(Acta Anaesth. Belg., 2008, 59, 27-32)

Comparison of midazolam sedation with or without fentanyl in cataract surgery

O. Yalcin Cok (*), A. Ertan (**) and M. Bahadir (**)

Abstract : We compared the effect of midazolam sedation with or without fentanyl on the hemodynamic parameters, sedation, and pain and satisfaction profile in cataract surgery. Two hundred and ten patients were randomly allocated to receive either midazolam 1 mg iv (Group M, n = 101) alone or with fentanyl 25 µg (Group MF, n = 100) before retrobulbar injection. Hemodynamic parameters, observer's assessment of alertness/sedation (OAA/S) scores, pain during block and surgery, satisfaction of patient and surgeons were assessed. Heart rate and diastolic arterial pressure decreased after retrobulbar injection in comparison to baseline whereas systolic arterial pressure values increased in both groups. The majority of patients in both groups experienced mild pain during retrobulbar injection but no pain during surgery. There was a significant decrease in OAA/S scores in both groups (p = 0.001) and this decline was more significant in Group MF (p = 0.038). We suggest that midazolam alone may produce optimal block conditions for the patient and it is satisfactory during the procedure while the addition of fentanyl has not improved the effect on the examined parameters.

Key words : Fentanyl ; midazolam ; pain ; sedation ; patient's satisfaction.

Introduction

Cataract operation is the most common surgery in the elderly patients. Regional techniques are frequently performed following the administration of sedatives in cataract surgery. The choice of sedatives is highly variable and opioids may be added for better pain relief and higher patient satisfaction. Any side-effects delaying the discharge after sedation are undesirable (1). Midazolam and fentanyl have been favored for sedation in cataract surgery under retrobulbar block (2).

In this study, we planned to compare the effect of midazolam sedation with or without fentanyl on the hemodynamic parameters, sedation, and pain and satisfaction profile in cataract surgery examined if fentanyl addition may improve these parameters.

Methods

After approval by the Hospital Evaluation Committee of Scientific Studies for ethical purpose and written informed consent, patients scheduled for cataract surgery by phacoemulsification in one week were randomly allocated to two study groups to receive midazolam either alone (Group M) or with fentanyl (Group MF). Randomisation was established according to computer-generated random numbers list. Enrollment was limited to patients who were aged 18 years or older, American Society of Anesthesiologists (ASA) physical status I-III. Patients with ASA status IV, allergy to drugs used in the study, history of drug abuse, and disorders preventing the use of regional anesthesia or sedation were excluded. Patients' characteristics as age, weight, and gender and ASA physical status were noted prior to surgery.

An intravenous cannula was inserted on the dorsum of left hand in the preparation room where sedation and block were applied and routine monitors in place were electrocardiogram, non-invasive blood pressure and pulse oxymetry (PETAS-KMA275, PETAS, Ankara, Turkey). Drugs were administered by an anesthesia technician who was not involved in the study. Patients in Group M (Group M, n = 101) received midazolam 1 mg intravenously whereas Group MF (Group MF, n = 100) received midazolam 1 mg and fentanyl 25 µg.

Oya Yalcin Cok, M.D. ; Aylin Ertan, M.D. ; Mehmet Bahadir, M.D.

(*) Department of Anesthesiology and Reanimation, Baskent University, Faculty of Medicine, Ankara, Turkey – formerly working at Kudret Eye Hospital, Ankara, Turkey.

(**) Department of Ophthalmology, Kudret Eye Hospital.

Correspondence address : Dr. Oya Yalcin Cok, Baskent University, Adana Teaching and Research Hospital, Dadaloglu Mah. 39. sok No : 6, Yuregir, Adana / Turkey. Tel. : +90 533 4306963. E-mail : oyacok@yahoo.com

This study was presented as poster in 2nd World Congress on Regional Anesthesia and Pain Therapy, 4th-8th March 2006, Rio de Janeiro, Brazil.

Retrobulbar nerve block was performed by the same ophthalmic surgeon who was unaware of group allocation with 4 ml lidocaine 2% via the percutaneous route with a 25 G, 38 mm Atkinson needle (John Weiss & Son Limited, Milton Keynes, England), at inferotemporal site. No patient received an additional facial nerve block.

Heart rate (HR), systolic (SAP) and diastolic (DAP) arterial pressure values were recorded 3 minutes after the sedation as baseline and after retrobulbar injection to assess the effect of sedatives during the block.

After sedation and retrobulbar block, all patients were transferred to the operating room where recording of all parameters was continued. In the operating room, patients received supplemental oxygen 5 L min^{-1} insufflated by a tray under the drapes.

We assessed the pain immediately after block and surgery. Patients were asked to score pain as 'no pain, mild pain, moderate pain, severe pain'. Recall of the retrobulbar block was questioned at 5 minutes after the injection. Patients and the surgeon were also asked to verbally rate their level of satisfaction according to five-degree scale as "very bad, bad, moderate, good and very good" after the operation. The sedation level of patients was assessed by the Observer's Assessment of Alertness/Sedation (OAA/S) scale (Table 1) (3, 4). Until discharge any adverse events such as bradycardia, tachycardia, hypertension or hypotension, respiratory depression, nausea and vomiting were registered. All parameters and observations were recorded by the same anesthesia technician not being part of the study team. Patients complaining of nausea and vomiting were treated with metoclopropamide 10 mg. All patients were discharged from the hospital on the day of the surgery.

SPSS 11.0 and Stat Pac version 3.0 were used for statistical analyses. Aiming at a 20% difference between groups with alfa = 0.05, for a 0.8 power, our analysis revealed that total 50 patients in each group would be sufficient for the study. Taking into account several drop-outs, all patients scheduled during one week were enrolled in the study. All statistical tests were two-tailed, with statistical significance defined as $p < 0.05$. Descriptive variables were analyzed by using independent samples t-test and $\chi 2$-test. Recall of the block and adverse events were analyzed by a $\chi 2$-test. For hemodynamic values, independent samples t-test was used for between group analyses whereas paired samples t-test was used within group. Pain and satisfaction scores were analyzed by two sample t-test between percents.

Results

Two hundred and one patients were recruited during one week. No patients were excluded from the study groups due to a complication or failure of the block or operation. Patient demographics and operation time were comparable in both groups (Table 2).

Heart rate values significantly decreased after the block in both groups ($p = 0.0001$) (Table 3). Systolic arterial pressure significantly increased after the block in both groups ($p = 0.0002$) and this rise was significantly more pronounced in Group M

Table 1

Observer's Assessment of Alertness/Sedation (OAA/S) scale

Category	Observation	Score Level
responsiveness	responds readily to name spoken in normal tone	5
	lethargic response to name spoken in normal tone	4
	responds only after name is called loudly and/or repeatedly	3
	responds only after mild prodding or shaking	2
	does not respond to mild prodding or shaking	1
speech	normal	5
	mild slowing or thickening	4
	slurring or prominent slowing	3
	few recognizable words	2
facial expression	normal	5
	mild relaxation	4
	marked relaxation (slack jaw)	3
eyes	clear, no ptosis	5
	glazed, or mild ptosis (less than half the eye)	4
	glazed and marked ptosis (half of the eye or more)	3

Table 2

Patients' characteristics (Mean ± SD or number of patients)

	GROUP M	GROUP MF
Number of patients	101	100
Age (years)	67.2 ± 12.7	68.9 ± 11.3
Weight (kg)	72.2 ± 12.2	72.7 ± 11.3
F/M	55/46	63/37
ASA I/II/III	46/54/1	47/50/3
Operation duration (min)	9.4 ± 2.7	8.9 ± 3.3

in comparison to the Group MF ($p = 0.015$) (Table 3). Diastolic pressure decreased in Group MF in comparison to both baseline and Group M ($p = 0.008$ and $p = 0.031$, respectively).

The pain scores during retrobulbar injection and surgery were similar in both groups (Fig. 1a & 1b). The majority of patients in both groups experienced mild pain during retrobulbar injection (Fig. 1a) but no pain during the surgery (Fig. 1b). The proportion of patients experiencing moderate or severe pain during the block and the operation were also comparable in both groups. Nine patients in Group M and 12 in Group MF did not even remember the retrobulbar injection ($p = 0.49$).

Although overall satisfaction rate was high and comparable in both groups, the percentage of patients who rated their level of satisfaction as "good" was higher in group M ($p = 0.01$) (Fig. 2a). Also the surgeon's satisfaction was high and comparable between groups (Fig. 2b).

OAA/S scores were similar following sedation, but OAA/S scores significantly decreased in both groups after retrobulbar block ($p = 0.001$) and this decline was more significant in the Group MF ($p = 0.038$).

Two patients in Group M and 5 patients in Group MF reported nausea in the postoperative period. In both groups no other adverse events were registered until discharge.

Discussion

Cataract operation is the most common surgery performed in elderly patients (5). Current anesthetic approaches in cataract surgery vary from topical to needle techniques. While eye blocks provide excellent anesthesia for ophthalmic surgery, many clinicians combine these blocks with sedation. The choice of the technique depends on the needs and preferences of patients, surgeons and anesthetists (1, 2). Published data claim that the patients prefer sedation during eye blocks in cataract operations ; both ophthalmic surgeons and the anaesthetists prefer this practice (6-8). Sedation during a block also increases the degree of satisfaction with pain management (1).

The main objectives of sedation in cataract surgery are pain relief during the block with less or no serious adverse events. Ideally sedation should allow patients to be awake and cooperative during the operation and early discharge. A variety of sedatives and analgesic agents, especially opioids, have been used alone or in combination to ensure comfort of the patient during performance of a retrobulbar block (1, 5). Midazolam is the commonly used benzodiazepine for producing amnesia and sedation (9). Following a single intravenous sedative dose, the onset of effect is rapid (30 to 60 seconds), and its duration ranges from 15 to 80 minutes. However, hemodynamic and respiratory depressant effects of this drug have been reported being more pronounced in conjunction with opioids or in the elderly (10). When an opioid is added to a sedative, the expected benefits are to reduce the incidence of pain and to increase the satisfaction during procedure (1, 11). Fentanyl exhibits a rapid onset of action between 3-5 minutes and short duration of effect following a single intravenous dose and may be recommended for ophthalmic use in the elderly for its lower incidence of side effects (5, 10, 12).

Table 3

Hemodynamic parameters (mean ± SD, # : $p < 0.05$ in comparison to baseline within group ; * : $p < 0.05$ between groups)

		GROUP M (n = 101)	GROUP MF (n = 100)
Heart rate (pulse/min)	Before block	81.5 ± 10.7	79.0 ± 11.0
	After block	75.0 ± 15.3#	72.1 ± 13.2#
Systolic arterial pressure (mmHg)	Before block	132.4 ± 15.4	130.5 ± 16.8
	After block	148.2 ± 22.6#*	140.8 ± 20.1 #
Diastolic arterial pressure (mmHg)	Before block	83.6 ± 7.8	81.3 ± 8.2
	After block	81.5 ± 11.6	77.4 ± 14.9 #*

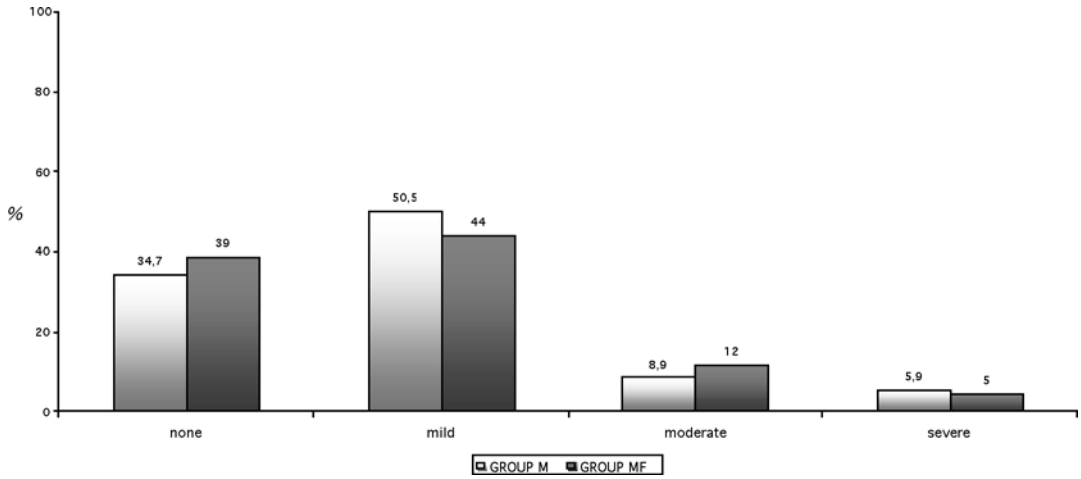

Fig. 1a. — Pain profile of patients during retrobulbar block, (%)

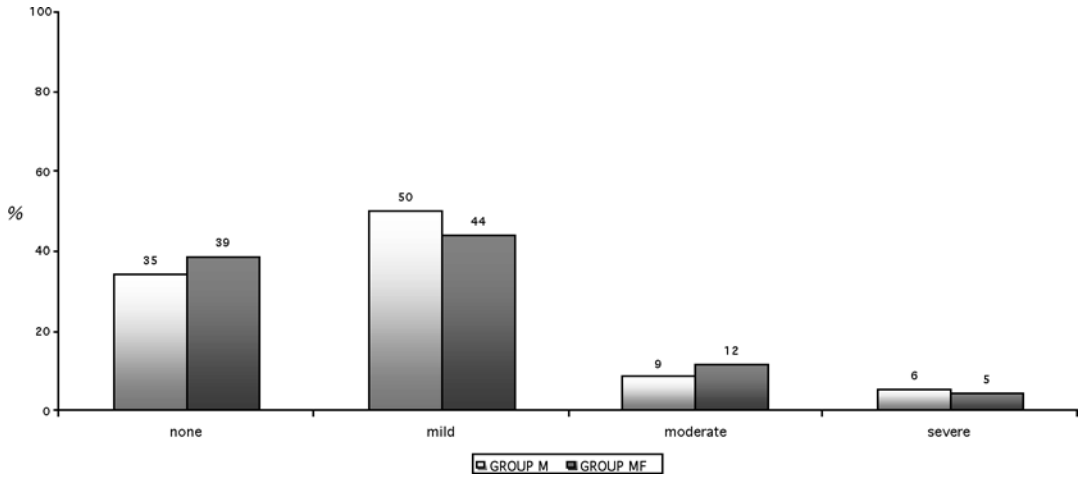

Fig. 1b. — Pain profile of patients during the operation, (%)

The combination of a benzodiazepine with an opioid appears to be promising but a synergistic potential for marked depressant effects should not be ignored.

This study evaluated the effect of midazolam alone or with fentanyl on hemodynamics, pain relief, and sedation level during retrobulbar injection and surgery. We also noted the satisfaction of patients and surgeon and adverse events until discharge. Main objective was to examine if fentanyl addition to midazolam could be beneficial in terms of pain relief and satisfaction in cataract surgery during the block and operation. In this study, the hemodynamic alterations were similar to other reports and kept in a clinically acceptable range (1, 5, 12). The majority of patients in both groups experienced mild pain during retrobulbar block and noticed no pain during surgery. Although no patient in either group was excessively sedated, addition of fentanyl significantly decreased OAA/S scores in comparison to midazolam alone. Satisfaction of the patients and the surgeon was very high in both groups. The high satisfaction of patient may be attributed to absent or mild pain during block and surgical procedure, short duration of surgery and the absence of repeat or rescue injections. However, we did not observe any benefit of adding fentanyl in decreasing pain sensation or increasing satisfaction. The amnesic effect of midazolam also might have affected the assessment of pain and helped the patients to forget the unpleasant feelings associated with the surgery (13). The incidence of nausea and vomiting which usually leads to delayed discharge from the hospital was low and similar in both groups. Except for nausea no other adverse events were noticed.

The most important limitation of this study was that we examined the effect of a fixed dose of midazolam 1 mg and fentanyl 25 µg being consistent with current practice in our clinic. Titration of medication according to weight might have resulted in different results.

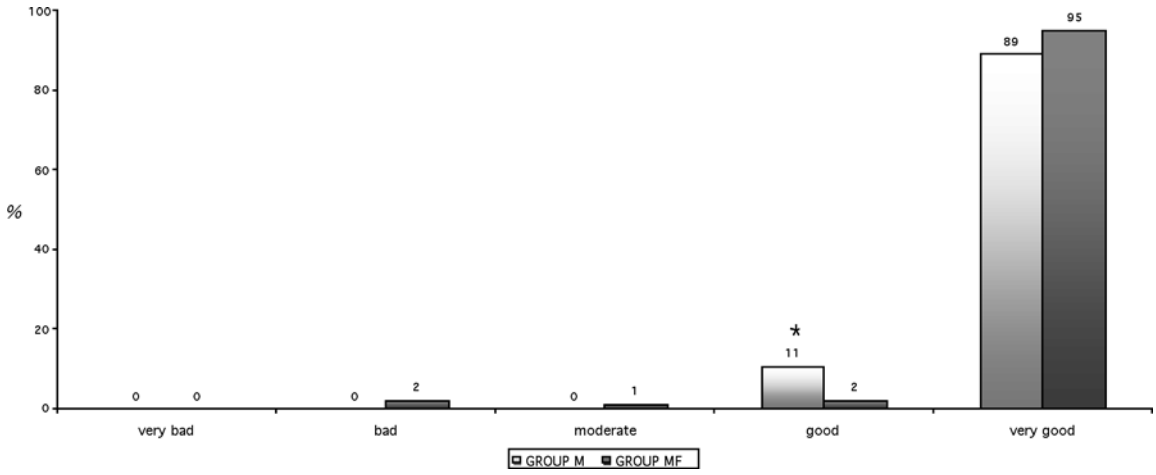

Fig. 2a. — Satisfaction profile of the patients, (%) (* : $p < 0.05$ between groups)

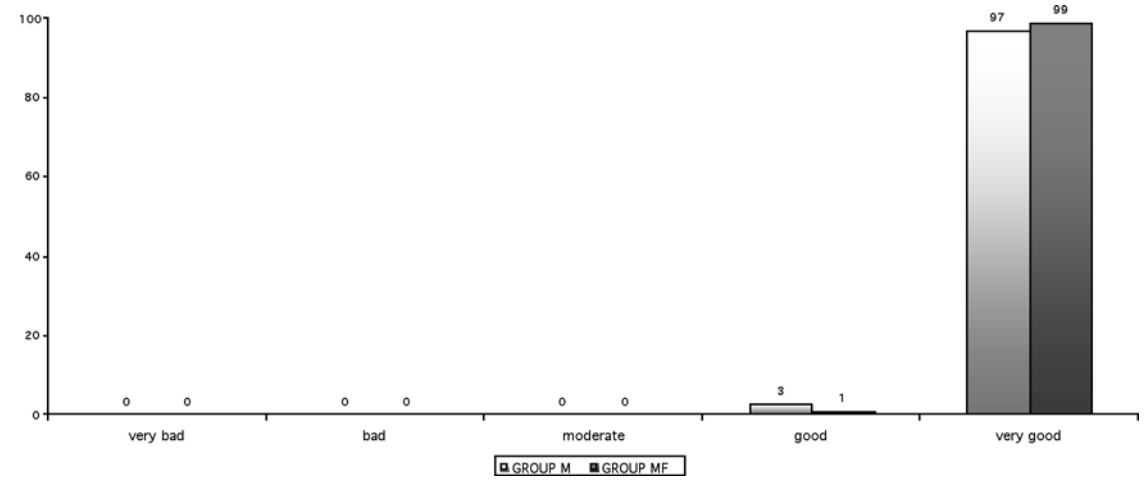

Fig. 2b. — Satisfaction profile of the surgeon, (%)

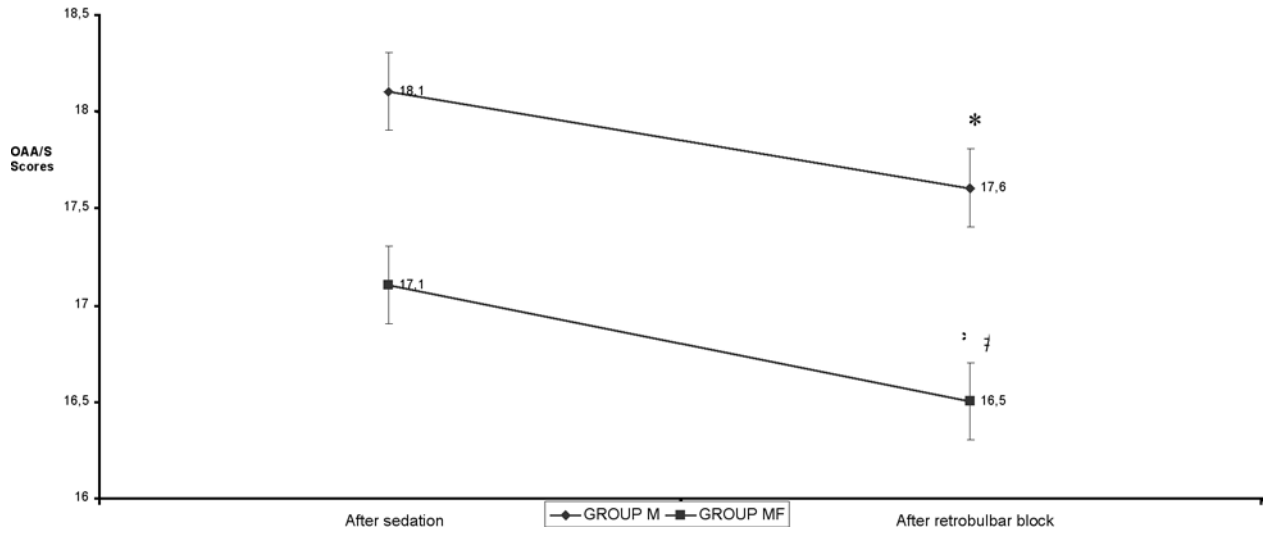

Fig. 3. — Observer assessment of alertness/sedation scores after sedation and retrobulbar block (* : $p < 0.05$ within group)

In conclusion, the addition of fentanyl to midazolam during regional anesthesia for cataract surgery did not result in a significant difference in sedation, pain relief, satisfaction or adverse events. Therefore the authors suggest that sedation with midazolam alone may be sufficient to provide optimal block conditions for this procedure.

References

1. Katz J., Feldman M. A., Bass E. B., *et al.*, *Study of Medical Testing for Cataract Surgery Study Team. Adverse intraoperative medical events and their association with anaesthesia management strategies in cataract surgery*, Ophthalmology, **108**, 1721-6, 2001.
2. Kumar C. M., Dodds C., *Ophthalmic regional block*, Ann. Acad. Med. Singapore, **35**, 158-10, 2006.
3. Avramov M. N., White P. F., *Methods for monitoring the level of sedation*, Crit. Care Clinics, **11**, 803-826, 1995.
4. Chernik D. A., Gillings D., Laine H., *et al.*, *Validity and reliability of the Observer's Assessment of Alertness/ Sedation Scale* : *Study with intravenous midazolam*, J. Clin. Psychopharm., **10**, 244-251, 1990.
5. Inan U. U., Sivaci R. G., Ermis S. S., Ozturk F., *Effects of fentanyl on pain and hemodynamic response after retrobulbar block in patients having phacoemulsification*, J. Cataract. Refract. Surg., **29**, 1137-42, 2003.
6. Boezaart A. P., Berry R. A., Nell M. L., van Dyk A. L., *A comparison of propofol and remifentanil for sedation and limitation of movement during periretrobulbar block*, J. Clin. Anesth., **13**, 422-6, 2001.
7. Friedman D. S., Reeves S. W., Bass E. B., *et al.*, *Patient preferences for anaesthesia management during cataract surgery*, Br. J. Ophthalmol., **88**, 333-5, 2004.
8. Reeves S. W., Friedman D. S., Fleisher L. A., *et al.*, *A decision analysis of anesthesia management for cataract surgery*, Am. J. Ophthalmol., **132**, 528-36, 2001.
9. Habib N. E., Mandour N. M., Balmer H. G., *Effect of midazolam on anxiety level and pain perception in cataract surgery with topical anesthesia*, J. Cataract. Refract. Surg., **30**, 437-43, 2004.
10. Colson J. D., *The pharmacology of sedation*, Pain Physician, **8**, 297-308, 2005.
11. Ben-Shiomo I., Abd-el-Khalem H., Ezry J., *et al.*, *Midazolam acts synergistically with fentanyl for induction of anesthesia*, Br. J. Anaesth., 64, 45-7, 1990.
12. Baris S., Karakaya D., Aykent R., *et al.*, *Comparison of midazolam with or without fentanyl for conscious sedation and hemodynamics in coronary angiography*, Can. J. Cardiol., **17**, 277-81, 2001.
13. Katz J., Feldman M. A., Bass E. B., *et al.*, *Injectable versus topical anesthesia for cataract surgery* : *patient perceptions of pain and side effects. The Study of Medical Testing for Cataract Surgery study team*, Ophthalmology, **107**, 2054-60, 2000.