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Low-dose oral clonidine as premedication before intraocular surgery in retrobulbar anesthesia

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PURPOSE. *We investigated whether low-dosed oral clonidine premedication before elective intraocular surgery in retrobulbar anesthesia is effective in terms of anxiolysis, sedation, stable hemodynamics, lower intraocular pressure and perioperative endocrine stress response.*
METHODS. *In a prospective, randomised, double-blind study, 44 patients scheduled for elective intraocular surgery received either 0.15 mg clonidine (n=22) or a matched placebo (n=22) orally 60 minutes before retrobulbar anesthesia. The main study parameters were sedation, anxiolysis, hemodynamics and intraocular pressure. Additionally, mediators of endocrine stress responses were measured five times, in 13 patients after clonidine and 12 after placebo.*
RESULTS. *After clonidine 86% of the patients showed sedation and after placebo 90.9% showed no sedation ($p<0.01$). Clonidine produced effective anxiolysis (Erlanger-Anxiety-Scale: 31.6 ± 2.6 points vs. 38.1 ± 8.5 points) before the operation ($p<0.01$).*
Systolic blood pressure was significantly lower after clonidine. Effects on mean and diastolic blood pressure were small but statistically significant. Norepinephrine and cortisole plasma concentrations were significantly lower after clonidine. Intraocular pressure was significantly lower too ($p<0.05$). No clinically relevant adverse effects were observed e.g. inappropriate sedation, hypotension (<100 mmHg), bradycardia (<50 bpm) or hypoxemia (SpO_2<90%).
CONCLUSIONS. *Oral low-dose clonidine produces light sedation, significant anxiolysis and stable hemodynamics, and attenuates the endocrine response to perioperative stress. Thus, clonidine seems sufficient to increase patient comfort for intraocular surgery and might even offer clinically worthwhile benefits such as stable hemodynamics and a reduced response to perioperative stress. (Eur J Ophthalmol 2000; 10: 248-56)*

KEY WORDS. *Clonidine, Intraocular surgery, Low dose, Oral premedication*

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INTRODUCTION

Success in ophthalmological microsurgery, especially during intraocular procedures, depends on optimal surgical conditions. Disturbances caused by agitated patients during surgery in local anesthesia, e.g. abrupt arousal, must be avoided to prevent damage to intraocular structures and potential vision loss (1).

The most common indications for ophthalmological surgery are cataracts and retinal detachments in the aged population. A large percentage of these patients already suffer from conditions such as diabetes, ischemic heart disease, hypertension and respiratory disorders (2). Combined with age-related physiological changes and often intensive and multiple drug therapy, these patients are particularly at risk of pe-

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rioperative complications (3).

Up to 80% of ophthalmological surgery is performed in local anesthesia (4). However, at least in Germany, the majority of these patients do not profit from perioperative anesthesiological management. Only patients at obvious high risk are referred to monitored anesthesia care. Thus, premedication is not routine, although it might be particularly beneficial for these patients. There are at least three reasons for this situation. First of all, ophthalmologists do not have routine experience with the sedative drugs used for premedication. Second, they are therefore not familiar with the adverse effects of these drugs and their treatment. Third, the ophthalmologist may not be informed about well-validated benefits of premedication.

We therefore set out to demonstrate that even a low-dose premedication regimen is sufficient to increase patient comfort for intraocular surgery by producing sedation and anxiolysis. We chose low-dose oral clonidine, on the basis that it might produce the following desirable premedication effects: sedation, anxiolysis, decrease in intraocular pressure, stable perioperative hemodynamics and some attenuation of the endocrine stress response (5-9).

MATERIALS AND METHODS

Patients

After approval of the study and obtaining written informed consent, we admitted 44 ASA-physical status I-III patients in this prospective, randomised, double-blind study. Patients scheduled for elective intraocular surgery in retrobulbar anesthesia (RBA) received either 0.15 mg clonidine (group I: n=2) or a matched placebo (group II: n=22) per os 60 minutes before retrobulbar block. Clonidine and placebo tablets were identical in shape, size and colour and coded corresponding to the allocation schedule, with the unopened code being retained by the principle investigator. The dosage was chosen after preliminary trials with higher doses of clonidine (0.3-0.45 mg), which corresponds to a recommended dose of about 5 µg/kg as reported by Ghignone and Kumar (10, 11). However, in our elderly patients, doses of 0.3 mg and more produced undesired deep and prolonged sedation and pronunced cardiovascular effects, as in previous reports (12-14). Thirteen patients in group I and 13 in group II (one sample was lost in processing) were randomly assigned to analysis of the endocrine parameters, which could only be done in 13 patients because of restricted finances (Tab. I).

Monitoring

All patients were fitted with an 18-gauge venous line, preferably in a large cubital vein, for crystalloid infusion. After oral premedication, patients were monitored with a three-lead ECG, non-invasive blood pressure measurements (NIBP) and pulse-oximetry, using (a Dinamap) instrument, throughout the observation period. During the operation, patients received fresh air at 5 L per minute through a nasal tube.

Inclusion/exclusion criteria

Co-operative ASA-class I-III patients were admitted to the study after giving informed written consent. Patients had to be scheduled for the RBA between 7.30 and 8.30 a.m.

Patients were not included if they had recent therapy with clonidine, known endocrinological disorders (with the exception of diabetes), a history of psychodrug medication, sick sinus syndrome or history of severe arrhythmic disorders as contraindications to clonidine.

Sedation

Sedation was assessed 45 minutes after premedication, using a modified rating-sclae, as previously described by Kumar et al (1992) (11) (Tab. II).

Perioperative anxiety

Trait-anxiety was measured with the Spielberger State-Trait-Anxiety-Inventory (STAI-X2) (1972) one day before the operation (15). There were no patients with abnormally high scores (>50 points), indicating an anxiety disorder. Situative anxiety was studied with the Erlanger Anxiety Scale (EAS), a validated instrument for assessing situative anxiety (16). Perioperative situative anxiety was measured at five time points: before premedication (bPM), 30 minutes after premed-

ication (30"aPM), before RBA (bRBA) and 45 minutes after the end of the operation (45"aOP).

Intraocular pressure

Intraocular pressure (IOP) was measured by Goldmann applanation-tonometry, at five times: preoperative evening, before premedication, before RBA, 10 minutes after RBA and 45 minutes after the operation.

Hemodynamics

Systolic, diastolic and mean blood pressure, heart rate and pulse-oximetry were automatically recorded and analysed at the following times: 5 minutes before premedication (5PM), 15, 30 and 45 minutes after premedication (PM 15,30,45), 5 minutes before RBA (5RBA), 1-5 minutes after RBA (RBA1-5), 10, 15, 20 minutes after RBA (RBA 10, 15, 20), 5 minutes before incision (5OPI), 2 and 15 minutes after incision (OP12, 15) and 240 minutes after the operation (OP240).

Endocrine parameters

Endocrinological analyses focused on the main mediators of the endocrine stress response: adrenocorticotropic hormone (ACTH), somatotropic hormone (STH), cortisol and the catecholamines epinephrine, norepinephrine and dopamine. To standardise the influence of the circadian endocrine rhythm of secretion, only patients receiving RBA between 7.30 and 8.30 a.m. were included. The hormones were determined at five time points: 5 minutes before premedication (5PM), 5 minutes before RBA (5RBA), 2 minutes after RBA (RBA2), 5 minutes before incision (5OP) and 60 minutes after surgery (OP60). Blood samples were drawn from a venous access (minimum 16 gauge), placed in a large cubital or antecubital vein after warming the arm to "arterialise" the sample. Samples for STH, ACTH and cortisol were collected in EDTA tubes (Sarstedt, Germany). Catecholamine samples were collected into pre-cooled sodium-heparinate tubes (Sarstedt, Germany). The tubes were immediately cooled in ice-water and centrifuged at once. Plasma was then stored at –20°C until analysis. ACTH, STH and cortisol plasma concentrations were determined by radioimmunoassays. The catecholamines were separated by high pressure liquid chromatography (HPLC). Their concentrations then were determined by electrochemical detection (ED) (17). All measurements were done twice to enhance accuracy.

Retrobulbar anesthesia

After including akinesia of the eyelid using the O'Brien technique with articaine 2% (Ultracain®), the retrobulbar block was administered using a 21G needle (Sterican® Nr. 2, B. Braun, Melsungen, Germany) with 4.5 ml of a standardised solution of bupivacaine 0.75% (Carbostesin®) and articaine 2%, 1:1, with addition of 0.05 ml naphazolinenitrate (Privine®) per ml of solution. Oculopressure (Vörösmarthy-Oculopressor®, Storz, Germany) of 40 mmHg was then applied for 10 minutes.

Statistical analysis

A blocked randomisation procedure was used to assign the patients to group I or II. In each group 13 patients were randomised to participate in the endocrine analyses. Statistical analysis was done using the SPSS® statistical software. Normal distribution was tested with the Kolmogoroff-Smirnoff test. Data not normally distributed were transformed (log x) and retested for normal distibution. Normally distributed data were then analysed with a two-way analysis of variance for repeated measurements. For significant results the Scheffé test was performed.

Data that were not normally distributed were then analysed by the Kruskal-Wallis H-test, and a pairwise comparison was done with the Mann-Whitney U test. For repeated analyses an α-adjustment was made, according to the Bonferoni rule. For all tests α was set at 5%.

RESULTS

Biometric data and baseline values for hemodynamic variables and endocrine parameters showed no significant differences in both groups (Tab. I).

Sedation

After placebo 20 patients (90.9%) showed no sedation, 2 (9.1%) light sedation and none deeper sedation (Tab. II). Clonidine induced sedation in 19 patients (86.4%, $p<0.05$), and no sedation in 3 (13.6%). No inappropriate deep sedation was observed with clonidine (Tab. II).

Perioperative anxiety

There were no significant differences between the groups concerning trait-anxiety (STAI-X2: clonidine: 26.6 ± 4.7 points, placebo: 28.3 ± 7.4 points). Situative anxiety did not differ before premedication. After clonidine, situative anxiety was reduced, whereas it increased after placebo. Just before the operation, situative anxiety was signifciantly lower in the clonidine group (EAS score: 31.6 ± 2.6 points, $p<0.01$) than with placebo (EAS score: 38.1 ± 8.5 points). For both groups, the scores for sitautive anxiety were lowest after the operation (Fig. 1).

Intraocular pressure

Initial IOP, IOP before premedication and before RBA did not differ in the two groups. A significant reduction of IOP was found with clonidine 10 minutes after RBA and 45 minutes after the operation (13.8 ± 2.4 vs; 14.9 ± 1.6 mmHg, 13.4 ± 3.3 vs. 14.9 ± 1.4 mmHg, $p < 0.05$).

Hemodynamics

A significant reduction of systolic BP ($p<0.01$) was observed with clonidine. Excluding the values immediately after RBA, which did not differ significantly, systolic BP after clonidine was significantly lower than with placebo throughout the entire observation period, up to 4 hours postoperatively. Systolic BP after clonidine remained below baseline at all times, whereas with placebo it rose considerably above baseline (Fig. 2). The baseline mean arterial pressure (MAP) was higher, though not significantly, in the clonidine group. After premedication, MAP decreased to values comparable to the placebo group. The decrease in MAP after clonidine reached statistical significance for RBA15, RBA20, 50P and OP15 ($p<0.05$).

No real difference was observed for diastolic blood pressure (DBP), except at 4 hours after the operation, when it was significantly lower after clonidine (Tab. III). Heart rate and pulse-oxymetric oxygen saturation (Tab. III) were not different. No clinically relevant adverse effects were observed using the following definitions: bradycardia (<50 bpm), hypotonia (systolic BP <100 mmHg) or hypoxemia (SpO_2 <90%).

Endocrinological parameters

Before premedication, the endocrine parameters were within normal ranges for both groups. Biometric data were similar in all endocrinological subgroups. The values for STH, ACTH and cortisol are seen in Table IV. STH showed extreme intraindividual and interindividual variability, but no sig-

TABLE I – PATIENTS' CHARACTERISTICS, CONCOMITANT DISEASES AND SURGICAL PROCEDURES (mean ± SD)

Patients' characteristics	Group I: Clonidine (n=22)	Gorup II: Placebo (n=22)
Age (yrs)	66.6 ± 10.8	69.4 ± 7.9
Height (cm)	169.4 ± 10.6	163.4 ± 4.6
Male/female	14/8	16/6
Weight (kg)	76.4 ± 11.4	71.6 ± 8.9
ASA: I/II/III	1/8/13	0/10/12
Concomitant diseases		
Diabetes mellitus	7	7
Hypertension	11	13
COPD	1	1
Congestive heart failure	4	7
Arhythmias	3	9
Ischemic heart disease	7	11
Surgical procedures		
ECCE & PCL	4	7
Phaco & PCL	12	12
Others	6	3

ECCE: extracapsular cataract extraction; Phaco: phaco-emulsification, PCL: posterior chamber lens

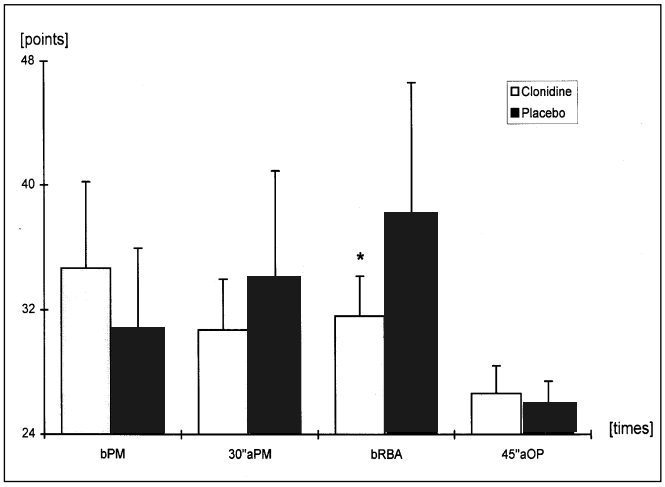

Fig. 1 – *Erlanger-Anxiety-Scale scores for perioperative situative anxiety before premedication (bPM), 30 minutes after premedication (30" aPM), before retrobulbar anesthesia (bRBA) and 45 minutes after the end of the operation (45" aOP) (mean ± SD, *: p<0.01).*

nificant differences. Baseline ACTH was similar. Surprisingly in both groups ACTH before and after RBA was significantly higher than 60 minutes after the operation ($p<0.01$). For both groups, plasma peaks were seen immediately after RBA. The plasma ACTH peak after placebo was considerably higher than after clonidine (Tab. IV). Intraoperative plasma cortisol gradually decreased in both groups, with a plasma peak 60 minutes after the operation (Fig. 3). The peak concentration was lower after clonidine ($p<0.05$). For the catecholamines see Table IV and Figure 4. There were no significant differences for plasma epinephrine, both groups showing peaks 2 minutes after RBA, but the peak after placebo was higher. In both groups epinephrine was lowest 60 minutes after the operation. Baseline norepinephrine was comparable for both groups. After clonidine, all norepinephrine concentrations were significantly lower than after placebo ($p<0.05$).

With placebo were neorepinephrine concentrations highest after RBA and with clonidine the highest were prior to premedication. The results for dopamine and STH showed tremendous variability, with no significant differences.

DISCUSSION

The effects of clonidine are amply described and validated in the anesthesiological literature. However, doses of about 5 µg/kg are usually used, with a view to the complete suppression of perioperative responses to stress, or stabilisation of hemodyanmics during major surgery (7, 18-21). For premedication, higher doses have also been used, but on considerably younger groups. At doses of 4-6 µg/kg clonidine has been reported to produce sedation and anxiolysis, stabilisation of perioperative hemodynamics and suppression of the perioperative stress reaction (19, 20-26). Kumar et al (1992) already suggested that age might be a limiting factor for the use of oral clonidine and that dosage adjustments may be required for the aged population to minimise adverse cardiovascular effects (11). Our aim was to show that even low-dose clonidine has beneficial effects in the elderly ophthalmological patient, and the probability of adverse effects is less than with higher doses (12-14).

The sedative effect of clonidine doses of 3-5 µg/kg is widely validated. Adequate sedation levels after 0.15-0.3 mg oral clonidine were shown by Filos et al (1993)

TABLE II – ASSESSMENT OF SEDATION WITH CLONIDINE AND PLACEBO. RATING SCALE, CRITERIA, SCORES AND STATISTICAL DIFFERENCES

Score	Sedation	Rating criteria	Clonidine (n=22)	Placebo (n=22)
0	None	Patient awake and talkative	3	20 +
I	Light	Awake but uncommunicative	13 +	2
II	Moderate	Quiet, drowsy and easily arousable upon call	6 +	0
III	Deep	Asleep and only arousable upon tactile stimuli	0	0
IV	Very deep	Hardly arousable	0	0

+, $p<0.05$

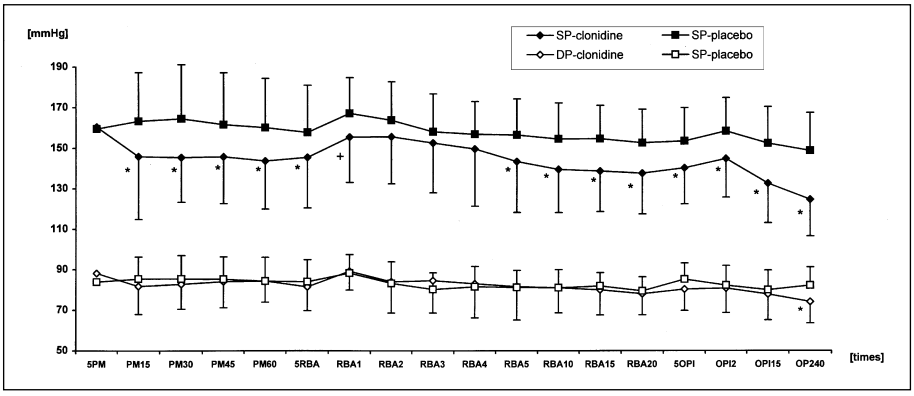

Fig. 2 - *Systolic (SP) and diastolic (DP) blood pressure after clonidine and placebo 5 minutes before premedication (5PM), 15, 30 and 45 minutes after premedication (PM 15, 30, 45), 5 minutes before RBA (5RBA), 1-5 minutes after RBA (RBA1-5), 10, 15, 20 minutes after RBA (RBA 10, 15, 20), 5 minutes before incision (5OPI), 2 and 15 minutes after incision (OP12, 15) and 240 minutes after the operation (OP240). Results (mean ± SD) and significance of differences between groups (Scheffé-Test; *: p<0.01, +: p<0.05).*

TABLE III - MEAN BLOOD PRESSURE, HEART RATE AND PULSE-OXYMETRIC OXYGEN SATURATION (mean ± SD) FIVE MINUTES BEFORE PREMEDICATION (5PM), 15, 30 AND 45 MINUTES AFTER PREMEDICATION (PM 15, 30, 45), 5 MINUTES BEFORE RBA (5RBA), 1-5 MINUTES AFTER RBA (RBA 1-5), 10, 15, 20 MINUTES AFTER RBA (RBA 10, 15, 20), 5 MINUTES BEFORE INCISION (5OPI), 2 AND 15 MINUTES AFTER INCISION (OPI2, 15) AND 240 MINUTES AFTER THE OPERATION (OP240)

	Mean blood pressure (mmHg)		Heart rate (bpm)		Pulse-oxymetric O2 Saturation	
	Placebo	Clonidine	Placebo	Clonidine	Placebo	Clonidine
5PM	100.1 ± 17.1	112.4 ± 17.4	69.8 ± 11.5	75.5 ± 12.7	97.5 ± 1.0	96.9 ± 1.3
PM15	103.0 ± 16.0	111.9 ± 14.4	69.9 ± 11.5	72.2 ± 11.7	97.0 ± 1.1	96.9 ± 1.3
PM30	105.4 ± 18.2	109.8 ± 14.0	70.4 ± 11.3	72.0 ± 11.1	96.6 ± 1.8	96.6 ± 1.4
PM45	105.5 ± 17.8	107.9 ± 14.5	72.8 ± 13.1	71.9 ± 10.3	96.8 ± 1.9	96.8 ± 1.5
PM60	105.2 ± 17.7	104.8 ± 15.1	72.5 ± 15.2	73.8 ± 12.5	96.6 ± 1.3	96.7 ± 1.3
5RBA	104.2 ± 12.1	101.0 ± 13.5	74.5 ± 16.6	75.7 ± 12.9	96.4 ± 1.8	96.5 ± 1.4
RBA1	108.3 ± 13.9	109.5 ± 20.7	75.6 ± 15.9	78.2 ± 12.9	96.1 ± 2.3	96.4 ± 1.7
RBA2	106.0 ± 11.7	102.6 ± 15.9	74.6 ± 16.4	74.7 ± 13.0	96.1 ± 1.3	96.4 ± 1.5
RBA3	100.8 ± 14.2	105.3 ± 22.3	73.3 ± 16.5	74.0 ± 13.5	96.5 ± 1.6	96.2 ± 2.1
RBA4	101.1 ± 12.9	105.3 ± 23.4	72.8 ± 16.7	73.6 ± 14.0	96.3 ± 1.5	96.3 ± 1.7
RBA5	101.9 ± 11.8	103.4 ± 20.0	72.5 ± 16.4	72.8 ± 12.3	96.0 ± 1.8	96.0 ± 2.0
RBA10	100.7 ± 14.7	98.4 ± 13.5	72.3 ± 14.2	72.5 ± 11.5	95.7 ± 2.1	96.4 ± 1.9
RBA15	101.5 ± 12.2	98.9 ± 11.4+	72.7 ± 16.0	71.5 ± 11.0	96.6 ± 2.0	96.3 ± 1.8
RBA20	101.6 ± 15.5	97.9 ± 13.8+	72.4 ± 15.4	70.1 ± 11.6	96.2 ± 1.5	96.3 ± 1.6
5OPI	107.6 ± 12.0	99.1 ± 15.9+	71.4 ± 14.7	71.0 ± 11.0	95.5 ± 2.1	96.5 ± 1.6
OPI2	104.4 ± 10.2	99.8 ± 14.2	71.9 ± 14.5	72.5 ± 11.4	85.4 ± 2.0	96.1 ± 1.7
OPI15	100.5 ± 11.4	94.4 ± 12.5+	69.9 ± 15.2	69.7 ± 11.7	95.5 ± 2.3	96.0 ± 1.8
OP240	97.6 ± 15.0	95.4 ± 12.9	72.2 ± 13.7	71.4 ± 9.0	97.0 ± 1.2	97.0 ± 1.3

(Scheffé-Test*: p<0.01, +: p<0.05)

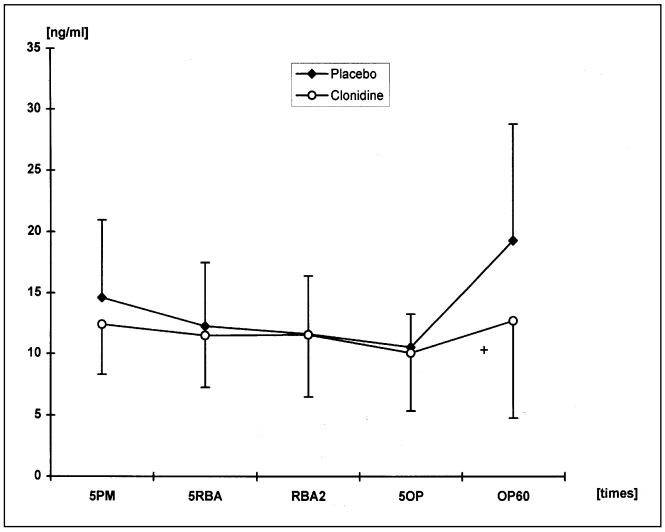

Fig. 3 - *Cortisol plasma concentrations (mean ± SD) 5 minutes before premedication (5PM), 5 minutes before RBA (5 RBA), 2 minutes after RBA (RBA2), 5 minutes before incision (5OP) and 60 minutes after surgery (OP60), and significant differences (+: p<0.05).*

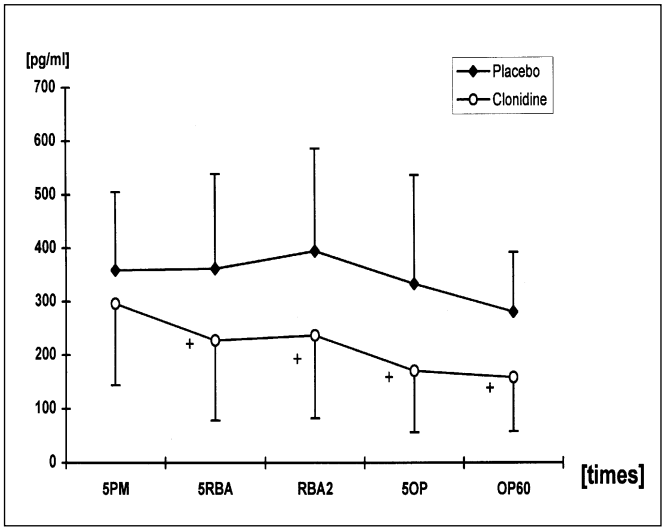

Fig. 4 - *Norepinephrine plasma concentrations (mean ± SD) 5 minutes before premedication (5PM), 5 minutes before RBA (5RBA), 2 minutes after RBA (RBA2), 5 minutes before incision (5OP) and 60 minutes after surgery (OP60), and significant differences (+: p<0.05).*

and Laurito et al (1991) (12, 22). Filos et al also investigated an aged population and confirm our unpublished observations that 0.3 mg clonidine may cause too deep sedation in these patients; those authors report that this dosage produced prolonged sedation, for up to six hours postoperatively. Our findings confirm the sedative effect of 0.15 mg oral clonidine.

There are only few studies of the anxiolytic effect of clonidine. Although they all describe an anxiolytic effect, the methods were either descriptive or were based on visual analogue scales (VAS) (11). There are well-validated psychological instruments to assess both trait and state-anxiety and these can be considered more sensitive and specific for assessing anxiety. Our results suggest there is a significant reduction in situative anxiety in patients given clonidine rather than placebo. Our data agree with a psychiatric study by Mizuki et al (1996), who found significant anxiolysis after 0.15 mg of clonidine using the state-trait-inventory (STAI-X1) for state anxiety (26).

The use of clonidine in ophthalmology for the treatment of glaucoma has been discontinued now that

TABLE IV – PLASMA CONCENTRATIONS OF ACTH, STH, EPINEPHRINE AND DOPAMINE (mean ± SD) 5 MINUTES BEFORE PREMEDICATION (5PM), 5 MINUTES BEFORE RBA (5RBA), 2 MINUTES AFTER RBA (RBA2), 5 MINUTES BEFORE INCISION (5OP) AND 60 MINUTES AFTER SURGERY (OP60)

	ACTH (pg/ml)		STH (ng/ml)		Epinephrine (pg/ml)		Dopamine (pg/ml)	
Time	**Placebo**	**Clonidine**	**Placebo**	**Clonidine**	**Placebo**	**Clonidine**	**Placebo**	**Clonidine**
5PM	25.18 ± 11.73	22.35 ± 12.35	1.50 ± 2.25	0.72 ± 0.71	48.0 ± 23.6	59.1 ± 37.9	43.4 ± 32.2	74.5 ± 47.8
5RBA	20.81 ± 10.47	21.85 ± 13.86	0.98 ± 1.10	1.90 ± 3.36	63.3 ± 28.4	58.0 ± 29.4	50.7 ± 38.8	54.1 ± 39.5
RBA2	40.45 ± 33.17	28.42 ± 27.43	2.00 ± 3.01	1.99 ± 3.71	112.0 ± 133.9	97.8 ± 76.3	43.3 ± 26.8	73.3 ± 48.3
5OP	16.27 ± 5.02	14.57 ± 7.61	2.16 ± 3.12	1.96 ± 3.87	66.0 ± 42.2	62.5 ± 35.8	78.9 ± 102.4	62.4 ± 89.1
OP60	9.81 ± 5.21	11.00 ± 4.83	1.76 ± 1.66	1.61 ± 1.74	46.3 ± 21.1	33.4 ± 14.2	36.8 ± 29.4	52.1 ± 37.0

more specific adrenergic agonists have been developed, such as apraclonidine or brimonidine. Clonidine at a dose of 0.5 mg/kg, given as an oral premedication before intraocular surgery, significantly lowered IOP, as reported by Ghignone et al (1988), Kumar et al (1992) and Filos et al (1993). In general anesthesia doses of 4-6 µg/ml even suppressed the rise in IOP after laryngoscopy and intubation. However, with 0.15 mg clonidine only Filos et al (1993) have so far reported a significant reduction in IOP confirmed by our results.

The hemodynamic effects of 4-6 mg/kg clonidine are amply validated in the literature. Indications in anesthesiological management range from perioperative stabilization of hemodynamics to use as an adjunct in deliberate hypotension. For intraocular surgery, transient increases in BP must be avoided, to prevent expulsive hemorrhage. Previous studies in ophthalmological patients using clonidine 0.3 mg did not report clinically relevant hypotension. However, Ghignone et al used a well-defined anesthesiological algorithm for BP management, whereas Kumar et al do not give details of how BP was controlled; Filos et al showed that more than 30% of their patients required at least one treatment for hypotension after 0.3 mg clonidine. Wright et al (1990) and Carabine et al (1991) reported that intraoperative and postoperative hypotension was common after 0.3 mg clonidine (13, 14). There is growing evidence, however, that 0.15 mg clonidine does not induce clinically relevant hypotension, despite its significant effect on systolic BP (12, 18).

Clonidine's ability to blunt the perioperative response to major surgical stress intra- and postoperatively has been studied widely. Clonidine 4-6 µg/kg suppressed the main mediators of the endocrine stress response (5, 6, 18-20, 23) but so far there are no reports about lower doses. The present results suggest a dose-related effect on the endocrine response. At higher doses, suppression is almost complete, with a significant reduction in epinephrine and norepinephrine plasma levels. Only plasma norepinephrine was significantly attenuated and this is known to be a direct effect of clonidine. However, in respect to the cardiovascular effects of norepinephrine, this might be beneficial, especially among the elderly, who often suffer from cardiovascular disease. The suppression of the postoperative cortisol peak after clonidine suggests a prolonged positive effect well into the postoperative period.

In conclusion, 0.15 mg clonidine before intraocular surgery produces adequate sedation and anxiolysis, lowers intraocular pressure, moderately influences hemodyanmics and attenuated the perioperative endocrine response to stress. Thus, low-dose oral clonidine may be useful for premedication before intraocular surgery in local anesthesia.

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