A comparison of midazolam, alfentanil and propofol for sedation in oupatient intraocular surgery

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Purpose: To determine the ideal sedative regimen for intraocular surgery under peribulbar or retrobulbar block. The addition of alfentanil and or propofol to midazolam was evaluated with regard to hemodynamic variables, respiratory rate, pain, anxiety, sedation, postoperative recovery and patient satisfaction.

Methods: Eighty two patients aged between 50 and 85 were recruited into this prospective, randomised, double blind study. Patients, in four groups, received 0.015 mg·kg^{-1} midazolam, 5 μg·kg^{-1} alfentanil and 0.15 mg·kg^{-1} propofol; 0.015 mg·kg^{-1} midazolam and 0.15 mg·kg^{-1} propofol; 0.015 mg·kg^{-1} midazolam and 5 μg·kg^{-1} alfentanil or 0.015 mg·kg^{-1} midazolam alone. Blood pressure, heart rate, respiratory rate, pain, anxiety and sedation scores were measured. Times to discharge from the Post Anesthesia Care Unit (PACU) and Day Surgery Unit (DSU) were documented. A 24 hr telephone interview was carried out to determine patient satisfaction.

Results: Systolic blood pressure of patients in groups that had received alfentanil was 6% lower than that of patients who had not ($P < 0.05$) at the time of insertion of intraocular block. Patients in the alfentanil groups also had lower respiratory rates during the first 15 min after drug administration, but all patients were given supplemental oxygen therefore oxygen saturation was unaffected. Pain scores of patients who had been given alfentanil were lower during the first postoperative hour than those who had not.

Conclusion: The addition of alfentanil to midazolam is advantageous in providing sedation for insertion of intraocular block.

Objectif : Déterminer le régime sédatif idéal pour une intervention intra-oculaire lors d'un blocage péribulbaire ou rétrobulbaire. L'ajout d'alfentanil et/ou de propofol au midazolam a été évalué sous l'angle des variables hémodynamiques, de la fréquence respiratoire, de la douleur, de l'anxiété, de la sédation, de la récupération postopératoire et de la satisfaction du patient.

Méthode : On a recruté 82 patients de 50 à 85 ans pour une étude prospective, randomisée et en double aveugle. Les patients, répartis en quatre groupes, ont reçu 0,015 mg·kg^{-1} de midazolam, 5 μg·kg^{-1} d'alfentanil et 0,15 mg·kg^{-1} de propofol; 0,015 mg·kg^{-1} de midazolam et 0,15 mg·kg^{-1} de propofol; 0,015 mg·kg^{-1} de midazolam et 5μg·kg^{-1} d'alfentanil ou 0,015 mg·kg^{-1} de midazolam employé seul. La pression sanguine, la fréquence cardiaque, la fréquence respiratoire, la douleur, l'anxiété et la sédation ont été mesurées, de même que le temps passé à la salle de réveil et à l'unité de chirurgie d'un jour. Un interview téléphonique, mené 24 h plus tard, a permis d'évaluer la satisfaction du patient.

Résultats : La tension artérielle systolique des patients qui avaient reçu de l'alfentanil était de 6 % plus basse que celle des patients qui n'en avaient pas eu ($P < 0,05$) au moment de l'insertion du bloc intra-oculaire. Les patients des groupes alfentanil présentaient une fréquence respiratoire plus basse pendant les 15 premières min suivant l'administration du médicament, mais tous les patients ont reçu de l'oxygène d'appoint si bien que la saturation en oxygène est demeurée stable. Les scores de douleur des patients qui avaient reçu de l'alfentanil, comparés à ceux des patients qui n'ont pas eu d'alfentanil, ont été plus bas pendant la première heure postopératoire.

Conclusion : L'ajout d'alfentanil au midazolam est avantageux et fournit la sédation nécessaire à l'insertion d'un blocage intra-oculaire.

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CATARACT extraction and intraocular lens implantation is one of the most frequently performed surgical procedures in the world. A sociodemographic analysis of 351 cataract patients revealed that the mean age was 70.6 ± 12.4 yr and 76.6% of the patients took medication for cardiovascular disease, diabetes, asthma or mental disorder.[1] Cognitive impairment has been demonstrated in patients undergoing cataract surgery under local anesthesia with sedation, which has important implications for discharge.[2] Sedation should increase comfort and provide amnesia, but not increase intraoperative complications, delay recovery or discharge.

Midazolam 0.015 mg·kg^{-1} provides effective sedation for cataract surgery in combination with fentanyl.[3] Alfentanil 5 μg·kg^{-1} and 20 mg propofol have been used in combination with midazolam.[4] We hypothesised that careful sedation with short acting drugs would be well accepted by patients and that increasing drug combinations may lead to more complications.

Method

Following ethics committee approval, informed consent was obtained from 82 patients aged 50 - 85 yr, ASA I - III, who were to undergo intraocular surgery under peribulbar or retrobulbar block. Surgery included cataract extraction, excision of pterygium, corneal transplant, trabeculectomy or a combination of these. Patients were excluded if they had: contraindications to any of the study drugs, visual impairment of the non operative eye, weight < 40 kg or > 100 kg, a history of drug or alcohol abuse, confusion, dementia, or communication difficulty resulting from deafness or language barrier. Baseline pain and anxiety scores were measured using a 100 mm visual analogue scale. Sedation scores were obtained on a 5 point scale with 1 = fully alert and oriented, 2 = drowsy, 3 = eyes closed but rousable to command, 4 = eyes closed but rousable to mild physical stimulation and 5 = unrousable to mild physical stimulation. Psychomotor testing was carried out using the Trieger Dot[5] and Digit Symbol Substitution[6] tests.

Patients were randomised by computer generated codes into one of four groups to receive: Group MAP - 0.015 mg·kg^{-1} midazolam + 5 μg·kg^{-1} alfentanil + 0.15 mg·kg^{-1} propofol; Group MP - 0.015 mg·kg^{-1} midazolam + placebo + 0.15 mg·kg^{-1} propofol; Group MA - 0.015 mg·kg^{-1} midazolam + 5μg·kg^{-1} alfentanil + placebo; Group M - 0.015 mg·kg^{-1} midazolam + placebo + placebo. Syringes were prepared by pharmacy and contained 1 mg·ml^{-1} midazolam, 500 μg·ml^{-1} alfentanil or an equivalent volume of saline, and 10 mg·ml^{-1} propofol or an equivalent volume of intralipid.

In the operating room, standard monitoring was instituted. Supplemental oxygen was administered at 6 l·min^{-1} by face mask. A 20 gauge intravenous cannula was inserted and attached to an infusion of normal saline. The anesthesiologist, who was blinded to the contents of the syringes, administered the drugs at 30 sec intervals in the order midazolam, alfentanil/placebo, propofol/placebo and the block was performed 30 sec later. If sedation was inadequate, further 0.0075 mg·kg^{-1} midazolam could be given every five minutes. Blood pressure, heart rate and respiratory rate were recorded every minute for five minutes and then every five minutes during surgery. Pain, anxiety and sedation scores were done after administration of the drugs, after the block and then every 20 min.

On arrival in the PACU, hemodynamic variables, respiratory rate, pain, anxiety and sedation scores were recorded every 30 min. The time to achieve a Post Anesthesia Discharge Scoring System[7] score of 9 was noted. At 24 hr, patients were telephoned and asked whether they had experienced any nausea and vomiting, dizziness, drowsiness or pain.

Statistical analysis

The data were analysed using factorial analysis of variance, chi-square test, and Fisher's exact test, where appropriate. $P < 0.05$ was considered statistically significant. All analyses were carried out using SAS (version 6:12) statistical software.

Results

Data from 81 patients were analysed. There were 20 patients in groups MAP, MP and M, and 21 patients in group MA. There were no differences in demographic data among groups. The MAP group patients

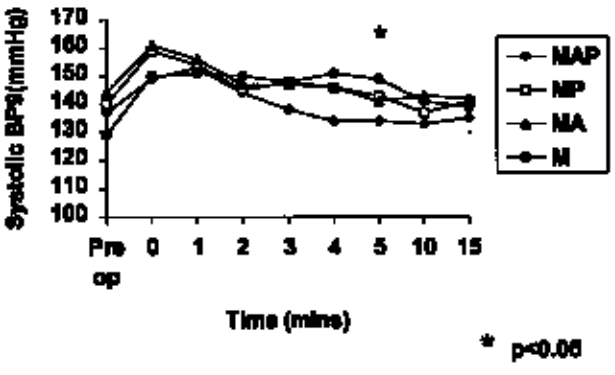

FIGURE 1 Graph of systolic blood pressure against time

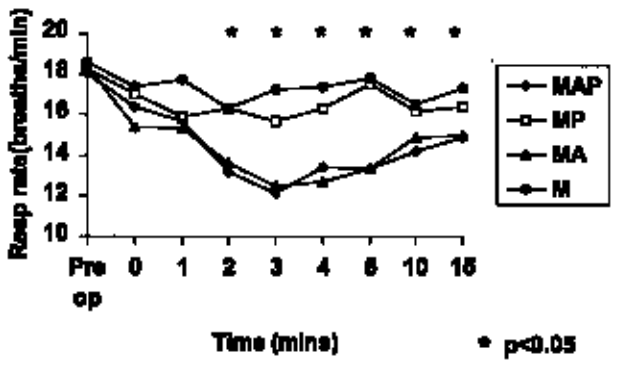

FIGURE 2 Graph of respiratory rate against time

TABLE I Postoperative pain scores.

	0 min	*30 min*	*60 min*
Group MAP	0.05 ± 0.22*	0.05 ± 0.22*	0
Group MP	0.85 ± 1.4	0.8 ± 1.5	0.5 ± 1.3
Group MA	0.3 ± 0.6*	0.1 ± 0.5*	0.2± 0.5
Group M	0.9 ± 1.5	0.7 ± 1.6	0.6 ± 1.5

* $P < 0.05$

TABLE II Results of the Digit Symbol Substitution (DSST) and Trieger Dot tests (TDT).

	MAP	*MP*	*MA*	*M*
DSST				
Preop	20	20	21	20
0 min	17	16	18	15
30 min	16	19	17	17
60 min	17	17	19	16
90 min	5	7	4	6
TDT				
Preop	20	20	21	20
0 min	19	18	21	20
30 min	19	20	20	18
60 min	18	17	20	17
90 min	5	7	6	6

received 1.2 ± 0.4 mg midazolam, 345 ± 73 μg alfentanil and 10 ± 2 mg propofol. The MP group patients received 1.3 ± 0.4 mg midazolam and 11 ± 2.0 mg propofol, the MA group patients received 1.3 ± 0.3 mg midazolam and 365 ± 64.1 μg alfentanil, and group M received 1.2 ± 0.3 mg midazolam.

Systolic blood pressure of patients who received alfentanil, was 6.0% lower at five minutes than that of patients who had not ($P < 0.05$, Figure 1). This is the time at which the intraocular block was inserted. These patients also had lower respiratory rates for 15 min after drug administration, the lowest mean being 12.1 bpm at three minutes in Group MAP ($P < 0.05$, Figure 2). Oxygen saturation was unaffected.

Intraoperatively, addition of alfentanil and or propofol to midazolam did not affect pain, anxiety or sedation scores. Although postoperative pain scores were low in all groups, those of patients who had received alfentanil were lower during the first postoperative hour ($P < 0.05$, Table I).

Increasing the number of sedative agents used did not have a deleterious effect on performance in the Trieger Dot and Digit Substitution tests (Table II).

Average time spent in the PACU ranged from 29.5 min(Group MAP) to 35.5 min (Group M), and in the DBU from 41.8 min (Group MA) to 50.5 min (Group MAP). No patient suffered from nausea and vomiting.

Discussion

In our study, alfentanil minimized the hemodynamic response to local anesthetic injection and reduced pain scores in the first postoperative hour. Neither midazolam alone or in combination with propofol was found to have these effects. Comparison of premedication for outpatient cataract surgery with intramuscular injections of alfentanil 12.5 $\mu g \cdot kg^{-1}$, midazolam 20 $\mu g \cdot kg^{-1}$ or placebo 15 min preoperatively,[8] also found that alfentanil obtunded the hemodynamic response to block insertion. The importance of reassurance and gentle technique when performing the local anesthetic block cannot be overemphasised.[9] We would also recommend that supplemental oxygen be administered to all patients who receive sedation.

We have demonstrated that the use of alfentanil is advantageous as part of a sedative regimen for ambulatory patients undergoing ophthalmic surgery. There was no increase in the incidence of postoperative nausea and vomiting or respiratory depression associated with its use.

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