Comparison of Dexmedetomidine Versus Midazolam-Fentanyl Combination for Monitored Anesthesia Care During Burr-Hole Surgery for Chronic Subdural Hematoma

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Background: Intraoperative movements are marker of inadequate level of sedation and are undesirable during burr-hole surgery under monitored anesthesia care (MAC). It distracts surgeon, hinders surgical procedure, and may lead to iatrogenic complication. Dexmedetomidine has shown to provide excellent analgesia, cooperative sedation with fewer fluctuations in sedation level during MAC. We compared the effect of dexmedetomidine on intraoperative patient movement, postoperative recovery time, and the surgeon and patient satisfaction scores with commonly used midazolam-fentanyl combination.

Methods: Fifty-two patients undergoing burr-hole surgery for chronic subdural hematoma under MAC were randomly assigned to receive either IV dexmedetomidine 1 μg/kg over 10 minutes followed by continuous infusion 0.03 to 0.07 μg/kg/h (group D) or IV fentanyl 0.5 μg/kg and midazolam 0.03 mg/kg over 10 minutes followed by continuous infusion of 0.5 to 1.16 μg/kg/h fentanyl and 0.03 to 0.07 mg/kg/h midazolam (group M/F) titrated to maintain Ramsay sedation scale 3. Total number of intraoperative patient movements, postoperative recovery time, and patient and surgeon satisfaction scores were recorded.

Results: Demographic and baseline characteristics were comparable between the 2 groups. Intraoperative patient movements were significantly less in group D than group M/F (median interquartile range, 1.00 [0.00 to 2.00] vs. 3.00 [1.00 to 3.25], $P = 0.007$). Group D patients showed faster postoperative recovery (mean ± SD, 7.00 ± 6.96 vs. 13.69 ± 6.18 min, $P = 0.000$). Surgeon satisfaction scores were better in group D compared with group M/F (median interquartile range, 1.00 [1.00 to 1.25] vs. 2.00 [1.00 to 2.00], $P = 0.014$). However, patient satisfaction score and hemodynamic parameters were comparable ($P > 0.05$) between both the groups.

Conclusions: Use of dexmedetomidine for MAC is associated with lesser number of intraoperative patient movements, faster postoperative recovery, better surgeon satisfaction score, and comparable patient's satisfaction compared with midazolam-fentanyl combination.

Key Words: monitored anesthesia care, dexmedetomidine, fentanyl-midazolam, intraoperative movement

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Chronic subdural hematoma (CSDH) is one of the most frequently encountered intracranial hemorrhage in neurosurgical practice.[1] Burr-hole trepanation with closed system drainage is the method of choice for its initial treatment. This procedure can safely be performed variously under general anesthesia, local anesthesia, or intravenous (IV) conscious sedation. General anesthesia usually poses a higher risk in the elderly and those with coexisting systemic illness, both of which are common in CSDH. On the contrary, local anesthesia alone may be uncomfortable for the patient and the resultant noncooperation inconvenient to the surgeon. IV conscious sedation under monitored anesthesia care (MAC) is a logical middle ground between full general anesthesia and isolated local anesthesia. It can improve patient comfort and facilitate smooth conduct of surgical procedure. Preliminary results indicate that conscious sedation under MAC is safe and effective for burr-hole trepanation surgery.[2]

Conscious sedation can be provided using IV midazolam, propofol, or fentanyl or a combination of drugs.[3] However, each of the drugs possesses inherent limitations. Midazolam has no analgesic property and may cause respiratory depression by decreasing respiratory response to carbon dioxide.[4] The use of repeated doses of midazolam may result in prolonged sedation.[5] Although propofol is a very potent anesthetic agent, it is devoid of any analgesic property. It carries risks for loss of airway control besides respiratory depression and marked lowering of blood pressure. Fentanyl provides effective analgesia but is not a potent sedative. It causes respiratory depression when used in high doses or in combination with other sedative agents such as benzodiazepines.

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Dexmedetomidine is a highly selective α_2 adrenoreceptor agonist. It has sympatholytic effect that can attenuate the stress response to surgery mitigating tachycardia and hypertension. It produces excellent analgesia and cooperative sedation, while retaining the ability to arouse the patient, if needed.[6] Its use as an effective baseline sedative under MAC has been shown to provide greater patient satisfaction, less opioid requirements, and less respiratory depression.[3,7] The present study was designed to compare the efficacy of dexmedetomidine with midazolam-fentanyl combination on patient movement score in patients undergoing burr-hole surgery for CSDH under conscious sedation. Secondary outcomes were postoperative recovery time, patient and surgeon satisfaction with the conduct of the procedure.

MATERIALS AND METHODS

Following institutional ethical committee approval, 52 subjects aged between 18 and 80 years with ASA grade I-III and Markwalder's neurological grading score (MGS) 0 to 2 slotted to undergo burr-hole surgery for CSDH under MAC were included in this prospective, randomized, double-blind study.[8] Written informed consent was obtained from all subjects before enrollment in the study. Subjects with predicted difficult airway, a history of allergy to midazolam, fentanyl, dexmedetomidine, or local anesthetics, memory or cognitive dysfunction, history of drug/alcohol abuse, and those who received sedatives within 2 weeks before surgery were excluded from the study.

During the preanesthetic checkup, all subjects were explained about the operative procedure, use of local anesthesia, conscious sedation, and the 7-point Likert-like verbal rating satisfaction scale.[9] The patient demographic characteristics, American Society of Anesthesiology status, MGS score, and hematoma volume were noted.

No premedication was administered. On arrival in the operating theater, an IV cannula was placed under local infiltration anesthesia. Standard monitoring included 5-lead electrocardiogram, noninvasive arterial blood pressure, peripheral arterial oxygen saturation (SpO_2), respiratory rate (RR), and capnography (by placing the carbon dioxide sample line of the capnograph in close vicinity of one of the nostrils). Oxygen supplementation at FiO_2 of 0.35 was achieved through a suitable air entrainment mask.

Subjects were randomized into 2 groups using a computer-generated random number table. Group D received dexmedetomidine 1 μg/kg IV over 10 minutes followed by continuous infusion starting at 0.3 μg/kg/h (0.1667 mL/kg/h); this was scaled up at an increments of 0.1 μg/kg/h (0.0556 mL/kg/h) in each step up to 4 times or till the maximum infusion dose of dexmedetomidine (0.7 μg/kg/h) was reached to achieve target sedation level, that is, Ramsay sedation scale (RSS) of 3. Group M/F received fentanyl 0.5 μg/kg IV and midazolam 0.03 mg/kg IV bolus over 10 minutes followed by continuous infusion starting at 0.1667 mL/kg/h (0.03 mg/kg/h midazolam and 0.5 μg/kg/h fentanyl). Infusion was scaled up in an increment of 0.0556 mL/kg/h (0.01 mg/kg/h midazolam and 0.165 μg/kg/h fentanyl) in each step up to 4 times or till the maximum infusion dose of midazolam (0.07 mg/kg/h) and fentanyl (1.16 μg/kg/h) was reached to achieve RSS of 3.

Loading and infusion doses of dexmedetomidine and loading doses of midazolam-fentanyl combination were chosen from previous studies.[10] To determine the optimal infusion doses of the combination of midazolam-fentanyl, a pilot study was carried out in 12 patients aged between 18 and 80 years. Infusion doses in a range of 0.01 to 0.10 mg/kg/h of midazolam and 0.3 to 1.5 μg/kg/h of fentanyl were titrated to achieve the optimum sedation during the procedure. On the basis of our pilot study, a loading dose of 0.03 mg/kg midazolam with 0.5 μg/kg fentanyl and a infusion of 0.03 to 0.07 mg/kg/h midazolam along with 0.5 to 1.16 μg/kg/h fentanyl were optimal for conduct of burr-hole surgery under MAC.

Loading doses of drug were prepared in a masked 10 mL syringe containing either dexmedetomidine (1 μg/kg) or midazolam (0.03 mg/kg) and fentanyl (0.5 μg/kg) combination. Infusion doses were prepared in a masked 50 mL syringes containing either dexmedetomidine (1.5 μg/kg) or midazolam (0.15 mg/kg) and fentanyl (2.5 μg/kg) combination. To ensure blinding drug concentration in the infusion syringe was chosen such that the desired amount of drug is delivered with same rate of infusion in either group (0.0556 mL/kg/h infusion = 0.1 μg/kg/h of dexmedetomidine, or 0.01 mg/kg/h of midazolam and 0.165 μg/kg/h fentanyl). The anesthesia resident who prepared the drugs did not participate in the study. The attending anesthesiologist, operating surgeon, and the subjects were blinded to the study drug. A blinded observer assessed the level of sedation using RSS scale.[11]

After achieving a predefined target sedation level (RSS of 3), surgeons were allowed to operate. Lignocaine with adrenaline (1:200,000) solution containing 2% lignocaine was infiltrated locally at the site of incision in the dose of 3 mg/kg, at least 5 minutes before surgical incision. Burr-hole craniotomy followed by the hematoma evacuation was accomplished by dural and hematoma membrane incisions. Infusion of sedative was discontinued just after placement of the final skin suture. Intraoperative patient's movement was defined as those likely to interfere with surgical procedure such as bending of hand and/or leg and movement of head. Tiny movement of body parts or movements of finger or toes were not deemed significant enough to record for the purpose of this study as they were unlikely to be of hindrance to the successful conduct of surgical procedure. If the patient moved during the procedure, the first intervention was to attempt patient reassurance for 30 seconds. If movement continued then the infusion dose of test drug was increased in the previously described manner till the maximum dose of test drug was achieved. If the patient movement persisted despite the maximum infusion dose of test drug, then fentanyl 0.5 μg/kg IV bolus was administered as rescue drug in both the groups. Induction of general anesthesia was deemed the final intervention in

TABLE 1. Demographic and Baseline Hemodynamic Characteristics

	Group D (n = 26)	Group M/F (n = 26)	*P*
Age (y)	62.04 ± 11.60	54.92 ± 14.85	0.06
Weight (kg)	65.58 ± 12.13	62.4 ± 8.36	0.226
Sex (male/female)	23/3	20/6	0.233
ASA (I/II/III)	15/8/3	13/12/1	0.379
Preoperative MNG (0/1/2)	0/11/15	0/16/10	0.165
Hematoma volume (mL)	70.38 ± 21.63	61.62 ± 15.62	0.884
Duration of surgery (min)	54.81 ± 20.22	61.15 ± 20.07	0.261
Duration of anesthesia (min)	73.52 ± 20.28	74.23 ± 20.33	0.399
Baseline heart rate (beats/min)	73.88 ± 17.05	77.62 ± 18.00	0.447
Baseline mean arterial pressure (mm Hg)	100.77 ± 14.30	98.65 ± 13.53	0.586
Baseline respiratory rate (breaths/min)	17.42 ± 4.10	18.19 ± 4.19	0.506
Baseline SpO_2 (%)	98.54 ± 1.84	99.08 ± 1.23	0.220

Values are expressed as mean ± SD or as numbers.
ASA indicates American Society of Anesthesiology status; MGS, Markwalder's Neurological Grading Scale; SpO_2, pulse oximetry/arterial oxygen saturation.

case satisfactory condition was not achieved within the rescue fentanyl.

The following parameters were recorded intraoperatively: total number of intraoperative patient movements, number of intraoperative patient movements managed with reassurance for 30 seconds, number of intraoperative patient movements managed with dose adjustments, and the number of intraoperative patient movements managed with rescue drug (fentanyl 0.5 μg/kg) or finally, those who needed a complete general anesthesia. Hemodynamic and respiratory parameters were noted at predefined intervals (at baseline, before and after bolus administration of test drug, before skin incision, and at 1, 2, 5, and 10 min after skin incision) and at 10-minute intervals thereafter. In the postoperative period following variables were noted: immediate postoperative Aldrete score, postoperative recovery time (Aldrete score ≥ 9), and patient satisfaction score using 7-point Likert-like verbal rating scale.[9,12] The surgeon satisfaction was scored at the end of procedure as: extremely satisfied (1), satisfied (2), not satisfied but able to manage (3), and extremely dissatisfied (4).

Statistical Analysis

Statistical analysis was carried out using Statistical Package for Social Sciences (version 15.0 for Windows; SPSS Inc., Chicago, IL). Mean and medians were calculated for all quantitative variables, whereas for measures of dispersion SD or interquartile range (IQR) was calculated. Normality of quantitative data was checked by Kolmogorov-Smirnov tests. For normally distributed data means of 2 groups were compared using *t* test. For skewed data or for ordinal data Mann-Whitney test was applied. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using the χ^2 or the Fisher exact test. For comparison of hemodynamics variables a repeated measure ANOVA was applied. All statistical tests were 2-sided and were performed at a significance level of $\alpha = 0.05$. Sample size was estimated based on the results of our pilot study. The pilot study in 12 patients (6 in each group) showed mean number of intraoperative patient movement 1.65 in group D and 3.42 in group M/F with SD of 2.1. To detect a 50% change in movements with SD of 2.1, our sample size resulted in 23 per group at a power of 80% and confidence interval of 95%. For possible dropouts, we decided to include 26 patients in each group.

RESULTS

Both groups were comparable with respect to demographic and baseline hemodynamic characteristics (Table 1). Duration of surgery and duration of anesthesia were comparable between the 2 groups (Table 2). Total number of intraoperative patient movements was 1.0 (median IQR, 0.0 to 2.0) in group D and 3.0 (median IQR, 1.0 to 3.2) in group M/F ($P = 0.007$). The number of patient movements managed with reassurance for 30 seconds was 0.0 (median IQR, 0.0 to 1.0) in group D and 1.0 (median IQR, 0.75 to 2.00) in group M/F ($P = 0.019$). The number of times dose adjustment required was 0.0 (median IQR, 0.0 to 1.25) in group D and 1.0 (median IQR, 0.75 to 2.0) in group M/F ($P = 0.045$). No rescue drug was needed in either group (Table 2). HR remained within 15% of baseline values at most time point in both the groups. Decreases of >15% in HR were noticed at 60 and 80 minutes in group D and at 80 minutes in group

TABLE 2. Intraoperative Patient Movement Score

	Group D (n = 26)	Group M/F (n = 26)	*P*
Total intraoperative patient movements	1.00 (0.00-2.00)	3.00 (1.00-3.25)	0.007
No. movements managed with reassurance for 30 s	0.00 (0.00-1.00)	1.00 (0.75-2.00)	0.019
No. times dose adjustment required	0.00 (0.00-1.25)	1.00 (0.75-2.00)	0.045
No. times rescue drug used	0.00 (0.00-0.00)	0.00 (0.00-0.00)	1.000

Values are expressed as median (IQR).

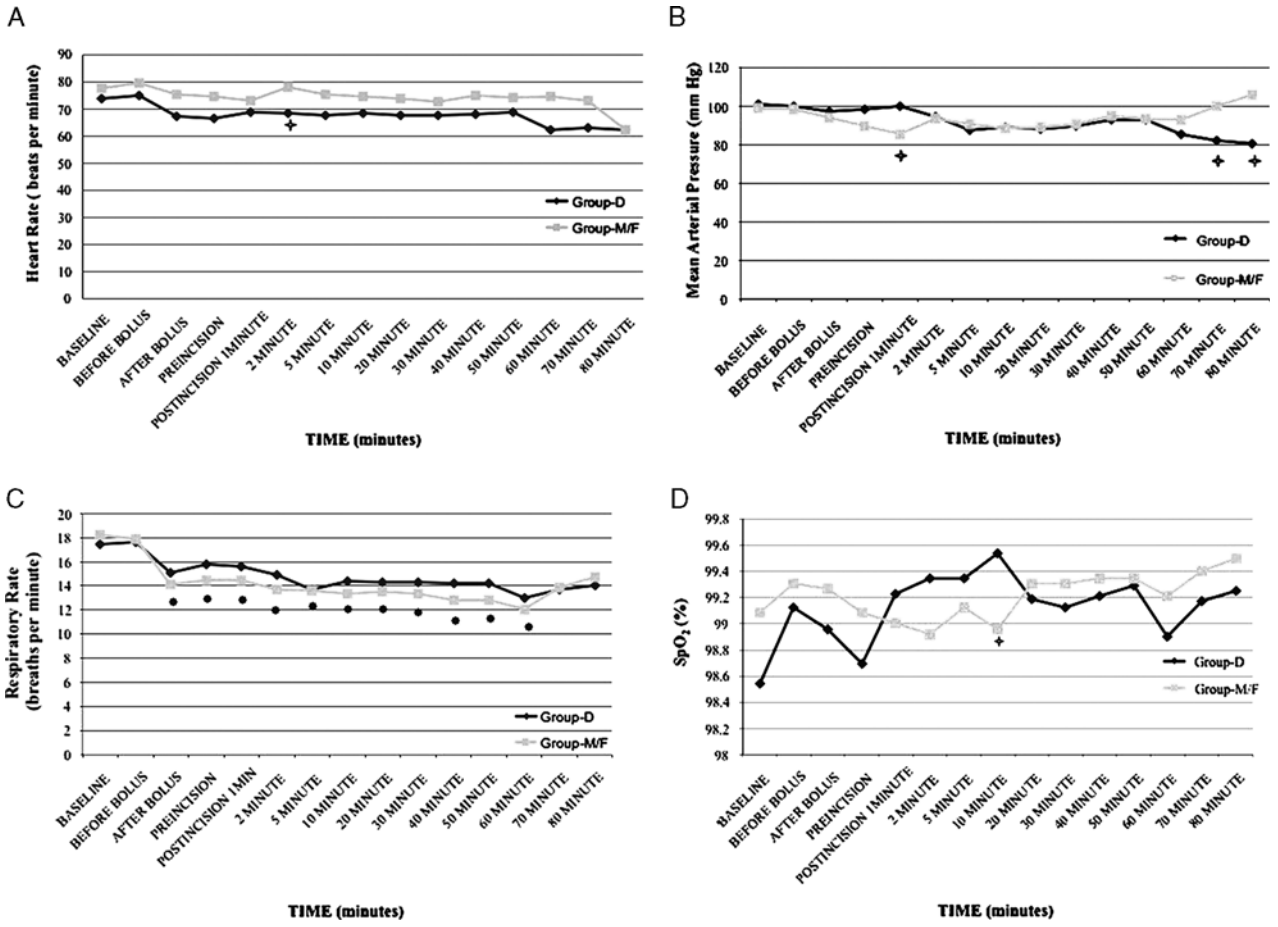

FIGURE 1. A, Variation in heart rate. *Point of significant difference between the groups ($P < 0.05$). B, Variation in mean arterial pressure. *Point of significant difference between the groups ($P < 0.05$). C, Variation in respiratory rate. *Point of significant difference from baseline ($P < 0.05$) within the group M/F. D, Variation in SpO_2. *Point of significant difference between the groups ($P < 0.05$). SpO_2 indicatses pulse oximetry/arterial oxygen saturation.

M/F. However, at no point were these changes statistically significant from baseline (Fig. 1A). Mean arterial pressure observations were comparable between the 2 groups at all time points except at 1 minute postincision when it was significantly lower in group M/F than group D ($P = 0.012$), whereas at 70 minutes ($P = 0.024$) and 80 minutes ($P = 0.033$) it was significantly higher in group M/F. Mean arterial pressure remained within 15% of baseline values at most time point in both the groups. Decrease of >15% in MAP was noticed at 60, 70, and 80 minutes in group D, but these values were statistically not significant (Fig. 1B). Decrease in RR was recorded in both the groups after bolus administration of drugs, but it remained comparable between 2 groups at all time point during the study period (Fig. 1C). None of the patient in either group had respiratory depression (RR < 8/minute). Postoperative Aldrete score was comparable in both the groups. Postoperative recovery time (time to an Aldrete score ≥ 9) was significantly lower in the group D (mean ± SD, 7.00 ± 6.96 min) in comparison with group M/F (mean ± SD, 13.69 ± 6.18 min) ($P = 0.000$). Postoperative surgeon satisfaction score was assessed at the end of surgical procedure in all 3 neurosurgeons who operated the case. It was significantly better in group D than group M/F (median IQR, 1.00 [1.00 to 1.25] vs. 2.00 [1.00 to 2.00], $P = 0.014$). However, the patient satisfaction score was comparable between both the groups (Table 3). The average drug requirement per patient in group M/F was fentanyl 66.90 + 22.66 μg and midazolam 4.01 + 1.35 mg, whereas in group D was dexmedetomidine 79.51 + 16.94 μg.

DISCUSSION

The results of our study suggest that the use of dexmedetomidine for conscious sedation in patients undergoing surgery for CSDH were associated with significantly reduced intraoperative patient movements. The need for reassurance and frequency of dose adjustment required to manage patient movement were also significantly lower in group D compared with group M/F. However, no rescue drugs were needed in either group. The postoperative recovery time was significantly less and surgeon satisfaction score was better with group D than group M/F. However, patient satisfaction score, intraoperative changes in RR and oxygen

TABLE 3. Postoperative Characteristics

	Group D (n = 26)	Group M/F (n = 26)	*P*
Postoperative Aldrete score	9.00 (8.00-9.00)	8.50 (8.00-9.00)	0.076
Postoperative recovery time (time to Aldrete score ≥ 9) (min)	7.00 ± 6.96	13.69 ± 6.18	0.000
Patient satisfaction score	7.00 (5.75-7.00)	7.00 (5.75-7.00)	0.474
Surgeon satisfaction score	1.00 (1.00-1.25)	2.00 (1.00-2.00)	0.014

Values are expressed as median (IQR) or mean ± SD.

saturation (SpO_2), and hemodynamic parameters were comparable among the groups.

Intraoperative patient movement during MAC may interfere with surgery and is one of the features that suggest inadequate level of sedation. Drugs that maintain more sustained desired level of sedation are expected to cause less intraoperative patient movements and less frequent dose adjustments after achieving the desired level of sedation. Earlier Bekker et al[13] have demonstrated that dexmedetomidine use results in fewer fluctuations from the desired sedation level in patients undergoing awake carotid endarterectomy under MAC compared with the other commonly used sedatives. The decreased number of intraoperative patient movements, reduced need for reassurance, and dose adjustments in group D of our study could be because of the ability of dexmedetomidine to maintain sustained level of desired sedation when compared with midazolam-fentanyl combination.

Use of dexmedetomidine as anesthetic adjuvant has been shown to decrease opioid and inhalational anesthetics requirement while shortening recovery time from anesthesia.[14,15] In contrast, comparison of dexmedetomidine with midazolam in patients undergoing cataract surgery under MAC demonstrated delayed recovery among dexmedetomidine sedated patients.[16] Our study results show significantly shorter postoperative recovery time (time to Aldrete score >9) in group D compared with group M/F. The difference in the result from previous study may be because of different methodology used in our study.

Patient satisfaction reflects the anesthetic care quality during the perioperative period. Candiotti et al[3] while evaluating the safety and efficacy of 2 doses of dexmedetomidine for sedation of patients undergoing a broad range of surgical and diagnostic procedures, concluded that dexmedetomidine provides better patient satisfaction and less opioid requirements than the placebo group. Authors attributed this result to additional analgesic property of dexmedetomidine. Similar result of better patient satisfaction was also observed by Alhashemi,[16] while comparing dexmedetomidine and midazolam for MAC during cataract surgery. Our results of comparable patient satisfaction score between both groups could be because of addition of fentanyl with midazolam, which may have provided adequate analgesia and improved patients' perception in M/F group.

Surgeon's perception of quality and responsiveness is key metric of quality of anesthesia service being delivered. Parikh et al[17] comparing dexmedetomidine with combination of midazolam-fentanyl for tympanoplasty under MAC, showed higher surgeon's satisfaction with dexmedetomidine group. Our results also suggested better surgeons satisfaction with use of dexmedetomidine when compared with midazolam-fentanyl combination. This may possibly be due to lesser intraoperative patient movements observed in group D patients.

Dere et al[18] showed that dexmedetomidine provides more efficient hemodynamic stability than midazolam during colonoscopy under conscious sedation. In our study, both groups maintained stable hemodynamics. HR and MAP were lower than baseline value in both the groups throughout the surgery.

Parikh et al[17] found comparable RR between dexmedetomidine and combination of midazolam-fentanyl during tympanoplasty under MAC. In a comparative study of dexmedetomidine with midazolam for cataract surgery, Alhashemi[16] observed a higher ventilatory frequency with decreased tidal volume and trend toward lower SpO_2 in midazolam group. Other investigators have also observed low SpO_2 readings among patients who received midazolam sedation. This has been attributed to hypoventilation or lack of supplemental oxygen administration.[19] We observed comparable RR and SpO_2 between both the groups. None of the study subjects experienced bradypnea (RR < 8/min) or desaturation (SpO_2 < 90%). There was a significant fall in RR from baseline value in M/F group, which was not observed in group D. The unique property of dexmedetomidine to preserve respiratory function may have accounted for the difference between the 2 groups in our study.[20] None of the patient in either group required conversion of MAC into general anesthesia. No other intraoperative and postoperative complications were encountered in either group during the study period. Considering higher cost of dexmedetomidine in our country, we evaluated cost of sedation per patient in each group. It was higher in group D ($3.52 + 0.99) compared with group M/F ($0.96 + 0.13).

Limitations

Although small difference in need for reassurance (0 vs. 1) and frequency of dose adjustment required (0 vs. 1) is statistically significant, it may not be of clinical significance. We did not compare anesthesiologist satisfaction score for administering anesthesia between the 2 groups. However, less number of total intraoperative movement, and movement that required intervention with similar hemodynamic and respiratory stability, may result in better satisfaction score with use of dexmedetomidine.

In conclusion, dexmedetomidine is a better alternative to midazolam-fentanyl combination in preventing

intraoperative patient movements, providing faster postoperative recovery, and better surgeon satisfaction in patients undergoing burr-hole surgery for CSDH. However, its use was associated with comparable patient satisfaction, hemodynamics, and respiratory parameters.

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