenance was same as in Group D, except for the administration of Dexmedetomidine. Fentanyl infusion at a rate of 0.02-0.03 µg/kg/hr. Before applying skull pin, local infiltration of 8-10 ml lignocaine 2% was done at the skin incision site. All patients were mechanically ventilated on volume control mode of a ventilator (tidal volume:8-10 ml/kg and respiratory rate: 12-16/min to maintain $etco_2$ 25-30 mmHg). All patients were catheterized and urine output was maintained at 0.5 ml/kg/hr. Before the opening of the dura, corticosteroids (8mg i.v.bolus), furosemide(0.5-1mg/kg), and mannitol(1mg/kg) were given as per the requirement. After the dura was opened, surgeons were asked to evaluate the cerebral swelling status.

Dexmedetomidine and Fentanyl infusions were continued until the skin sutures were initiated. Anaesthesia was stopped when sutures were completed. Neuromuscular blockade was antagonized with 0.008 mg/kg of glycopyrrolate and 0.05 mg/kg of neostigmine. After sufficient respiratory activity was observed and consciousness was regained, patients were extubated. Extubation time, recovery time and time to reach Aldrete Score 8 was recorded. Patients were taken to the postoperative unit and hemodynamic parameters and complications like bradycardia, hypotension, tachycardia, hypertension, shivering, nausea-vomiting were watched for.

We had defined following parameters for study: Hypotension was defined as MAP<20% of baseline value or 60 mm Hg, whichever was lower. The rescue drug was atropine 0.3mg if HR <50 BPM. OR Mephentermine 6mg if MAP<20% of baseline. Hypertension was defined as MAP>20% of baseline value or 110 mmHg, whichever was greater. Tachycardia was defined as HR>100 BPM. Bradycardia was defined as HR<50 BPM. The mean value was calculated for each parameter and Statistical analysis was done by unpaired t-test using the Graph Pad software. P value < 0.05 was considered significant.

OBSERVATION AND RESULTS

This comparative study includes 100 adult patients aged 18-65 years belonging to ASA group 1 and 2 undergoing supratentorial craniotomy. They were randomly assigned to two groups of 50 each. All the patients were given the drug according to methodology of our study and HR, SBP, DBP, and MAP were recorded in both the groups.

Table 2: comparison of heart rate (beats per minute) in both groups

Time	Dexmedetomidine Group (mean±SD)	Fentanyl Group (mean±SD)	P-value	Results
BASELINE	77.22±6.76	77.86±5.96	0.6	NS
AFTER INFUSION OF DRUG	70.86±5.83	76.8±4.95	<0.0001	S
AFTER INDUCTION	68.5±5.31	73.38±4.45	<0.0001	S
AFTER INTUBATION	75.06±6.76	82.84±8.11	<0.0001	S
BEFORE SKULL PIN INSERTION	69.58±5.86	72.04±5.57	0.03	S
AFTER SKULL PIN INSERTION	74.78±3.91	85.34±6.16	<0.0001	S
30 MINS	69.62±4.14	78.28±4.59	<0.0001	S
1 HR	69.56±3.54	76.48±5.07	<0.0001	S
1 HR 30 MINS	69.86±2.53	77±3.81	<0.0001	S
2 HR	70.26±2.76	78.82±4.88	<0.0001	S
2 HR 30 MINS	70.31±3.10	73.41±4.47	0.0001	S
3 HR	70.28±3.49	77.78±4.06	<0.0001	S
EXTUBATION	77.42±3.41	84.68±5	<0.0001	S

Table 2 shows comparison of HR in both the groups. P value is statistically significant between dexmedetomidine and fentanyl group. (p-value <0.05)

Table 3: Comparison of sbp in both groups

Time	Dexmedetomidine Group (mean±sd)	Fentanyl group (mean±sd)	P-value	Results
BASELINE	130.52±5.93	131.24±6.68	0.5	NS
AFTER INFUSION OF DRUG	115.7±7.33	123.02±6.84	<0.0001	S
AFTER INDUCTION	110.42±6.23	116.36±6.31	<0.0001	S
AFTER INTUBATION	123.58±5.83	133.82±6.84	<0.0001	S
BEFORE SKULL PIN INSERTION	115.34±4.87	119.78±6.38	0.0002	S
AFTER SKULL PIN INSERTION	122.88±3.74	135.8±5.3	<0.0001	S
30 MINS	107.62±5.98	118.72±6.73	<0.0001	S
1 HR	112.52±8.3	119.58±6.73	<0.0001	S
1 HR 30 MINS	110.52±8.3	119.06±6.01	<0.0001	S
2 HR	114.41±7.1	118.93±5.66	0.0007	S
2 HR 30 MINS	112.73±6.03	121.68±5.73	<0.0001	S
3 HR	111.78±5.29	121.68±5.95	<0.0001	S
EXTUBATION	127.28±6.7	135.34±5.97	<0.0001	S

Table 3 shows comparison of SBP in both the groups p value between two groups is statistically significant. (p value<0.05)

Table 4: comparison of dbp in both groups

Time	Dexmedetomidine Group (mean±SD)	Fentanyl Group (mean±SD)	P-value	Results
BASELINE	78.64±7.11	80.14±4.7	0.2	NS
AFTER INFUSION OF DRUG	71.3±6.71	76.24±4.41	<0.0001	S
AFTER INDUCTION	68.02±5.03	72.74±3.86	<0.0001	S
AFTER INTUBATION	75.26±4.48	84.36±6.05	<0.0001	S
BEFORE SKULL PIN INSERTION	68.12±6.36	77.32±4.07	<0.0001	S
AFTER SKULL PIN INSERTION	76.54±4.63	84.62±5.03	<0.0001	S
30 MINS	73.16±4.26	76.08±6.65	0.01	S
1 HR	75.38±4.23	78.28±5.34	0.003	S
1 HR 30 MINS	73.62±4.26	76.06±4.19	0.004	S
2 HR	75.76±3.85	78.34±4.01	0.001	S

2 HR 30 MINS	75.19±3.9	78.26±4.6	0.0005	S
3 HR	73.71±3.42	77.37±3.55	<0.0001	S

Table 4 shows comparison of DBP in both the groups. P value is statistically significant (p value<0.05). In postoperative period DBP came back to normal.

Table 5: comparison of map (mmhg) in both groups

Time	Dexmedetomidine Group (mean±sd)	Fentanyl Group (mean±sd)	P-value	Results
BASELINE	95.92±5.17	97.12±4.98	0.24	NS
AFTER INFUSION OF DRUG	86.12±5.49	91.78±4.59	0.0001	S
AFTER INDUCTION	82.18±4.52	87.32±3.8	<0.0001	S
AFTER INTUBATION	91.38±3.66	100.86±5.46	<0.0001	S
BEFORE SKULL PIN INSERTION	83.84±4.83	91.42±3.67	<0.0001	S
AFTER SKULL PIN INSERTION	91.98±3.5	101.66±4.19	<0.0001	S
30 MINS	84.64±3.54	90.26±5.09	<0.0001	S
1 HR	87.74±4.68	92.12±4.09	<0.0001	S
1 HR 30 MINS	85.9±5.18	90.38±3.68	<0.0001	S
2 HR	88.6±4.61	91.86±4.01	0.0003	S
2 HR 30 MINS	87.7±4.19	92.73±4.2	<0.0001	S
3 HR	86.35±3.38	92.18±3.7	<0.0001	S

Table 5 shows comparison of MAP in both the groupsl. P value between two groups is statistically significant (p value<0.05).

Table 6: comparison of spo_2 (in percentage) in both groups

Time	Dexmedetomidine Group	Fentanyl Group	P-value Result
BASELINE	99	100	NS
AFTER INFUSION OF DRUG	100	99	NS
AFTER INDUCTION	100	100	NS
AFTER INTUBATION	99	100	NS
BEFORE SKULL PIN INSERTION	100	100	NS
AFTER SKULL PIN INSERTION	99	99	NS
30 MINS	100	100	NS
1 HR	100	100	NS
1 HR 30 MINS	100	99	NS
2 HR	100	99	NS
2 HR 30 MINS	99	100	NS
3 HR	100	100	NS

No statistically significant difference was found between two groups with regard to SpO_2.

Table 7: extubation time (in min.)

	Group d (mean±sd)	Group f (mean±sd)	P-value	Result
EXTUBATION TIME	9.82±2.96	11.72±4.23	<0.01	S

Table 8: time to reach aldrete score 8(in min.)

	Group d (mean±sd)	Group f (mean±sd)	P-value	Result
TIME TO REACH ALDRETE 8	13.74±3.62	17.32±4.05	<0.0001	EXTREMELY SIGNIFICANT

Table: ALDRET SCORE

ACTIVITY	
2	Able to move sponteously or on command four extremities
1	Able to move voluntarily or on command two extremities

0	Unable to move any extremities
RESPIRATION	
2	Able to deep breath and cough freely
1	Dyspnea,shallow or limited breathing
0	apneic
CIRCULATION	
	BP+20mmhg of pre-sedation
	BP+20-50 mmhg of pre-sedation level
	BP+50 mmhg of pre-sedation level
CONSCIOUSNESS	
2	Fully awake
1	Arousable on calling
0	Not responding
SKIN COLOR	
2	Normal
1	Pale,dusky,blotchy,jaundice,others
0	cynotic

Table 9: Adverse events

	Group d	Group f
BRADYCARDIA	3(6%)	NONE
HYPOTENSION	2(4%)	1(2%)
HYPERTENSION	NONE	3(6%)
NAUSEA/VOMITING	NONE	2(4%)
SHIVERING	NONE	4(8%)
ARRHYTHMIA	NONE	NONE

DISCUSSION

Dexmedetomidine is highly selective α_2 agonist with sedative, analgesic, anxiolytic, neuroprotective and anaesthesia sparing effects without causing respiratory depression. It also has a central sympatholytic effect. This, in turn, decreases BP and HR. In our study, we found that dexmedetomidine in a loading dose of 1 µg/kg followed by 0.4 µg/kg/hr was very effective in maintaining hemodynamic stability. Tanskanen PE *et al.*[1] found that intra-operative dexmedetomidine infusion decreased hemodynamic response to various noxious stimuli in patients undergoing intracranial tumor surgery. Ankita Batra *et al.*[2] found that progressive decrease in HR in Group D after giving the infusion, but intra-operative HR remained within 20% of baseline. In control group, HR remained within 20% of baseline during whole observed period except at the time of extubation , when the rise in HR was more than 20% of baseline and MAP also showed the same result. Time to reach aldret score 8 is less in group D as compared to group F. R N Soliman *et al.*[3] studied that dexmedetomidine significantly attenuated the hemodynamic response to laryngoscopy, intubation, Mayfield three pin head holder application, surgical stimulation and extubation in patients undergoing supratentorial craniotomy. Higher doses of sevoflurane, fentanyl and esmolol were used in control group. In our study baseline MAP was 95.92±5.17 and 97.12±4.98 in group D and group F respectively, which was comparable. After infusion of study drug, it decreased in both the groups, after induction it further reduced to 82.18±4.52 and 87.32±3.8 in group D and group F respectively with p-value <0.0001 which was statistically significant. It remained stable and below the baseline in group D. At the time of skull pin insertion (91.98±3.5) and extubation (95±3.83) MAP increased in group D, but it was below the baseline. While in group F MAP increased significantly at the time of skull pin insertion (101.66±4.19) and extubation (101.18±5.24) which was statistically significant as compared to group D. Jamali *et al.*[4] studied that when brain surgery patients were given sufentanil (0.8 µg/kg) and fentanyl (4.5 µg/kg) before skull pin insertion, there was decrease in HR and MAP, but it returned to baseline after skull pin application. John guy *et al.*[5] *et al.* studied effect of fentanyl and remifentanil for supratentorial craniotomy. They observed that remifentanil had a rapid onset of action and attenuation of hemodynamic response was better in remifentanil group as compared to fentanyl group. Shwethashri *et al.*[6] conducted a study and they observed that dexmedetomidine in dose of 0.5 µg/kg was more effective in attenuating hemodynamic responses to skull pin insertion as compared to a dose of 1 µg/kg. Osman *et al.*[7] found that there is no statistically significant difference between groups with regard to SpO_2. We found similar results in our study.

CONCLUSION

We concluded that dexmedetomidine HCL is better than fentanyl citrate for perioperative hemodynamic stability in a loading dose of 1 µg/kg followed by maintenance dose of 0.4 µg/kg/hr in patients undergoing supratentorial craniotomy.

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