Original Research Article

EVALUATION OF RECOVERY CHARACTERISTICS BETWEEN FENTANYL - PROPOFOL VERSUS DEXMEDETOMIDINE-PROPOFOL BASED ANESTHESIA IN SUPRATENTORIAL BRAIN TUMOR SURGERY

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Abstract

Background: The aim of the present study is to compare the recovery profiles,peri- operative hemodynamic changes and undesirable side-effects such as postoperative nausea and vomiting(PONV) and shivering of patients undergoing anaesthesia with fentanyl - propofol or dexmedetomidine–propofol in supratentorial brain tumor surgery.

Materials And Methods: In a prospective randomized double blind study 70 ASA I-II patients aged 18-65 yrs of either sex, scheduled for supratentorial craniotomy with a maximum anticipated duration of 300 minutes, was allocated into two equal groups. One group received Dexmedetomidine-Propofol and other group received Fentanyl-Propofol as induction and maintenance of anesthesia along with other drugs. Both the groups (n=35) received either i.v. dexmedetomidine or iv fentanyl 1 μg/kg 15mins prior to induction as loading dose followed by 0.5 μg/kg/ hr by continuous i.v. infusion preoperatively. At the end of surgery, recovery characteristics were assessed and recorded.

Discussion & Conclusion: Propofol-fentanyl and propofol-dexmedetomidine are both suitable for elective supratentorial craniotomy and provide similar intraoperative hemodynamic responses. Propofol-dexmedetomidine allows earlier cognitive recovery.

Keywords: Dexmedetomidine, Fentanyl, Propofol ,recovery characteristics, supratentorial brain tumors.

INTRODUCTION:

The goals of neuroanaesthesia are to provide good operating conditions and to ensure stable cerebral hemodynamics without sudden increases in intracranial pressure or acute brain swelling. Furtherm ore, fast recovery from anesthesia is often preferred to allow immediate neurological evaluation [1].During recovery, abrupt increase in arterial blood pressure can pose a risk for postoperative haematoma [2].Opioid analgesia prevents haemodynamic responses to awakening and

extubation but may result in respiratory depression and high carbon dioxide tension with subsequent increase in the intracranial pressure. Alpha2 adrenergic agonists have been introduced to clinical anaesthesia for their sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties. Dexmedetomidine has shown analgesic effects without significant respiratory depression[3][4]. As dexmedetomidine provides good peri-operative haemodynamic stability with decreased intra-operative opioid requirement. Studies in animals suggest that it might have been a suitable anaesthetic adjuvant to neuroanaesthesia as it has beneficial effects in terms of neural protection. On the other hand, fentanyl is an opioid analgesic which cause respiratory depression and delay in postoperative recovery[5].

OBJECTIVES OF THE STUDY: The objectives of present study were

1) To compare recovery profiles of patients undergoing anesthesia either with dexmedetomidine–propofol or with fentanyl – propofol in supratentorial brain tumor surgery.
2) To compare peri-operative hemodynamic changes in both set of patients
3) To compare the intra-operative consumption of propofol and muscle relaxant
4) To assess undesirable side-effects: postoperative nausea and vomiting (PONV) and shivering

MATERIALS AND METHODS

After obtaining approval from institutional ethics committee and written informed consent from each of the patients, this randomized prospective, double blind, parallel group, study was conducted in the Department of IPGMER and SSKM Hospital, Kolkata & Bangur Institute of Neurosciences from March 2014 to March 2015.In this study 70 patients of either sex, aged between 18 to 65 years, ASA (American Society of Anaesthesiologists) physical status I &II were assigned for supratentorial brain tumor surgery. The patients were randomly allocated into two groups comprising of 35 patients in each group. The allocation was done by a computer-generated codes based on a two-way randomization and which was kept in sequentially numbered envelops and was opened 3 hours before operation. Pre-anaesthetic check-up and investigations were done and the procedure was explained to the patients. On arrival at the operation theatre baseline hemodynamic parameters like heart rate, invasive BP and SpO_2 were recorded and an i.v line was established. Intra-arterial line was established with local anesthetic before induction.

Group 1(n=35) received dexmedetomidine and Group 2(n=35) received fentanyl in a dose of 1µg /kg15 mins prior to induction as loading dose and 0.5µg/ kg/ hr as maintenance. During the infusion SBP, DBP, HR and SpO_2 were recorded at 5 mins interval. After pre-oxygenation for at least 3 min, patients received 2 µg/kg fentanyl and inj. glycopyrrolate 3µg/kg before induction. Anesthesia was induced with propofol 1-2.5 mg/ kg in increments of 20 mg every 15s until the BIS reached a predetermined value of 50 and loss of verbal commands. Neuromuscular blockade was induced using atracurium in a bolus dose of 0.5mg/kg to facilitate endotracheal intubation when 95% neuromuscular block was achieved as indicated by train of four monitor (TOF count =0).Adequate oxygenation and normothermia was maintained throughout the procedure and the $EtCO_2$ was kept in between 30-35 mm of hg. Anesthesia was maintained with N_2O:O_2 (1:1), and propofol 50-150 µg /kg/ min. Depth of anaesthesia was monitored by using a BIS within a range of 40 and 50.Mannitol 1gm/kg was administered i.v. over approximately 30mins.

A urinary catheter was inserted for monitoring of urinary output. Muscle relaxation was maintained by continuous intravenous infusion to maintain 90% suppression of the single twitch response. Signs of inadequate analgesia defined as an increase in mean arterial pressure 20% above baseline value and tachycardia HR>100beats/min was treated by inj. fentanyl 0.5-1µg /kg i.v., provided the BIS score is in the recommended range. Hypotension (SBP<90 mm Hg) was treated with mephentermine 6mg i.v. and bradycardia (HR<40 beats /min) was treated with 0.6 mg boluses of i.v. atropine. Approximately 30mins before the expected end of surgery, atracurium infusion was discontinued and the infusion of dexmedetomidine or fentanyl was also stopped, propofol infusion however been continued till the start of skin closure. The patients were allowed to recover spontaneously until the return of T_1=25%.Then Inj. neostigmine 0.05mg/kg and inj. glycopyrrolate 0.01mg/kg was administered to reverse the neuromuscular blockade. The time needed to return ofT_1 to 25% and return of the TOF ratio(T_1/T_4) to 70% were recorded. The patients were extubated when BIS reached 80.Each patient was observed continuously after the termination of anesthesia and total doses of fentanyl, propofol, dexmedetomidine and atracurium were recorded. Any adverse events or side effects were recorded during perioperative period. Hemodynamics of the patients was monitored before and after (a) during study drugs administered (b) induction of anesthesia(c) endotracheal intubation(d)skin incision(d) opening of duramater and (e) extubation. At the end of surgery, recovery characteristics were assessed by

1) Time to response to verbal commands (starting from the time of discontinuation of anesthetic, a blinded investigator asked each patient at 1-min intervals, to open his or her eyes, squeeze the investigator's hand).
2) Time to extubation (spontaneous breathing with a minimum of 8 mL /kg body weight, ability to sustain a 5-sechead lift, and adequate negative inspiratory force [-40 cmH_2O],sustained hand grip and sustained arm lift).
3) Orientation time (for the patient to tell his name, birthday and the place he or she is in).

STATISTICAL ANALYSIS:

Data was summarized by routine descriptive statistics namely mean & standard deviation for numerical variables and count & percentage for categorical variables. Numerical data was compared between groups by student's unpaired't' test if normally distributed or by Mann Whitney 'U' test if otherwise. Chi-square test or fisher's exact test was employed for intergroup comparison of categorical variables. All analyses were two tailed and $p<0.05$ is considered statistically significant.

RESULTS

The present study was undertaken in 70 patients with ASA I and II in both male and female patients between 18-65 yrs for supratentorial brain tumor surgery.

Table 1: Shows the demographic data of the study subjects involved in the study

	Group1 (Mean ±SD)	Group 2 (Mean ± SD)	p-Value
Age	30.54	33.97	0.150
Weight	55.23±6.96	54.29±11.13	0.672
Hb%	12±1.26	11.94±1.23	0.833

Figure 1 shows that each group consists 35 patients with 18 females and 17 males

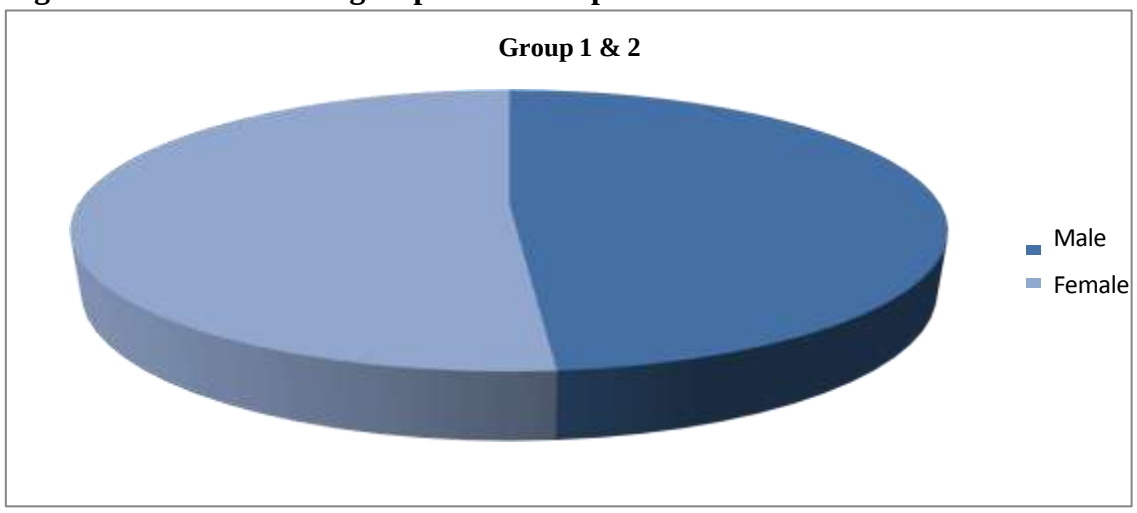


Table 2: Shows Baseline Clinical parameters in both the groups			
	Group1	Group 2	p-Value
No. of patients	35	35	
Baseline heart rate	76.37±8.32	75.8±11.48	0.812
Baseline SBP	121.83±8.28	122.49±9.95	0.765
Baseline DBP	76.54±5.92	74.26±8.47	0.195
Duration of surgery	2.2±0.529	2.35±0.708	

The following shows the trend of heart rate(HR),SBP and DBP during preoperative infusion and intraoperative period. There was no difference between groups. There were no significant difference in baseline heart rate(HR),systolic blood pressure(SBP),diastolic blood pressure(DBP).

Figure 2: Shows changes in Heart Rate

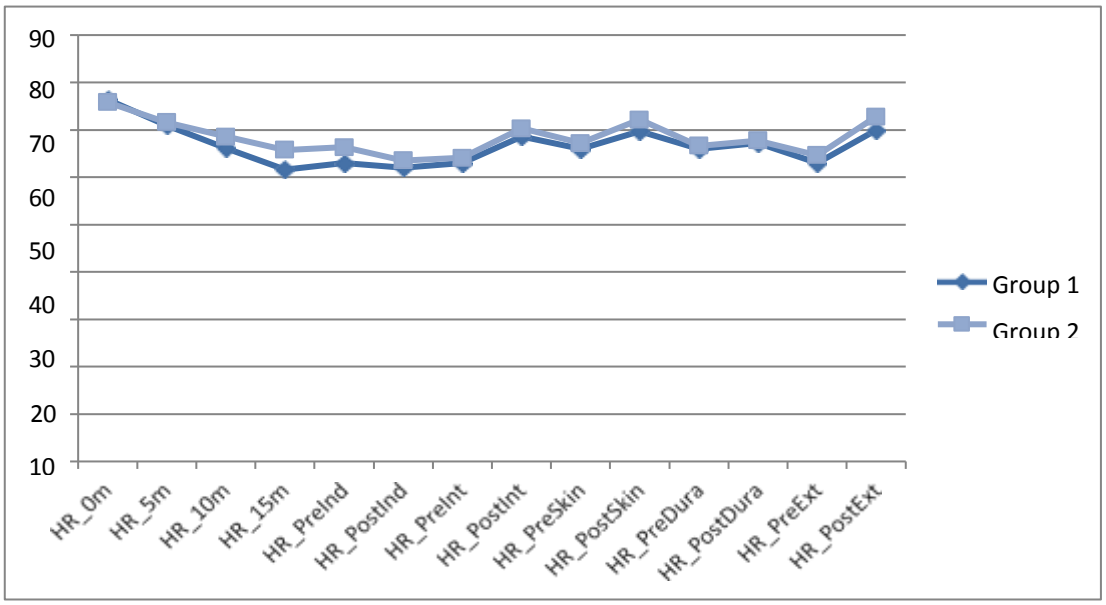


Figure 3: Changes in SBP (mm of Hg)

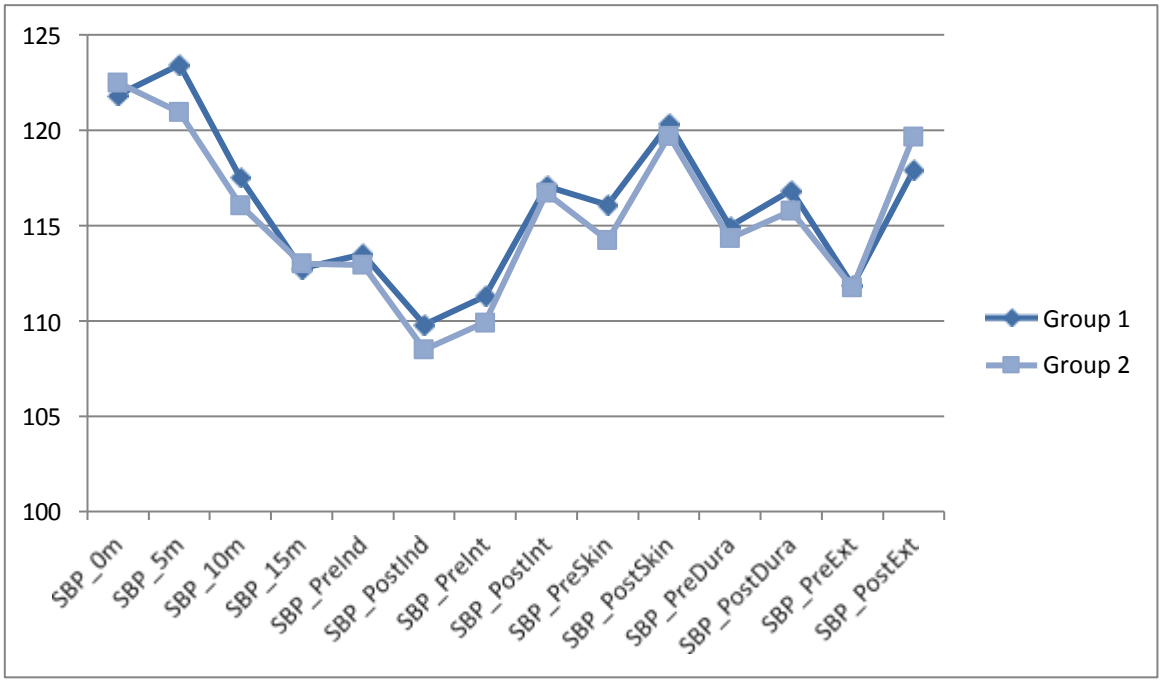


Figure 4: Shows the changes in DBP (mm of Hg)

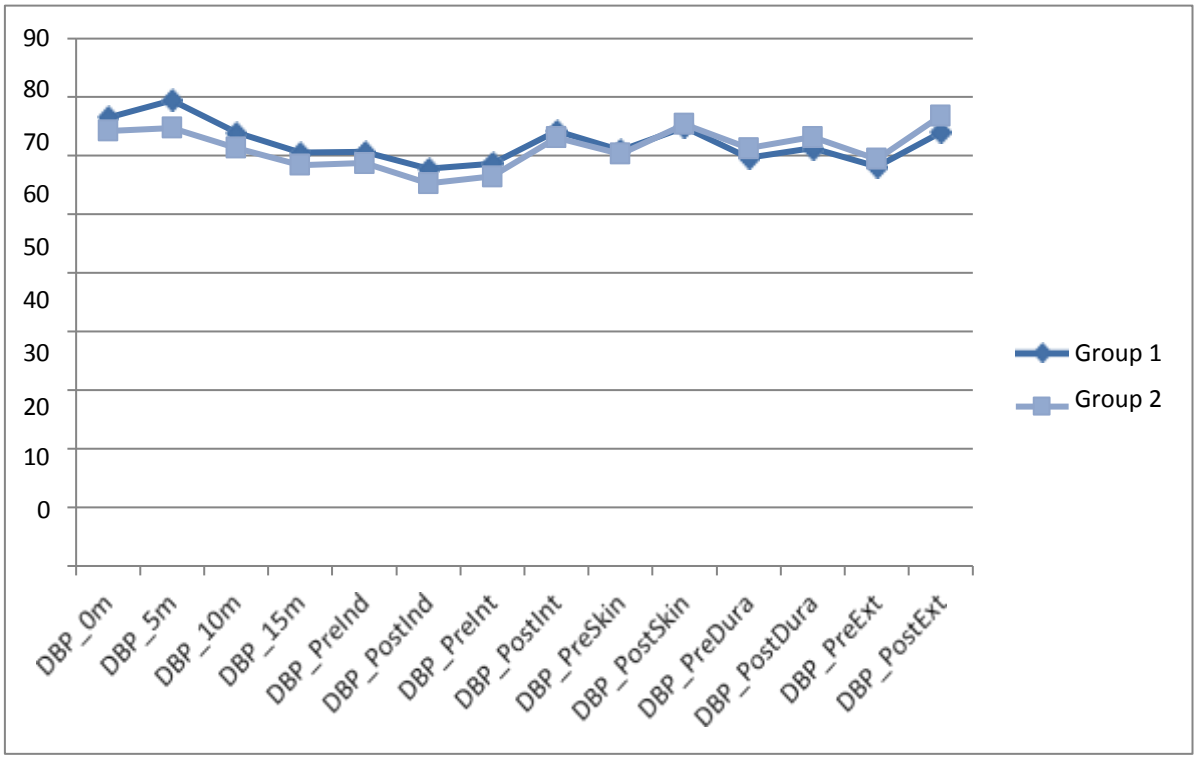
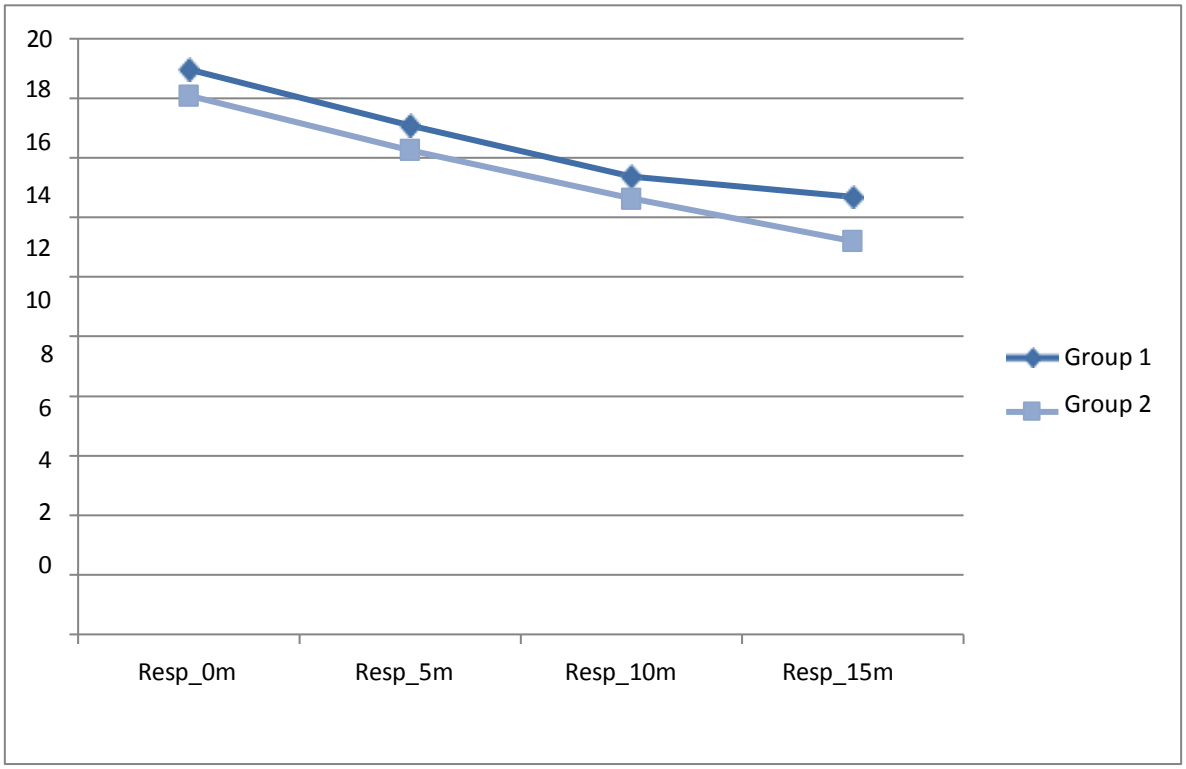
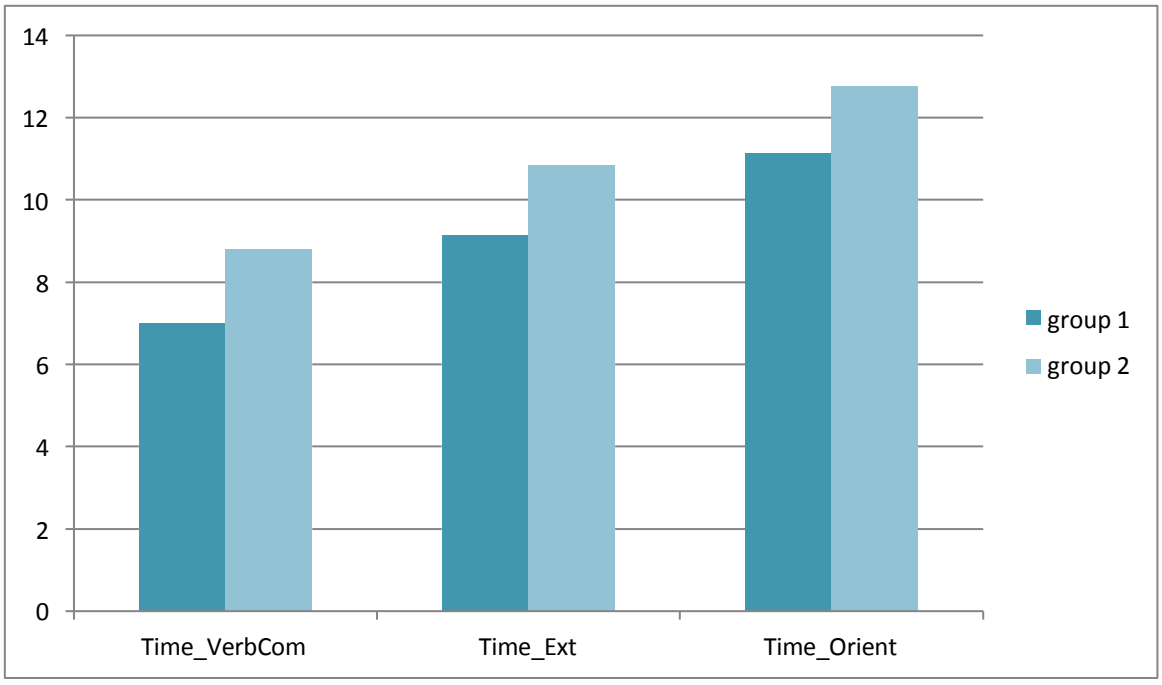


Figure 5: Changes in Respiratory rate (RR/min) during preoperative infusion of study drugs.



Decrease in respiratory rate was observed in Group 2 at 15 mins time of infusion which was found to be significant.

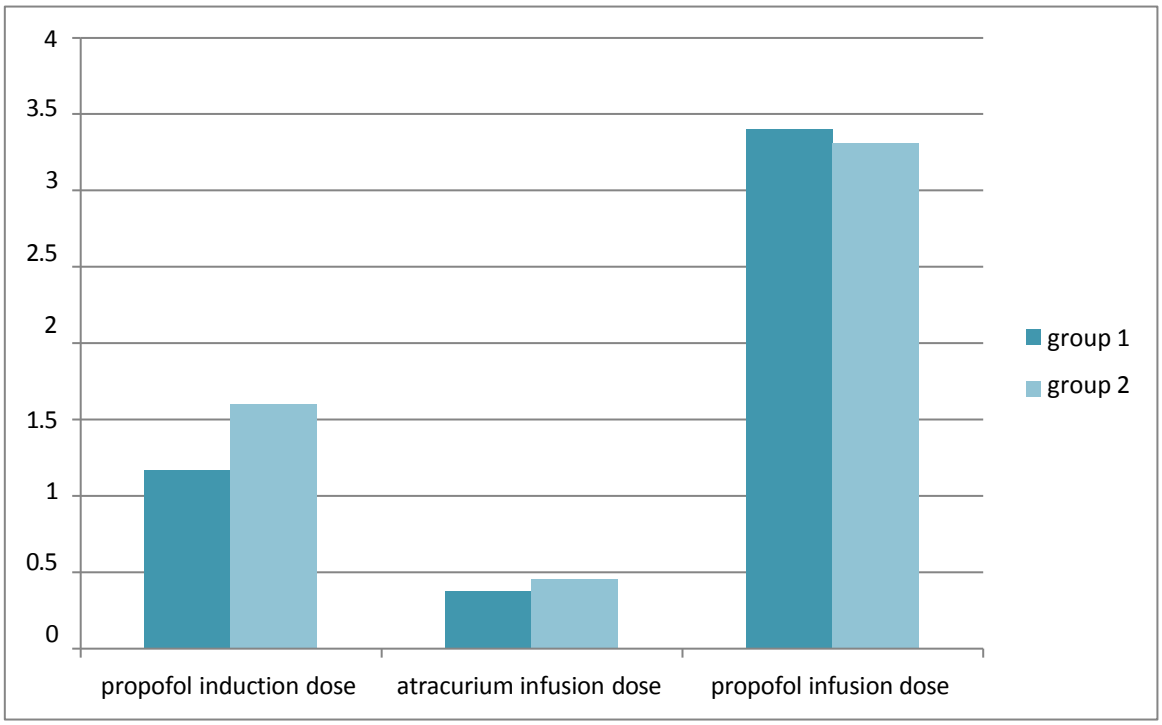
Figure 6: Time (in minutes) to verbal command, extubation and orientation after stoppage of anesthesia.



Patients in Group 1 recovered early compared to Group 2 in terms of response to verbal command (6.99±0.77 vs8.79±0.88), extubation time (9.14±0.91vs10.83±1.06) and orientation time

(11.14±0.703vs12.76±1.10) which were found to be statistically significant.

Figure 7: Induction dose (mg/kg) of propofol and infusion dose (mg/kg/hr) of atracurium and propofol



Induction dose of propofol and infusion dose of atracurium were significantly less in dexmedetomidine group in comparison to fentanyl group.

Table 3: Shows the adverse effects in both the groups		
	Group 1	Group2
No of patients	35	35
Nausea	1(2.86%)	2(5.71%)
Vomiting	0	1(2.86%)
Shivering	2(5.71%)	3(8.57%)
Bradycardia	0	0
Total	3	6

Though in both the groups adverse effects were seen, but it was very less(less than 9%).

DISCUSSION:

In elective intracranial surgery, faster recovery from anesthesia is especially important for detecting early complications and for performing the neurological examination. Neurosurgical patients are at higher risk of postoperative cerebral bleeding and detection of procedural complications are easier if patients recover early. The results of the present study demonstrates that dexmedetomidine and fentanyl both can be used in patients undergoing supratentorial brain tumor surgery, as this allows prompt neurological assessment and determination of the need for urgent intervention.
In our study patients of group 1 recovered early(orientation time11.14±.70 min) from anesthesia compared to group 2 . Turgut et al.[6] compared dexmedetomidine –propofol and remifentanil-

propofol in supratentorial brain tumor surgery and showed similar recovery profile in dexmedetomidine group though timing was slightly different(orientation time 12.52±3.01 min).
Tanskanen et al.[1] studied 54 patients undergoing supratentorial brain tumor surgery with continuous infusion of dexmedetomidine (plasma target concentration 0.2 or 0.4 ng/ ml) or placebo. Patients receiving dexmedetomidine had their tracheal tubes removed faster than placebo group,indicating preserved respiratory function.

He XY, Cao JP, Shi XY, Zhang H. [7]included 5 trials, consisting of 482 patients in total. There were no significant differences in the number of patients who required rescue analgesics in the postanesthesia care unit, the number of patients with emergence agitation, the number of patients with postoperative nausea and vomiting, or the time to extubation between patients who received dexmedetomidine and those who received opioids. Compared with opioids, dexmedetomidine was associated with a significantly decreased time to eye- opening in response to verbal stimuli.
'The golden standard' of neuroanaesthesia includes maintenance of anaesthesia with propofol or isoflurane and fentanyl[8].Recently, new alternatives, such as sevoflurane, desflurane and remifentanil, have been introduced to this paradigm. High concentrations of volatile anaesthetics can blunt the carbon dioxide response and render CBF pressure passively. In present study, we used fentanyl or dexmedetomidine for intraoperative analgesia because it has little effect on CBF regulation.
In dexmedetomidine group , there was significant reduction of induction dose of propofol and infusion dose of atracurium. Keniya, et al[9] concluded that dexmedetomidine ,as a pre- anesthetic medication and intraoperative infusion , decreased intraoperative anesthetic requirement.But in our study ,maintenance dose of propofol was similar in both the groups.
Ali AR, El GhoneimyMN[10] showed in 3-8 yr old children undergoing ESWL(extracorporeal shock wave lithotripsy) , that both propofol/fentanyl and propofol/dexmedetomidine combinations were effective and well tolerated. However, propofol/dexmedetomidine combination was accompanied with less propofol consumption, prolonged analgesia and lower incidence of intraprocedural and postprocedural complications.
In our study, fentanyl and dexmedetomidine were similar in overall efficacy. In both the groups, no hemodynamic and cardiovascular side effects were noted perioperatively. Similarly, Tanskenen PE et al.[1] reported that dexmedetomidine provided good perioperative hemodynamic stability in patients undergoing brain tumor surgery and that it also reduced intraoperative opioid requirements. Dexmedetomidine could be convenient as an adjuvant anesthetic in neurosurgical anesthesia. But llhan et al .[11]found that dexmedetomidine controlled the hemodynamic changes better than fentanyl perioperatively, after extubation and during early postoperative period.
Because of the ventilatory depressing effects of fentanyl, Feld JM et al.[12]studied various alternative methods for analgesia in bariatric surgery. In their study comparing dexmedetomidine to fentanyl, they reported that dexmedetomidine provided both stable perioperative hemodynamics and postoperative analgesia, thus reducing the use of supplementary morphine.
Dexmedetomidine, the highly selective alpha2adrenoreceptor agonist, has sedative and analgesic effects without causing postoperative respiratory depression[[13][14].Dexmedetomidine
0.5 to 1.0 μg kg-1 over 20 minutes followed by an infusion at rates of 0.01 to 1.0 μg kg-1 h-1 was used in awake craniotomy and enabled the performance of the neurological examination[15][16].
The major reported problem associated with dexmedetomidine is its hemodynamic effects such as hypotension, hypertension, and Bradycardia[13][14]. In our study, bradycardia (HR<60/min) was seen more in dexmedetomidine group similar to other studies, however it never caused hemodynamic

instability or there was no need of inj. Atropine. Hypotension or hypertension, was also not observed in our groups.
Commonly encountered complications in the early postoperative period in the recovery room in both the groups were shivering and nausea, vomiting, which were not statistically significant.
The analgesic profile of dexmedetomidine has not been fully characterized in humans[17]. However, the anxiolysis, blood pressure stabilization, analgesia, anesthetic sparing effects, and sedation without respiratory depression or significant cognitive impairment effects of dexmedetomidine, are known.

In our study, requirement of additional dose of analgesic was seen in fentanyl group without statistically significant difference.
Cormack et al.[18] suggested that alpha2-agonists are useful adjuncts for the management of the neurosurgical patient during surgery and in the intensive care unit.
This study protocol does not allow us to make any conclusions about possible neuroprotective or cerebral vasoconstrictive effects of dexmedetomidine in elective supratentorial tumor patients. We have, however, demonstrated the safety and feasibility of dexmedetomidine in these patients in terms of early extubation of trachea and stable cardiorespiratory profile. Larger outcome studies on neural protection are warranted in clinical settings.

CONCLUSION-

Propofol-dexmedetomidine and propofol-fentanyl are both suitable for elective supratentorial craniotomy and provide similar intraoperative hemodynamic responses and postoperative adverse events. Propofol-dexmedetomidine allows earlier cognitive recovery.

REFERENCES

1. Tanskanen PE, Kytta JV, Randell TT, Aantaa RE. Dexmedetomidine asan anaesthetic adjuvant in patients undergoing intracranial tumor surgery: a double-blind, randomized and placebo-controlled study. Br J Anaesth 2006; 97: 658-65.

2. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between peri-operative hypertension and intracranial haemorrhage after craniotomy. Anesthesiology 2000; 93: 48-54.

3. Maze M, Tranquilli W. Alpha-2 adrenergic agonists: defining the role in clinical anaesthesia. Anesthesiology 1991; 74: 581–605

4. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000; 93: 382–94

5. Guy J, Hindman BJ, Baker KZ, et al. Comparison of remifentanil and fentanyl in patients undergoing craniotomy for supratentorial space occupying lesions. Anesthesiology 1997; 86: 514-24

6. Turgut N, Turkmen A, Ali A, and Altan A. Remifentanil-propofol vs Dexmedetomidine-propofol- Anesthesia for supratentorial Craniotomy. Middle East J Anaesthesiol 2009;20(1):63-

70

7. He XY, Cao JP, Shi XY, Zhang H.dexmedetomidine versus morphine or fentanyl in the management of children after tonsillectomy and adenoidectomy: a meta-analysis of randomized controlled trials. Ann Otol Rhinol Laryngol. 2013;122(2):114-20.

8. Todd MM, Warner DS, Sokoll MD, et al. A prospective, comparative trial of three anaesthetics for elective supratentorial craniotomy. Propofol/fentanyl, isoflurane/nitrous oxide, and fentanyl/nitrous oxide.Anesthesiology1993; 78: 1005–20

9. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011; 55:352-7.

10. Ali AR, ElGhoneimyMN. Dexmedetomidine versus fentanyl as adjuvant to propofol: comparative study in children undergoing extracorporeal shock wave lithotripsy.Eur J Anaesthesiol. 2010 Dec;27(12):1058-64

11. Ilhan O, Koruk S, Serin G, Erkutlu I, and Oner U. Dexmedetomidine in the Supratentorial Craniotomy.Eurasian J Med. 2010 Aug; 42(2): 61–65.

12. Feld JM, Hoffman WE, Stechert MM, Hoffman IW, AnandaRC.Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery.J Clin Anesth; 2006, 18:24-28.

13. Sakaguchi Y, Takahashi S: Dexmedetomidine. Masui; 2006, 55:856-863.

14. Bekker A, Sturaitis MK. Dexmedetomidine for neurological surgery. Neurosurgery. 2005; 57:1–10.

15. ARD JL JR, Bekker AY , Doyle WK: Dexmedetomidine in awake craniotomy: a technical note. Surg Neurol; 2005, 63:114-11