Remifentanil versus fentanyl in combination with midazolam for retrobulbar block in cataract surgery

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ABSTRACT

الأهداف: مقارنة آثار عقار فينتانيل أو رامى فينتانيل مع عقار الميدازولام على قياسات حركيات الدم والألم وملف الرضى في عمليات المياة البيضاء.

الطريقة: أجريت هذه الدراسة الوصفية العشوائية في الفترة ما بين 10 و20 يوليو 2005م بمستشفى كوديرت للعيون. تم ترتيب المرضى في جدول لإجراء عملية إزالة المياة البيضاء عن طريق استحلاب محفظة العين بصورة عشوائية لتلقي التسكين مع ميدازولام 1mg عبر الوريد إما مع فينتانيل بمقدار 25µg (المجموعة الأولى،عدد= 54) أو رامي فينتانيل بمقدار 0.3µg/kg (المجموعة الثانية، عدد= 46). تم تسجيل معدل نبض القلب وضغط الشريان الانبساطي والانقباضي كخط قاعدي بعد الحقن خلف المقلة وأثناء العملية الجراحية، كما تم تسجيل رضا المريض والطبيب الجراح والآثار العكسية.

النتائج: كان هنالك تناوب ملحوظ في قياسات ضغط الشريان الانبساطي والانقباضي في المجموعتين (المجموعة الأولى: عدد=54 والمجموعة الثانية:عدد=46)، بينما تم إبقاؤهم جميعاً في معدل سريري طبيعي. لم يتذكر حتى الحقن خلف مقلة العين 24% من المرضى في المجموعة الأولى و15.2% من المجموعة الثانية. كانت نقاط الألم خلال الحقن خلف المقلة والعملية الجراحية متشابهة في كلتا المجموعتين. كما كان مستوى الرضا مرتفع لدى المرضى والطبيب الجراح وهو متقارب بين المجموعتين.

خاتمة: يعتبر عقاري الرامي فينتانيل والفنتانيل فعالين ومتقاربين لعقار الميدازولام من حيث قلة الشعور بالألم عند الحقن، كما إن مستوى الرضا مرتفع من حيث استقرار الحركة الدموية في عملية المياة البيضاء تحت الحقن خلف المقلة.

Objectives: To compare the effects of fentanyl or remifentanil in combination with midazolam on hemodynamic parameters, pain, and satisfaction profile in cataract surgery.

Methods: This randomized, double blind, prospective study was conducted between 10 and 20th July 2005 at Kudret Eye Hospital, Ankara, Turkey. Patients scheduled for cataract surgery by the phacoemulsification technique were randomly enrolled to receive sedation with midazolam 1 mg intravenous (iv) either with fentanyl 25 µg (group 1, n=54) or remifentanil 0.3 µg/kg (group 2, n= 46). Heart rate, systolic and diastolic arterial pressure values were recorded as baseline, after retrobulbar injection, and during the operation. We evaluated recall of retrobulbar block, pain during injection and operation, satisfaction of patient and surgeon, and the adverse effects.

Results: There were statistically significant alterations in systolic and diastolic arterial pressure measurements within and between groups, whereas all kept in the clinically normal range. Twenty-four percent of patients in group 1 and 15.2% in group 2 did not even remember the retrobulbar injection. The pain scores during retrobulbar injection and operation were similar in both groups. Also, satisfaction of patients and surgeon was high and comparable between groups.

Conclusion: Remifentanil and fentanyl are both efficient and comparable opioid adjuncts to midazolam providing low injection pain and high satisfaction level with hemodynamic stability in cataract surgery under retrobulbar injection.

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Cataract surgery patients constitute an increasing population in the world.[1] As the number of patients grows higher, the turnover in the operation room and the ward requires techniques that are suitable for day-case surgery reassuring low pain and high satisfaction. Sedation accompanying ophthalmic blocks is acceptable for the outpatient setting in cataract surgery, and the most preferred technique by the patients and the physicians.[2-4] Fentanyl and midazolam with retrobulbar block is a widely used combination for this purpose. While published data proved the short context-sensitive action time of remifentanil, this drug may also be a reasonable alternative for sedation in day case patients.[5-7] In this study, we aimed to evaluate if remifentanil or fentanyl provides stable hemodynamics, sufficient pain relief, and high satisfaction profile in patients undergoing elective cataract surgery under retrobulbar block in an outpatient setting.

Methods. After approval from the Hospital Scientific Committee for ethical purposes and informed consent of the patients, 110 patients were randomly enrolled to the double-blind, prospective study to receive midazolam either with fentanyl or remifentanil between 10-20 July 2005 at Kudret Eye Hospital, Ankara, Turkey. Patients with American Society of Anesthesiologists (ASA) status I-III scheduled for cataract surgery by the phacoemulsification technique under retrobulbar anesthesia were included in the study. Exclusion criteria were ASA physical status IV, allergy to drugs used in the study, history of drug abuse, and disorders preventing regional anesthesia or sedation. Patients' characteristics including age, weight, gender, and ASA physical status were noted before operation. All patients received 5 mg diazepam via the oral route for premedication one hour before operating theatre admission. Dentures and hearing aids were not removed before the operation, and patients were transferred in operation clothes to a room where the sedation and the block were performed. Routine monitors in place were electrocardiography, non invasive blood pressure, pulse oximetry (PETAS-KMA275, PETAS, Ankara, Turkey). A vein on the dorsum of the hand was cannulated, and the drugs were administered in 20 seconds. After midazolam 1 mg iv injection, patients in group 1 received fentanyl 25 µg, whereas remifentanil 0.3 µg/kg was administered in group 2 before the retrobulbar block. Both of the drugs had been diluted into a volume of 5 cc, and were administered by an anesthesia technician out of the study team in order to avoid any unfavorable impact on the double-blind study setting. Retrobulbar nerve block was performed by the same ophthalmic surgeon with 4 ml lidocaine 2% via the percutaneous route with 25 G, 38 mm Atkinson needle (John Weiss & Son Limited, Milton Keynes, England). Injection was at the inferotemporal site. No patient received additional facial block. After sedation and retrobulbar block, all patients were transferred to the operation room where all parameters continued to be recorded. In the operation theatre, patients received supplemental O_2 via a tray with 5 L/min. Heart rate (HR), systolic (SAP) and diastolic (DAP) arterial pressure values were recorded at intervals before the operation as baseline, 5 minutes after retrobulbar injection and intraoperatively. Recall and the pain of the retrobulbar injection were consulted 5 minutes after the block. The pain during the operation, satisfaction of the patient, and the surgeon were evaluated immediately after the operation. Patients evaluated their pain level by a 4-degree scale as "none, mild, moderate, severe." Satisfaction scoring was made according to a 5-degree scale as "very bad, bad, moderate, good, and very good." Adverse events were noted from the preanesthesia room admission to discharge. All the patients were discharged from the hospital on the same day as the surgery.

The SPSS and Stat Pac version 3.0 were used for statistical analyses. Recall of the block and adverse events were analyzed by x^2-test. For hemodynamic values, independent samples t-test was used for analysis between groups, whereas paired samples t-test was used for comparison with previous measurement within group. Pain and satisfaction scores were analyzed by 2-sample t-test between percents. A *p*-value less than 0.05 was considered to be statistically significant.

Results. One patient in the fentanyl group and 5 patients in the remifentanil group were excluded from the study due to procedural changes. Also 4 patients in the second group decided not to continue in the study by their own request. Patients' characteristics were comparable in both groups (**Table 1**). Heart rate values were similar between groups. Also, there was no significant difference within group measurements. There were statistically significant alterations in systolic and diastolic arterial pressure measurements within and between groups, whereas all kept in the clinically normal range (**Table 2**). Twenty-four percent of patients in group 1 and 15.2% in group 2 did not

Table 1 - Patients' characteristics.

Characteristics	Group 1 (n=54)	Group 2 (n=46)
Age (years)	66.7±13.13	66.86±11.0
Weight (kilograms)	71.38±9.63	75.0±10.0
Gender (Female/Male)	25/29	22/24
ASA I/II/III	35/17/2	25/19/2
Duration of operation (minute)	10.29±2.38	9.82±2.59

ASA - American Society of Anesthesiologists

Table 2 - Patients' Hemodynamics.

Parameters	Group 1	Group 2
Heart rate		
Baseline	78.1±12.1	80.9±11.1
After retrobulbar block	79.7±14.7	78.4±10.8
Intraoperative	78.1±11.8	80.3±7.7
SAP (mm Hg)		
Baseline	123.6±18.7	125.5±13.7
After retrobulbar block	130.8±17.9*	137.0±17.0*
Intraoperative	127.2±16.3	129.2±14.6*
DAP (mm Hg)		
Baseline	78.1±8.5	76.0±8.0
After retrobulbar block	80.8±13.6	87.8±11.5*†
Intraoperative	83.6±7.8	82.1±8.9*

*p<0.05 in comparison to previous measurement within group, †p<0.05 between group, SAP - systolic arterial pressure, DAP - diastolic arterial pressure

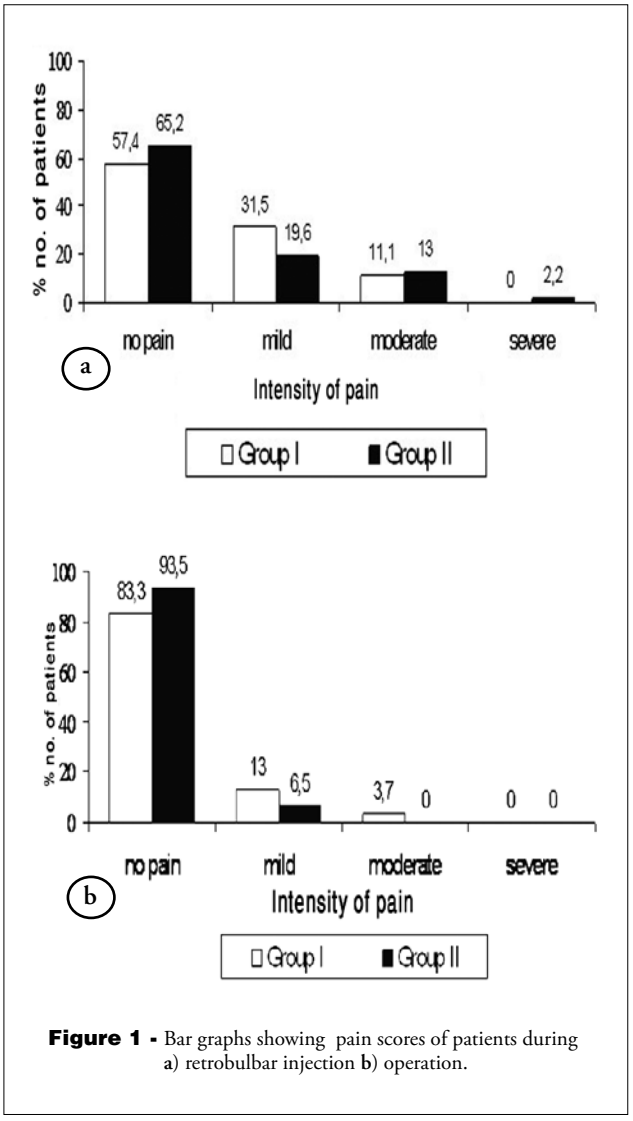

Figure 1 - Bar graphs showing pain scores of patients during **a**) retrobulbar injection **b**) operation.

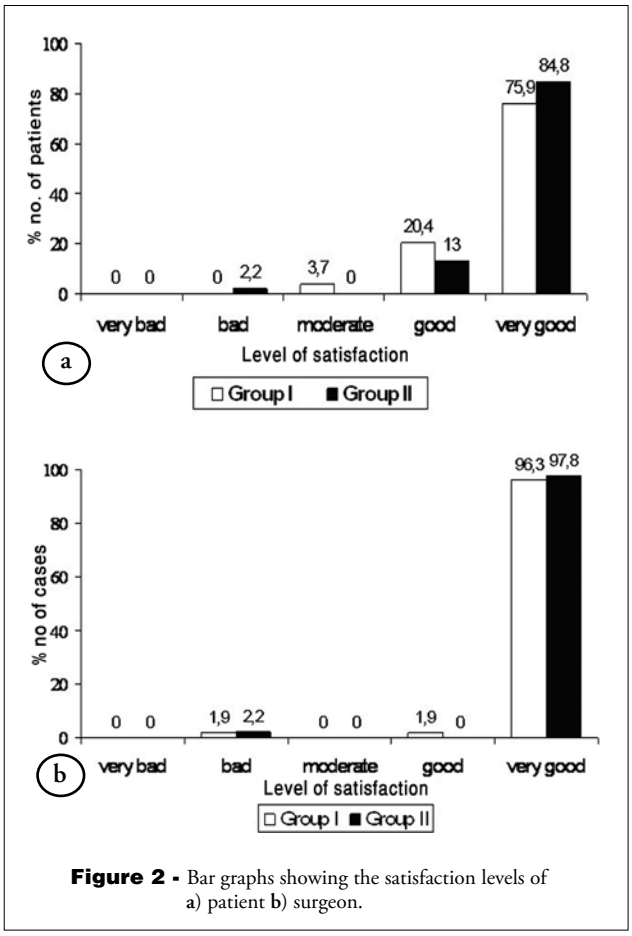

Figure 2 - Bar graphs showing the satisfaction levels of **a**) patient **b**) surgeon.

even remember the retrobulbar injection. However, there was no statistically significant difference between the groups. The pain scores during retrobulbar injection and operation were similar in both groups (**Figures 1a & 1b**). The satisfaction of patients and surgeons was also similar in the groups (**Figures 2a & 2b**). The majority of patients in both groups (96.3% in group 1, and 97.8% in group 2) rated their satisfaction as "good" or "very good". No adverse event occurred intraoperatively, and no additional medication was required during this period. Two patients reported nausea between the 2nd and 4th hours in postoperative period in the fentanyl group. They were treated with metoclopramide 10 mg. We did not observe vomiting in any patients. There was no other reported adverse event in any group.

Discussion. The care and provision of ophthalmic anesthesia for cataract surgery presents worldwide variation.[8] Current approaches vary from topical anesthesia to needle techniques such as retrobulbar and peribulbar. It is reported that 72% of patients prefer regional anesthesia over topical for cataract surgery.[4,9] These techniques are either practiced without sedation or

accompanied by oral or intravenous sedatives in various combinations.[4] The choice of anesthesia method largely depends on the preference of the anesthesiologists and surgeons, however, patients' perceptions of intraoperative pain and satisfaction also affect this selection.[4,9,10] Most patients have moderate to high levels of anxiety before cataract surgery.[11] Also visual experiences can be very disturbing during the operation.[12] Sedation decreases the unpleasant experience of retrobulbar injection and visual disturbances during the procedure. Although the use of sedation for regional techniques has been controversial, there is, clearly a need for sedation during administration of block from the patients' perspective.[13] Meeting the requirements of the procedure, sedation also provides the objective of a conscious and cooperative patient during both regional block and operation with limited movements decreasing the frequency of serious complications.[13,14] Without facial block, as in our study, cooperation of the patient is more important to remain akinetic.[13] Yet, short duration of the procedure mostly allows combination of ophthalmic regional blocks and sedation to meet the preferences of patients.[2] This combination significantly decreases the ratio of patients not entirely satisfied with pain management. Knowledge of patient satisfaction may provide an optimal anesthesia strategy.[4,10] However, preferences of physicians and anesthesiologists are reported to be similar to the patients'.[3]

The ideal sedative drug would produce sedation and pain relief without serious side effects for the short time required to perform the blocks in cataract surgery. The drugs used for the purpose should allow patients to be awake and cooperative during the operation, and permit early discharge from the hospital in elderly patients.[13,15,16] The ideal properties do not exist in one drug yet. For this reason, a combination of drugs may meet the requirements needed for cataract surgery. Sedatives in addition with opioids may reduce reports of any pain during surgery, increase satisfaction with pain management, and reduce postoperative drowsiness as opioid addition decreases the amount of sedatives used.[4] A combination of midazolam with fentanyl or remifentanil may provide optimal operation conditions. Midazolam used in a low dose may balance the possible risk of adverse events in cataract surgery patients who mostly represent an elderly population.[11] Midazolam and fentanyl and their combinations are widely used drugs, whereas remifentanil is an alternative to fentanyl with its unique properties. Remifentanil with its short context-sensitive half life of 3-5 minutes, a rapid offset and predictable emergence may be a safer choice over other opioids in supplementing sedation for retrobulbar nerve block in day case patients.[5-7,14,15] However, remifentanil alone may not provide optimal sedation for cataract surgery.[17]

In this study, neither fentanyl nor remifentanil addition could prevent a statistically significant rise in systolic arterial pressure after retrobulbar injection in both groups, whereas hemodynamics were kept in clinically normal range in all measurements. Without a significant difference, recall of retrobulbar injection rate was slightly higher in the remifentanil group, which might affect the pain perception and satisfaction of patients. A high percent of the patients declared to have no or a mild degree of pain during retrobulbar injection and operation. The number of painless patients was insignificantly more in the remifentanil group, which may suggest that titration according to weight may provide better dosing in comparison with a standard dose of fentanyl administration, or remifentanil may supply a more potent pain relief than fentanyl does. However, this was the limitation of our study, that we examined the effect of a fixed dose of fentanyl, which was a routine practice in our setting before the study was held. Hence, the medication titrated according to weight may get different results. Satisfaction of the patients and the surgeon was very high in both groups regardless of the drug administered. High patient satisfaction score may be attributed to the absence of periorbicular injection and absent, or minimum pain during the block and surgery.[18] The incidence of nausea and vomiting was low, which did not delay discharge from the hospital. We believe this was due to the low dose of the drugs. Although we did not observe any respiratory adverse event, the potential of remifentanil to depress respiration, especially in elderly people would be of concern.[19] In a pilot study, 0.5 μg/kg remifentanil was reported to reveal troublesome respiratory depression, and apnea in most patients.[13] Cost effectiveness is also a factor that influences the choice of drugs. The cost of remifentanil estimated according to mean weight of the patients in our study group was 0.117 Euros versus 0.095 Euros in the fentanyl group for one patient. Remifentanil cost was concordant with previously reported data in a similar study.[14] As the prices were similar, we suggest that both drugs may be preferable according to cost in a high-volume cataract surgery setting. However, the main concern of this study was not a cost analysis, and this information may just give a rough opinion to the reader only on the cost of opioids used in the study.

Cataract surgery is a short procedure, which improves quality of life.[20] Patients scheduled for cataract surgery demand a high level of comfort and satisfaction in addition to analgesia, which both represent important factors in quality of health care especially in such short cases and outpatient surgery. The combination of remifentanil 0.3 μg/kg or fentanyl 25 μg with midazolam 1 mg offered acceptable sedation for performing retrobulbar block. We achieved adequate

pain relief during the injection and operation, and high satisfaction in most of the patients in both groups.

In conclusion, we suggest that remifentanil and fentanyl are both efficient, and comparable opioid adjuncts to midazolam providing low injection pain, and high satisfaction level with hemodynamic stability in cataract surgery under retrobulbar injection.

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References

1. Asbell PA, Dualan I, Mindel J, Brocks D, Ahmad M, Epstein S. Age-related cataract. ***Lancet*** 2005 12-18; 365: 599-609.
2. Friedman DS, Reeves SW, Bass EB, Lubomski LH, Fleisher LA, Schein OD. Patient preferences for anaesthesia management during cataract surgery. ***Br J Ophthalmol*** 2004; 88: 333-335.
3. Reeves SW, Friedman DS, Fleisher LA, Lubomski LH, Schein OD, Bass EB. A decision analysis of anesthesia management for cataract surgery. ***Am J Ophthalmol*** 2001; 132: 528-536.
4. Katz J, Feldman MA, Bass EB, Lubomski LH, Tielsch JM, Petty BG, et al. Injectable versus topical anesthesia for cataract surgery: patient perceptions of pain and side effects. ***Ophthalmology*** 2000; 107: 2054-60.
5. Cohen J, Royston D. Remifentanil. ***Curr Opin Crit Care*** 2001; 7: 227-231.
6. Michelsen LG, Hug CC, Jr. The pharmacokinetics of remifentanil. ***J Clin Anesth*** 1996; 8: 679-682.
7. Beers R, Camporesi E. Remifentanil update: clinical science and utility. ***CNS Drugs*** 2004; 18: 1085-1104.
8. Kumar CM. Akinetic ophthalmic block with a short needle. ***CPD Anaesthesia*** 2001; 3: 97-102.
9. Gombos K, Jakubovits E, Kolos A, Salacz G, Nemeth J. Cataract surgery anaesthesia: is topical anaesthesia really better than retrobulbar? ***Acta Ophthalmol Scand*** 2007; 85: 309-316.
10. Wagle AA, Wagle AM, Bacsal K, Tan CS, Chee SP, Au Eong KG. Practice preferences of ophthalmic anaesthesia for cataract surgery in Singapore. ***Singapore Med J*** 2007; 48: 287-290.
11. Habib NE, Mandour NM, Balmer HG. Effect of midazolam on anxiety level and pain perception in cataract surgery with topical anesthesia. ***J Cataract Refract Surg*** 2004; 30: 437-443.
12. Tan CS, Au Eong KG, Kumar CM. Visual experiences during cataract surgery: what anaesthesia providers should know. ***Eur J Anaesthesiol*** 2005; 22: 413-419.
13. Boezaart AP, Berry RA, Nell ML, van Dyk AL. A comparison of propofol and remifentanil for sedation and limitation of movement during periretrobulbar block. ***J Clin Anesth*** 2001; 13: 422-426.
14. Leidinger W, Schwinn P, Hofmann HM, Meierhofer JN. Remifentanil for analgesia during retrobulbar nerve block placement. ***Eur J Anaesthesiol*** 2005; 22: 40-43.
15. Rewari V, Madan R, Kaul HL, Kumar L. Remifentanil and propofol sedation for retrobulbar nerve block. ***Anaesth Intensive Care*** 2002; 30: 433-437.
16. Katz J, Feldman MA, Bass EB, Lubomski LH, Tielsch JM, Petty BG, et al. Adverse intraoperative medical events and their association with anesthesia management strategies in cataract surgery. ***Ophthalmology*** 2001; 108: 1721-1726.
17. Avramov MN, Smith I, White PF. Interactions between midazolam and remifentanil during monitored anesthesia care. ***Anesthesiology*** 1996; 85: 1283-1289.
18. Fung D, Cohen MM, Stewart S, Davies A. What determines patient satisfaction with cataract care under topical local anesthesia and monitored sedation in a community hospital setting? ***Anesth Analg*** 2005; 100: 1644-1650.
19. Richardson SP, Egan TD. The safety of remifentanil by bolus injection. ***Expert Opin Drug Saf*** 2005; 4: 643-651.
20. Pesudovs K, Weisinger HS, Coster DJ. Cataract surgery and changes in quality of life measures. ***Clin Exp Optom*** 2003; 86: 34-41.