Topical Proxymetacaine Eyedrops in Fluorescein Angiography: A Randomized, Double-blind Placebo-Controlled Trial

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ABSTRACT

Background and Aims: Proxymetacaine eye drops are known to reduce subjects' blink rates[1] and are well tolerated compared with other topical anesthetic eye drops.[2,3] A randomized, controlled trial was performed to assess their routine use in fluorescein angiography, investigating their effect on patient comfort and image quality.

Methods: One hundred patients undergoing routine fluorescein angiography were randomized to receive either proxymetacaine (0.5%) or saline eye drops to both eyes. The degree of comfort of the patient and any stinging sensation induced by the eye drops were recorded, as were the photographer's independent assessment of image quality and overall procedural ease (using standardized linear analog scales). Requests made to hold the patient's eyelids open were also noted.

Results: The patients' comfort score data were not normally distributed and were negatively skewed. The comfort scores of the proxymetacaine group were significantly higher than those of the control group (proxymetacaine group: n = 50, median score 9; control group: n = 48, median 8; Mann-Whitney U test = 925, P = .044). Proxymetacaine had no significant effect on the photographer's scores for image quality and overall ease of procedure, or on the requests for eyelids to be held open.

Conclusion: Although proxymetacaine use was associated with a significantly higher comfort score than in the control group, it is difficult to recommend routine use of proxymetacaine in fluorescein angiography because most patients in both groups found the procedure very tolerable. Moreover, proxymetacaine use did not significantly improve the overall ease of the procedure or the image quality, as judged by the photographer.

INTRODUCTION

Fluorescein angiography is an investigation

Table 1. Demographic Details of the Patients.

Patient characteristics	Proxymetacaine group	Saline control group
Mean age (standard deviation)	75 (9.2)	70 (13.8)
Median age	76	75
Sex		
Male	18	26
Female	32	24
Diagnoses:		
Exudative macular degeneration	9	13
Atrophic macular degeneration	11	16
Diabetic-related disease	2	6
Retinal vein occlusion	11	7
Cystoid macular edema	3	0
Normal	5	3
Other	9	4

routinely performed in the diagnosis and management of retinal disease. A fluorescein angiogram can be quite an uncomfortable procedure for a patient to undergo—staring into the brightly illuminated lens of a camera for long periods of time can be difficult and may lead to loss of fixation, excessive blinking, poor image quality, and discomfort.

It was hypothesized that a proportion of the discomfort induced by trying not to blink for prolonged periods of time could be alleviated by the use of topical anesthetic eye drops. Subjects' blink rates are significantly lower following the administration of proxymetacaine (a benzoate ester) eyedrops.[1] By improving patient comfort, increased cooperation might lead to better fixation, improved photographs, and less need for intervention from a third party to hold patients' eyelids open during the procedure.

We conducted a prospective randomized, double-blind, placebo-controlled trial of 100 patients undergoing digital fluorescein angiography in our department. Proxymetacaine was chosen as the topical anesthetic agent due to its propensity to cause less stinging and ocular irritation than other topical agents,[2,3] and its documented lower blink rate in healthy volunteers.[1]

MATERIALS AND METHODS

Patients attending the department for routine digital fluorescein angiography were issued an information sheet regarding the procedure and the proposed trial. When satisfied with the information and provided that they were competent to consent, 100 consecutive patients were recruited into the study. Demographic details including their age, sex, and final diagnosis (after angiography) were recorded. Exclusion criteria included: allergy to proxymetacaine or fluorescein, functionally monocular patients, corneal conditions leading to reduced ocular surface sensation, and prior inclusion in the study. If patients were unable to read (due to cycloplegia or coexistent eye disease), they were only included in the study if an accompanying friend or relative was able to read the information sheet and post-procedure questionnaire to the patient.

After their pupils had been dilated with tropicamide (1%) and phenylephrine (2.5%), patients were then randomized to receive either: (i) a drop (50 μL) of proxymetacaine (0.5%) MINIMS to both eyes; or (ii) a drop of normal saline MINIMS to both eyes; immediately preceding angiography. The type of drops administered was concealed by code from the investigators, photographer, and patients. Patients were

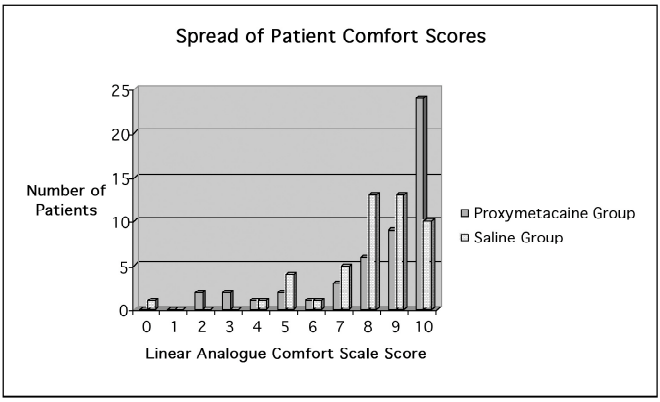

Figure 1. Distribution of patients' comfort scores.

specifically instructed not to discuss with the photographer any ocular sensation experienced.

Digital photography and angiography then proceeded routinely. After the end of each session, both the photographer and patient were questioned separately, through the use of written questionnaires. The patients were asked to rate their overall comfort during the procedure, using a standardized linear analogue scale from 0 (unbearable or intolerable) to 10 (no problems or very tolerable). They also recorded whether they found that the eye drops: (i) did not sting; (ii) stung a little; or (iii) stung a lot; upon administration. The photographer was asked to rate on standardized linear analogue scales from 0 (appalling) to 10 (excellent): (i) his overall satisfaction with the photographic result (given the ocular media of the patient); and (ii) the overall ease of the procedure and the patient's compliance. The photographer, patient, and supervising investigator all noted whether a request was made by the photographer to hold the patient's eyelids open during the procedure.

After completion of the study, the code was broken and results for each patient collated using Microsoft Access software. Statistical analysis was then performed using nonparametric techniques in consultation with a professional medical statistician.

RESULTS

The study was completed over a period of 5 months. A total of 100 patients were recruited into the study, with 50 patients in both the study and control groups. Two patients withdrew from the study, one during the procedure and one after the procedure was completed; both of these patients had received saline eye drops rather than proxymetacaine. The demographic details of the 100 patients are summarized in Table 1.

Figure 1 shows the distribution of the patients' comfort scores. The comfort scores of the patients were not normally distributed and had a negative skew, suggesting that more patients found the proce-

Table 2. The Stinging Sensations Produced by Saline and Proxymetacaine

Stinging sensation	Proxymetacaine (n = 50)	Saline control group (n = 48)
"None"	17	27
"A little"	30	21
"A lot"	3	0

Table 3. The Effect of Proxymetacaine on Requests for Holding Eyelids Open.

	Proxymetacaine (n = 50)	Saline (n = 49)
Lids held open	20	17
Lids not held open	30	32

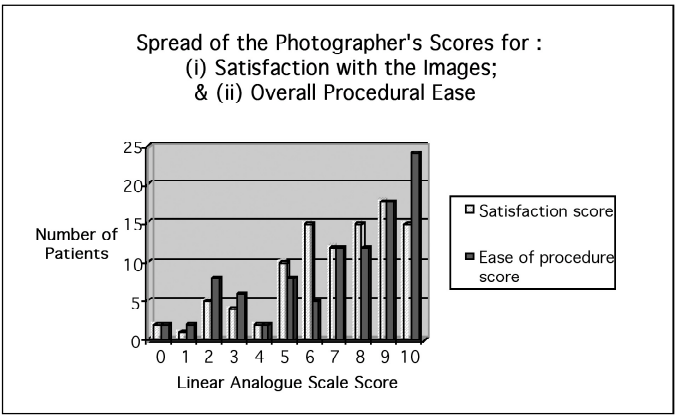

Figure 2. Distribution of photographer's scores.

dure tolerable than not. As one might expect, patients who had their lids held open supplied a lower comfort score (median score 8) than those who did not have their lids held open (median 9). There was a statistical difference in patient comfort scores between the proxymetacaine group and the control group (proxymetacaine group: n = 50, median = 9, lower quartile = 8.00, upper quartile = 10.00; saline group: n = 48, median = 8, lower quartile = 7.25, upper quartile = 9.00; Mann-Whitney *U* test = 925, *P* = .044).

Table 2 shows the results of the patients' questionnaire pertaining to the stinging sensation induced by the eye drops. For the purposes of statistical analysis, due to insufficient data in the third row (Table 2), it was necessary to regroup the data into "none" versus "a little" or "a lot". There was evidence to suggest an association between proxymetacaine use and an increased level of stinging sensation (χ^2 test with Yates correction = 0.4901, *P* = .044). Table 3 shows the effect of proxymetacaine eye drops on the number of requests made by the photographer to hold patients' eyelids open during the procedure. There was no evidence of an association between requests for eyelids to be held open and proxymetacaine use (χ^2 test with Yates correction = 0.114, *P* = .735). In patients whose eyelids were held open, there was no evidence that there was a significant difference in comfort according to the use of proxymetacaine or saline (Mann-Whitney *U* test=145.5, *P* = .325).

The distribution of the photographer's scores for: (i) his overall satisfaction with the photographic result; and (ii) the overall ease of the procedure and the patient's compliance; are shown in Figure 2. The data were not normally distributed. There was no evidence to suggest a difference in the photographer's score for his satisfaction with the photographic result (Mann-Whitney *U* test = 1144.5, *P* =.569), or in his score for the overall ease of the procedure (Mann-Whitney *U* test = 1155, *P* = .620), according to the use of proxymetacaine or saline.

DISCUSSION

Most patients who took part in the study found that fluorescein angiography was a tolerable procedure. However, proxymetacaine eye drops, the most tolerated widely available topical anesthetic,[2,3] with a documented lower blink rate than saline eyedrops,[1] were accorded a significantly higher comfort score than saline eye drops in this study. This is despite the finding that proxymetacaine was associated with significantly more stinging than saline, which might actually have led patients in this group to attribute a lower comfort score to the procedure as a whole, possibly introducing an element of negative bias.

Although there are numerous studies concerning the comparison of different topical anesthetics in terms of tolerability and efficacy,[3] there is little literature concerning their use in practical, nonsurgical situations, for example, in fluorescein angiography. In a different ophthalmological setting, Saunders et al compared the use of proxymetacaine and saline eyedrops on infant

stress during routine eye examinations for retinopathy of prematurity.[4] In their study, however, it was found that proxymetacaine offered no advantage over normal saline eyedrops during such examinations.

Proxymetacaine eyedrops did not lead to improved photographic images, as judged by the photographer. Although patients' blink rates might have been lower in the proxymetacaine group, it is certainly possible that increased breakup of the tear film induced by the topical anesthetic led to a reduction in image quality. Unfortunately, technical restraints meant that accurate measurements of both blink rate and tear film breakup time were not possible in this study.

CONCLUSION

Proxymetacaine use was associated with improved patient comfort during fluorescein angiography, although image quality and overall procedural ease were not significantly affected. Patients in both study and control groups found the procedure very tolerable on the whole. It is therefore difficult to justify recommending the routine use of proxymetacaine eyedrops in this procedure, however, they might have a useful role in individual patients who would otherwise struggle to participate.

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