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CORNEAL TRANSPARENCY CHANGES RESULTING FROM OSMOTIC STRESS

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Abstract—Corneal thickness and transparency changes were measured following exposure of the cornea to various levels of osmotic stress. Bathing the cornea in hypotonic solutions of NaCl caused an increase in corneal thickness and light scatter within the cornea.

Transparency changes with hypotonicity were determined by comparing the relative brightness of haloes around a bright lamp source for the various concentrations of NaCl solutions. Corresponding corneal thickness changes were determined by pachometry.

A nearly linear relationship was found between solution hypotonicity and the degree of corneal swelling, whilst an exponential relationship was found between hypotonicity and relative halo brightness. The rate of corneal recovery from osmotic stress was found to be constant with different degrees of tonicity, although the rate of thickness recovery was much slower than the recovery from haloes.

INTRODUCTION

It is well known that haloes can be a classic symptom of contact lens wear or can be produced experimentally by exposing the cornea to hypotonic bathing solutions or anoxic environments.

The use and measurement of haloes as a means of monitoring corneal epithelial response has previously been suggested (Wilson and Stevenson, 1981). It was shown that intersubject differences in epithelial response to a stress environment could be highlighted by a measurement of halo brightness when no changes were shown by conventional measurement of central corneal thickness. An implication of this finding is that if haloes are present their measurement could be a sensitive indicator of corneal epithelial change in contact lens wear. The relationship between structural changes within the epithelium and the phenomenon of light scatter giving rise to haloes has been described (Miller and Benedeck, 1973; Smelser, 1952).

In recognizing the significance of assessing epithelial changes relative to overall corneal response, attempts have been made to find alternatives to pachometry for either directly measuring epithelial thickness (Wilson *et al.*, 1980; O'Leary *et al.*, 1981), or quantifying epithelial response psychophysically (Remole, 1977, 1981; Hess and Garner, 1977).

Chan and Mandell (1975) used pachometry to measure corneal thickness changes in a small number of subjects following corneal exposure to NaCl bathing solutions of differing tonicities. They found a nearly linear relationship between solution hypotonocity and the degree of corneal swelling.

We therefore wanted to assess the relative significance and reliability of repeated corneal thickness and halo measurements to monitor epithelial response and recovery from osmotic stress. Also, by taking one subject and repeating the conditions several times, we aimed to determine the threshold level with respect to solution hypotonicity at which epithelial changes occur.

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MATERIALS AND METHODS

Fig. 1 shows the apparatus used to allow measurement of the relative brightness of haloes. This is based on the halometer described by Finkelstein (1952).

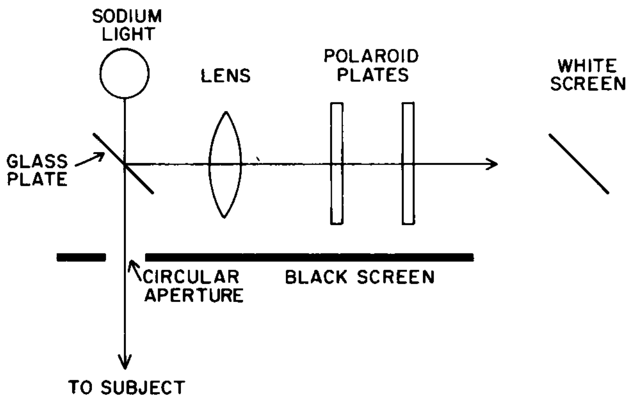

Fig. 1. Apparatus used to measure relative halo brightness.

The components were aligned on an optical bench; light from a sodium lamp was partially reflected by a 50/50 beam splitter to pass through a + 6.50-D lens and a pair of linearly-polarizing filters to give an evenly illuminated patch (4 × 3 cm) on a white screen. The luminance of this patch could be varied from maximum brightness down to zero by rotating one of the polaroid plates. The subject was seated 4.5 m away and viewed the light source through a circular aperture 25 cm in diameter in the black screen and through the beam splitter. This ensured that any variation in source intensity affected the halo source and the comparison patch equally. During an experimental run, following bathing an eye with NaCl solution, the subject reported if a halo was present whilst viewing the sodium source through the circular aperture. A halo, when described by a subject, corresponded to a circular haze of light surrounding the source, an arc of the halo being adjacent to the comparison patch. The subject was then required to make brightness matches of the halo against the comparison patch until this was no longer possible due to the diminution and eventual disappearance of the halo.

Corneal thickness was measured by a Hagg – Streit pachometer attached to a Nikon slit lamp. The modification of Mishima and Hedbys (1968) was adopted to ensure perpendicular alignment of the illumination slit, and a potentiometer attached to the pachometer allowed a permanent record of settings on a chart recorder. Previous calibration of the output of the electronic pachometer ensured linearity of the system. The corneal thickness at any one time was obtained by calculating the mean and SD of five successive readings.

Measurements were taken on several occasions of the left eye of one subject (JJ). NaCl bathing solutions of 1.5, 0.9, 0.7, 0.5 and 0.3%, and distilled water were used to "bathe" the eye by means of adapted swimming goggles with inlet and outlet ports. Base-line corneal thickness measurements were taken before and immediately after removal of the goggles. Measurements were repeated at short intervals for the first 5 min and then every 1 – 2 min for the next 20 – 25 min.

The procedure was repeated three times for each bathing solution with an interval of at least 1 day allowed between each trial.

During a pilot study it was found that generally haloes were not reported by the subject using solutions of a tonicity greater than 0.7%. Therefore a number of solutions within this range were chosen. These were 0, 0.1, 0.2, 0.3, 0.4 and 0.5%.

Halo and thickness measurements could not be performed on the same run due to the after-image effects from the slit-lamp source. Therefore a considerable time was required to perform repeated measures on the same subject. On removal of the goggles it was noted whether a halo was present, and, if so, relative brightness matches were made and repeated at 30-sec intervals until the halo could no longer be seen. Only one run in this case was carried out since results were very repeatable, within subjects, in a previous study (Wilson and Stevenson, 1981) and in a pilot study to this experiment.

RESULTS

Corneal thickness

Corneal hydration changes were measured for seven different concentrations of saline. Three sessions with each concentration gave 21 sets of results and the mean recovery of three sessions for each concentration is shown (Fig. 2). The SD of the mean of three sessions ranged from ± 0.002 to ± 0.013 mm.

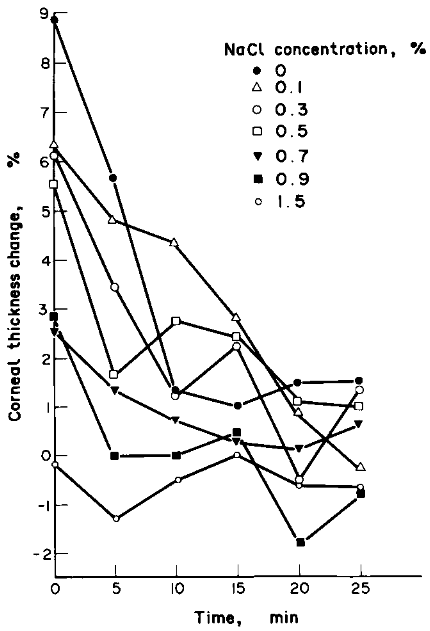

Fig. 2. Corneal thickness recovery of one subject's cornea from 30 min in NaCl bathing solution.

Table 1 shows the average corneal thickness change (%) immediately after the 30-min immersion period for all the concentrations of saline used. These values are plotted (Fig. 3), showing a nearly linear relationship between hypotonicity and degree of swelling (r = 0.95, $P < 0.01$).

Table 1. Summary of corneal thickness increases in one subject following immersion in NaCl bathing solutions

Concentration of NaCl bathing solution (%)	Average corneal thickening (%) immediately after 30-min immersion period
0	8.92
0.1	6.36
0.3	6.12
0.5	5.52
0.7	2.54
0.9	2.88
1.5	−0.18

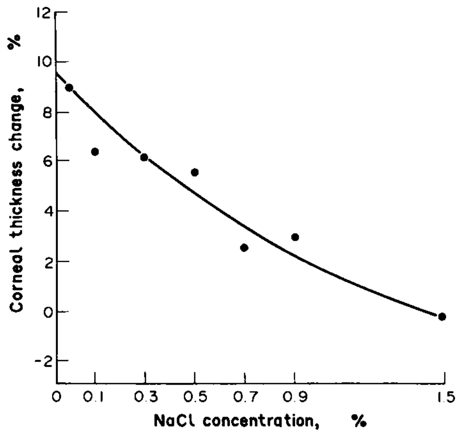

Fig. 3. Relationship between corneal thickness change (%) and NaCl solution tonicity.

The equation relating hypotonicity and thickness change is:

$$y = 7.73 - 5.4x,$$

where x = solution tonicity and y = % corneal swelling. The degree of corneal swelling produced by each of the bathing solutions was significantly different from the base-line thickness except for the 1.5% solution (t-test, $P < 0.01$).

The recovery of corneal thickness with time after being subjected to osmotic stress appears to be exponential. If this assumption is correct then a log transform using the equation:

$$\text{Log}_e (T_t - T_s) = \log_e (T_o = T_s) - at,$$

(where T_t = corneal thickness at time "t", T_s = initial corneal thickness, T_o = corneal thickness after removal of goggles, a = rate of change of the exponential curve and t = time) should give a straight line with slope "a". The slopes and intercepts are represented in Fig. 4. The result shows a relatively constant rate of recovery from corneal swelling with a mean slope of −0.158.

Halo measurements

Fig. 5 shows corneal recovery from haloes with time for solutions used. Haloes were not observed with saline solutions with concentrations greater than 0.7% NaCl.

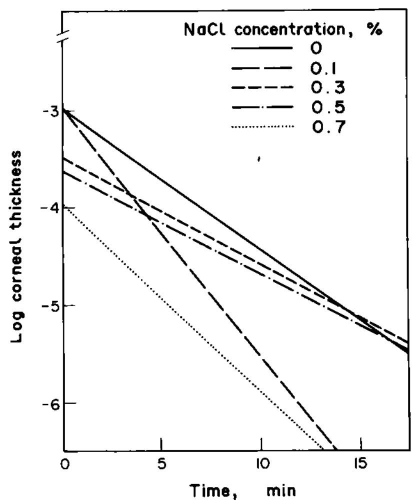

Fig. 4.

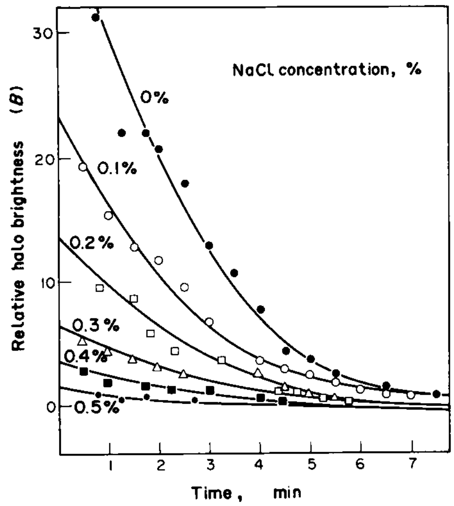

Fig. 5.

Fig. 4. Logarithmic transformation of corneal thickness recovery with time from NaCl bathing solutions.
Fig. 5. Corneal recovery from haloes from NaCl bathing solutions of different tonicity.

There appears to be an exponential recovery with time from haloes. Also the relationship between initial halo brightness and solution tonicity appears exponential (Fig. 6). To simplify data comparison, a logarithmic transform was done on this data using the equation:

$$\mathrm{Log}_e\,(B_t - B_s) = \log_e\,(B_o - B_s) - at,$$

where B_t = halo brightness at time t, B_s = halo brightness before treatment (i.e. $B_s = 0$) and B_o = halo brightness after removal of goggles. The slopes, intercepts and coefficients of correlation were all determined (Fig. 7). The mean slope was -0.519 and the correlation coefficients ranged from -0.77 to -0.99 (all significant, $P < 0.01$).

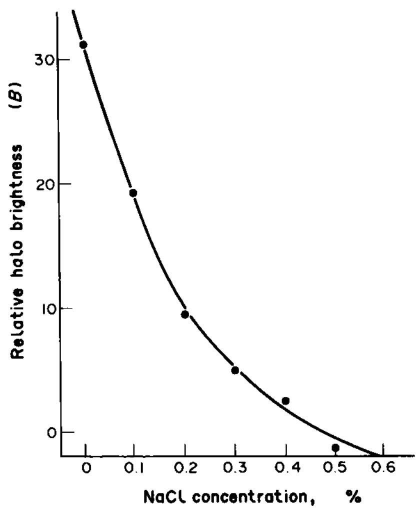

Fig. 6.

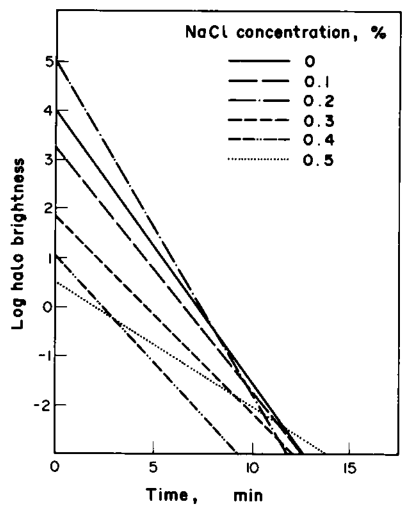

Fig. 7.

Fig. 6. Relationship of initial halo brightness and NaCl tonicity.
Fig. 7. Logarithmic transformation of halo recovery with time from NaCl bathing solutions.

DISCUSSION

The linear relationship found between solution tonicity and corneal thickness confirms the finding of Chan and Mandell (1975). The exact response of the cornea to hypertonic solutions cannot be confirmed since only one hypertonic solution was used in our experiment.

The exponential recovery of corneal thickness with time indicates a fairly rapid initial recovery after osmotic stress, slowing down as the cornea returns to normal. Maurice (1969) has suggested that the active pump mechanism operates at something like double its normal standby rate when the cornea is recovering from oedema. The logarithmic transformation of thickness recovery (Fig. 4) shows similar recovery response with each solution used (mean = 0.158). This finding suggests that the rate of removal of water from the oedematous cornea is the same regardless of the degree of oedema.

It is also shown that haloes diminish and disappear when often no significant recovery in corneal thickness has taken place. This would seem to suggest halometry indicating another process taking place, presumably with respect to epithelial cells. It may be that hypotonic solutions react with squamous epithelial cells allowing entrance to the epithelium, disturbing the intra-cellular fluid barriers, known as zonula occludentes (Bergmanson, 1981), and subsequently causing light scatter.

Scattering of light would then emanate not from an increased thickness of the epithelium but from an intercellular disturbance from droplets of fluid. This requires further work to demonstrate such a change.

The tonicity threshold for these changes for the subject we used was 0.7% NaCl. Therefore, hypotonic NaCl solutions of 0.7% or less produced changes in the epithelium resulting in haloes. Further experiments are being carried out to assess this on other subjects. At this level of hypotonicity an approximately 4% corneal thickness change occurred. It would therefore seem that although some overall corneal thickness changes can occur without the presence of haloes, this figure may well be within that which some contact lens wearers are subjected to. We would suggest therefore that halometry in a clinical context could be used in addition to conventional methods as a sensitive measure of epithelial change in contact lens wear, particularly extended wear, or in clinical trials of new lens materials to indicate differences in corneal response to such materials.

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