

Influence of pH on the efficacy of pilocarpine

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SUMMARY Pilocarpine 4% solutions at pH 4.1 and 5.8 were compared in a double-blind clinical trial on 24 eyes of patients with primary open-angle glaucoma. Each drug was used over a period of 1 week. No significant difference in the lowering of intraocular pressure was found, and the near-neutral solution of pilocarpine was found to be equally stable when compared to the acid solution over a 6-month period.

Commercially available pilocarpine is dispensed in acid solutions to prevent degradation during sterilisation and storage. Acid solutions, however, cause greater discomfort to the patients than neutral solutions. Riegelman and Vaughan (1958) suggested that pilocarpine buffered to a higher pH should be used routinely, even though this preparation may be less stable.

Andersen and Cowle (1968), using a single drop technique in combination with tonography, showed that the mean outflow responses to pilocarpine solutions of pH 6.5 were greater than for solutions at pH 4. In addition there was a significantly greater hypotensive action of the pilocarpine of pH 6.5 than with the more acid solution.

In the present study a randomised double-blind clinical trial was undertaken in an attempt to elucidate the role of the pH of a 4% pilocarpine solution in the management of patients with glaucoma. The main aim was to assess whether the efficacy of the drug in lowering intraocular pressure was affected by the pH.

Material and methods

Thirteen patients (24 eyes; 2 patients had absolute glaucoma in 1 eye) with primary open-angle glaucoma controlled on medical therapy were admitted to hospital for a period of 2 weeks.

Two solutions of 4% pilocarpine, one of pH 5.8 and one of pH 4.1, were provided for each patient in identical containers labelled with trial number 'A' and trial number 'B'. Drops from bottle 'A' were

*The pilocarpine solutions of both pH were supplied by Dispersa Pharmaceuticals.

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instilled in the patients' eyes, as a substitute for their previous pilocarpine therapy, for the first 7 days 4 times a day (6 a.m., 11 a.m., 5 p.m., 10 p.m.). This was replaced by bottle 'B' for the next 7 days under the same regimen.

The investigators were not aware of the content of the bottles, which were randomised.

Intraocular pressures were measured at 9 a.m., 12 noon, and 3 p.m. every day for the period of 14 days with the Goldmann applanation tonometer.

After 2 weeks the bottles were submitted for pH assessment to an independent laboratory. The intraocular pressure data was analysed statistically.

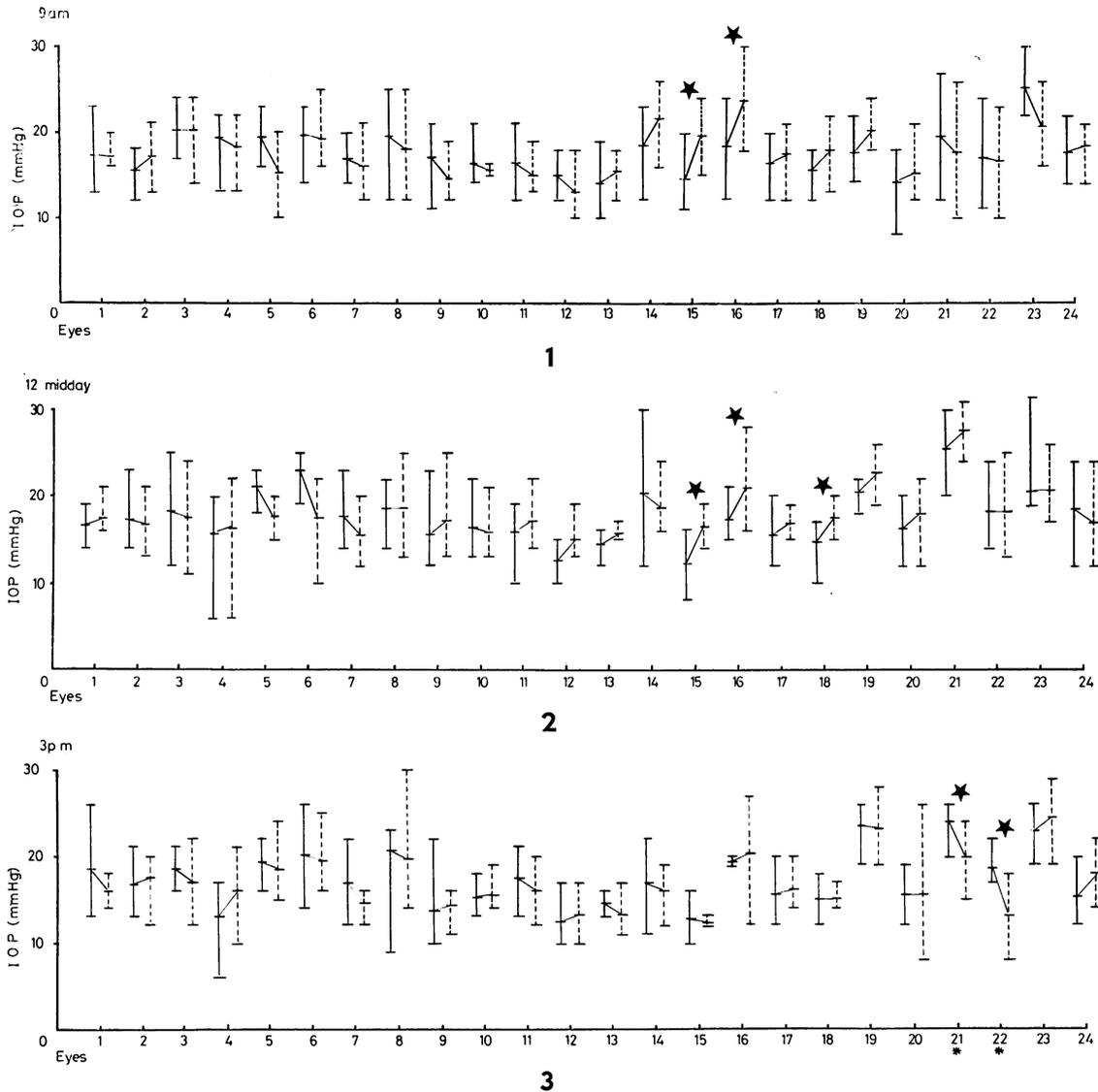
Results

The results are shown diagrammatically in Figs. 1-3. From this can be seen the close relationship between the average pressure readings of the first and second weeks. A significant difference in the average of the intraocular pressure measurement, with the 2 solutions for each measurement taken (i.e., at 9 a.m., 12 noon, and 3 p.m.), was found in only 7 readings (see Fig. 1*) from a total of 72 (3 daily assessments on 24 eyes); $P = 0.05$. Such a limited difference represents only 10% of the total as against the 90% which on statistical analysis showed no difference between the acid and alkali pilocarpine solutions.

Discussion

In this clinical trial no statistically significant difference in the intraocular pressure lowering effect was found between the 2 solutions. This shows that the efficacy of pilocarpine is not affected by the higher pH.

Both medicines were supplied for all the patients



Figs. 1, 2, 3 Average and range of intraocular pressures in 24 eyes using pilocarpine solutions buffered to pH 4.1 and pH 5.8. (----- pH 4.1 ————— pH 5.8)

at the beginning of the study and these bottles were used throughout the trial, which was completed after a period of 6 months. The results indicate that both the near-neutral and acid solutions are equally stable, at least over a 6-month period.

This finding, in addition to Ihler and Syversen's (1976) demonstration of patient comfort with a higher pH solution and 67% subjective patient preference, would indicate more routine clinical use of near-neutral pilocarpine solutions.

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References

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