A comparative study of proxymetacaine-fluorescein and lignocaine-fluorescein use during applanation tonometry

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Abstract

***Aims*—To evaluate the relative merits of proxymetacaine-fluorescein (PROX-FLU) and lignocaine-fluorescein (LIG-FLU) when used to perform applanation tonometry.**

***Methods*—This prospective, masked, double blind study assessed several aspects of the tonometry process—the duration of the stinging sensation and degree of discomfort, the extent of reflex lacrimation induced, the need for subsequent tear film manipulation to ensure an accurate tonometry reading, and total time to complete tonometry—for each preparation.**

***Results*—PROX-FLU caused significantly less discomfort and reflex lacrimation than LIG-FLU and accurate tonometry was more rapidly completed when it was used. PROX-FLU was preferred by 98% of the study patients.**

***Conclusion*—PROX-FLU is a well tolerated and useful alternative to the more widely used LIG-FLU mixture.**

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Applanation tonometry as describes by Goldmann and Schmidt[1] is generally regarded as the most accurate method of measuring intraocular pressure (IOP) in clinical practice and the technique requires instillation of a combination of topical anaesthetic and fluorescein, the latter to outline and make clearly visible to the observer the area of cornea applanated by the split prism tonometer head. The thickness and brightness of the resultant fluorecent tear meniscus govern the accuracy of IOP measurement.[2]

The ideal thickness of the visible fluorescein ring is about one quarter of the radius of the applanated area (0.4 mm) as shown in the Goldmann tonometer manual.[3] If the meniscus is too thin the IOP will tend to be underestimated[4] and too thick a meniscus will lead to overestimation of IOP—by about 2 mm Hg if the meniscus is 2 mm wide, and by up to 4.6 mm Hg in some eyes.[1] Underestimation of IOP may ensue if the fluorescein concentration in the meniscus is too low.[5]

A fixed dose combination of lignocaine and fluorescein in Minim form (Chauvin Pharmaceuticals) appears to be the most widely used agent for applanation tonometry . However, this agent often causes significant stinging discomfort and blepharospasm which may hamper and prolong the tonometry procedure. Reflex lacrimation may produce an excessively thick and/or dilute fluorescent tear meniscus leading to errors in IOP measurement.

Several studies have shown that proxymetacaine is generally better tolerated than other topical anaesthetic agents[6 7] and the aim of our study was to evaluate potential benefits of its use during tonometry compared to the more widely used lignocaine in terms of patient comfort, reflex lacrimation, time to complete the procedure, and patient preference.

Materials and methods

This randomised, masked, double blind, prospective study involved a sample of 60 consecutive suitable patients attending the ophthalmic outpatient department and requiring tonometry. Exclusion criteria were ophthalmic conditions likely to alter corneal sensation, ocular inflammatory conditions, infections, and use of any topical ophthalmic medication. The majority of patients were asymptomatic ocular hypertensives or glaucoma suspects on no treatment. Informed consent was obtained from participating patients.

Proxymetacaine 0.5% w/v with fluorescein 0.25% w/v (PROX-FLU) and lignocaine 4% w/v with fluorescein 0.25% w/v (LIG-FLU) eye drops in unit dose applicators (Minims, Chauvin Pharmaceuticals) were used for the study and contents of several minims of each combination were placed in separate sterile white unmarked dropper bottles. Each mixture was randomly assigned the letter "A" or "B" by an independent person and the assignment was unknown to the researchers until completion of the study. The study was performed during consecutive outpatient clinics on 5 different days and fresh preparations of drops were prepared each day to avoid potential contamination. Each drop was used first in half the patients to control for any potential reflex effects instillation of the first drop might have had on the second eye.

One drop (50 µl) of mixture "A" was instilled into the lower fornix of the right eye avoiding spillage onto the skin of the lid. The patient was asked to blink several times but avoid forced closure of the lids if possible and to report when any stinging sensation had ceased and the skin of the lids was examined to assess "spillage" of fluorescein stained tears as a measure of reflex epiphora according to a semiobjective ordinal scale of four categories arbitrarily scored from 1 to 4 respectively—"minimal wetting of the lid margin", "slight wetting of the lid skin", "moderate wetting of the lid skin", " heavy wetting of lid skin with

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tears running down cheek". Lids of all patients falling into categories 2–4 were wiped before completion of tonometry. If the fluorescent tear meniscus was felt to be too thick, thin, or faint to ensure an accurate IOP measurement it was adjusted by removing excess with absorbant tissue paper or adding an additional drop as necessary. Time taken to complete IOP measurement from initial drop instillation was recorded.

On completion of tonometry on each eye the patient scored the severity of stinging discomfort for that eye on a 100 mm linear analogue scale ranging from "no pain" to "very severe pain" and quantified the severity of ocular discomfort according to a descriptive discomfort scale of five categories: "no pain", "slight pain", "moderate pain", "severe pain", and "very severe pain". The procedure was then repeated for the left eye and patient preference for drop "A" or "B" ascertained.

Statistical analyses were performed using the two tailed z test to assess numerical variables of linear pain score, duration of stinging, and tonometry completion time and the χ^2 test to assess differences in the categorical variables of descriptive discomfort and lid wetting score.

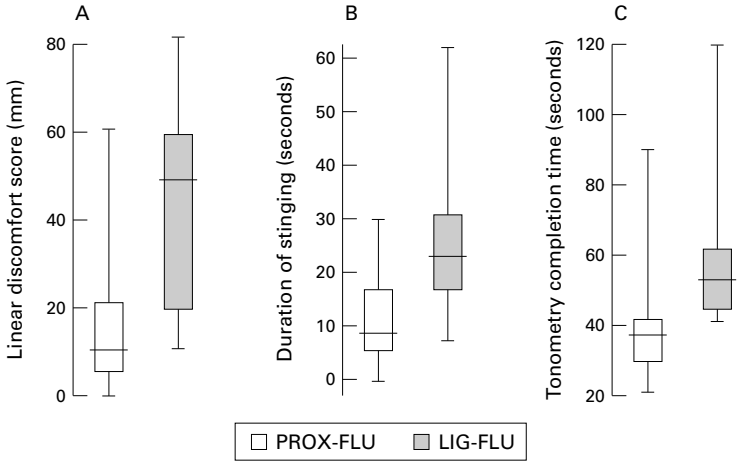

Figure 1 Box plot showing median values (horizontal lines), interquartile range (bars), and total range (vertical lines) for (A) linear discomfort score, (B) duration of stinging, (C) tonometry completion time.

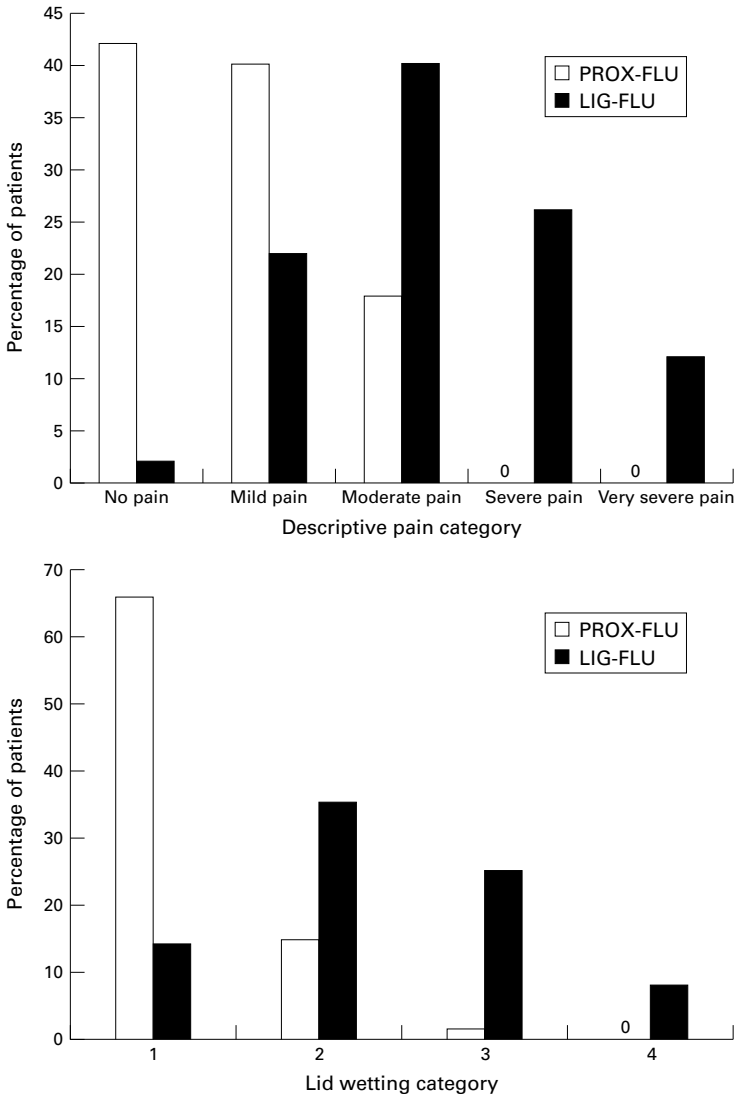

Figure 2 Percentages of patients in each descriptive pain category (top) and each lid wetting category (bottom).

Results

In the sample of 60 patients 23 were male and 37 female with a mean age of 63.2 years (SD 17.3, range 32–86). Results for linear pain score, stinging time, and tonometry completion time are summarised in Figure 1. The median pain score was 10 mm for PRO-FLU compared with 50 mm for LIG-FLU (z test, $p<0.001$). The median duration of stinging was 8 seconds for PROX-FLU and 22.3 seconds for LIG-FLU, (z test, $p < 0.001$). The median time for completion of tonometry was 36 seconds in the PROX-FLU eyes and 50 seconds in the LIG-FLU eyes (z test, $p<0.001$).

On the descriptive discomfort scale the distribution was skewed towards the lower discomfort categories for the eyes receiving PROX-FLU and towards the higher categories for those receiving LIG-FLU (χ^2, 4 df = 42.5, $p<0.001$) (Fig 2 top). Twenty patients reported LIG-FLU as causing "severe" or "very severe" discomfort but no patient scored PROX-FLU in these categories. On the lid wetting scale the distribution was skewed towards the lower categories for the PROX-FLU eyes and the higher categories for the LIG-FLU eyes (χ^2, 3 df = 40.4, $p<0.001$) (Fig 2 bottom). In five of the LIG-FLU eyes tearing was sufficient to cause overflow and running down the cheek but this occurred in none of the PROX-FLU eyes.

A meniscus of adequate thickness and fluorescence after initial drop instillation was obtained in 93% of the PROX-FLU eyes but in only 52% of the LIG-FLU eyes. Preference for the PROX-FLU mixture was expressed by 98% of the patient sample with only one patient expressing no preference. No patient preferred the LIG- FLU mixture.

Discussion

In terms of anaesthetic properties there is little to choose between commercially available topical agents[6] and though several studies have confirmed the superiority of proxymetacaine in

terms of patient discomfort[6 7] we found no comparative studies involving topical lignocaine. To our knowledge this is also the first study of the effect of reflex lacrimation induced by topical anaesthetic-fluorescein mixtures on the process and duration of applanation tonometry, including the need for tear film "manipulation" to produce an *accurate* IOP reading.

Manufacturers quoted range of pH for the agents used in this study is 4.8–5.3 for PROX-FLU and 3.0–4.2 for LIG-FLU and the greater acidity of the latter probably explains its poorer tolerance. Formulations of both agents are markedly hypotonic with respect to tears and have similar osmolarity, and while hypertonic solutions tend to sting, hypotonic solutions are generally well tolerated.[6] The influence of differences in chemical structure is unknown.

A potential drawback to routine use of PROX-FLU is the requirement for refrigerated storage but the manufacturer suggests PROX-FLU may be kept at room temperature before use for up to 28 days, significantly longer than the turnover time for a box in an average clinic.

In conclusion, this clinical study demonstrated within this group of patients the superiority of the proxymetacaine-fluorescein mixture for all the parameters studied and tear film manipulation was rarely required during its use. It would appear to be a useful and better tolerated alternative to the more widely used lignocaine-fluorescein mixture for applanation tonometry.

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Notes