

EFFICACY OF SODIUM HYALURONATE EYE DROPS OF DIFFERENT OSMALARITIES IN THE SYMPTOMATIC TREATMENT OF DRY EYE PATIENTS

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1. INTRODUCTION

High tear film osmolarity is often associated to keratoconjunctivitis sicca (KCS).¹ This increased osmolarity (up to 30–40 mosm/l) may be, at least in part, responsible for both symptoms and signs of KCS. In addition in vitro studies have demonstrated that such high osmolarity may be toxic to corneal epithelium.² Since the treatment of KCS is mainly based on the use of artificial tears solutions and/or ocular lubricants, an attempt has been made to reduce such osmolarity by applying hypotonic solutions.² However, the clinical results obtained by using hypo-osmolar or normally osmolar substances have been contradictory.^{1,3,4} Sodium hyaluronate (NaHa) solutions have beneficial effects in the relief of symptoms and conjunctival epithelial conditions in dry eye patients.^{5,6} The present study was designed to assess the effects of two NaHa solutions, with different molecular weight and tonicity, on symptom relief in KCS patients.

2. PATIENTS AND METHODS

This was a multi-centered, double masked, crossover clinical trial conducted in 158 patients with clinically well-defined dry eye syndrome. Only patients with history of dry eye for at least two months, tear film abnormalities (tear breakup time [BUT] < 10 sec and/or Schirmer's test < 5.0 mm in one or both eyes) and ocular surface damage (rose bengal

and/or fluorescein test score of at least 3 in at least one eye) were included in the study. Patients received two ophthalmic solutions, one hypotonic (215 mOsm/l) and the other isotonic (305 mOsm/l), both containing NaHa. Treatments were given over a period of 28 days for each study medication. A 7 day wash out period separated the two treatments. The viscosities of the two solutions were similar. Clinical symptoms and signs of ocular surface damage (stinging, burning, foreign body sensation, heaviness of the lids, photophobia, global ocular symptoms, tear BUT, fluorescein stain, rose bengal stain and anesthetized Schirmer's test) were performed at the end of each treatment period.

3. RESULTS

Data from 139 patients who completed the study were used for the statistical analysis. Efficacy analysis was based on pooled results from both treatment arms for each of the two compounds used. Both the hypotonic and isotonic solutions of NaHa were found to be effective for the resolution of symptoms in dry eye patients. Most of the maximally obtainable relief occurred within one month of treatment. For most symptoms and signs, there was no statistical difference between the two compounds (Fig. 1). However, tear BUT was significantly improved by the hypotonic solution ($P = 0.021$). The local tolerance was good and no adverse events were reported.

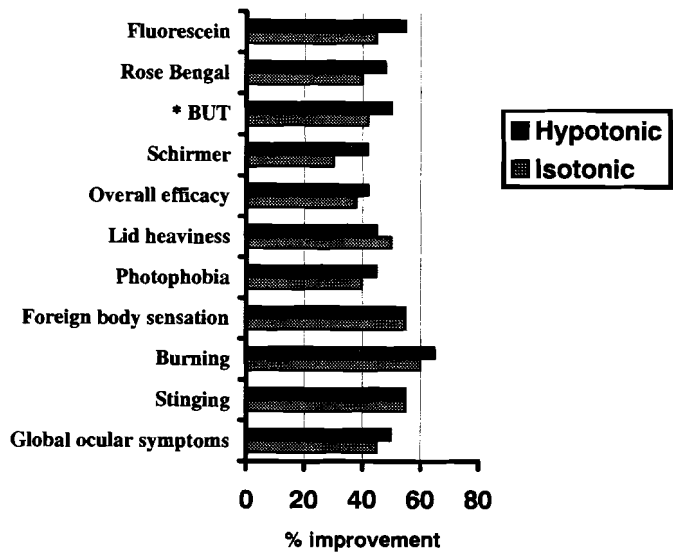


Figure 1. Efficacy of isotonic and hypotonic solutions on symptoms and signs of dry eye. Data are expressed as % improvement over baseline. * $P = 0.021$.

4. DISCUSSION

The treatment of dry eye is aimed to stabilize the tear film. To date no ideal tear substitute is available for relief of symptoms in such disorders. Damage to the ocular epithelium surface seems to be associated to KCS, and it was suggested that increased tear osmolarity could be responsible for such damage.^{1,2} However, clinical results obtained by using hypo-osmolar or normally osmolar substances have been contradictory. Some studies have demonstrated subjective improvements in eyes receiving hypotonic solutions^{1,3} but these findings were not confirmed in other reports.⁴ In the present study we tested two NaHa containing solutions with different osmolarity and found that both were equally effective in ameliorating both signs and symptoms of KCS. In particular our study showed that ocular surface damage, evaluated by either rose bengal or fluorescein stain, may be reduced with NaHa containing artificial tears despite their osmolarity. Interestingly, during the one week saline wash-out phase, symptoms worsened markedly in both treatment arms, suggesting that the improvement could indeed be related to the viscosity enhancing agent NaHa. In conclusion, although an increased tear osmolarity has been found in dry eye patients and it has been considered toxic for the corneal epithelium,^{1,2} the results of the present study indicate that greater importance should be ascribed to the substances which constitute the tear substitute solution rather than their physical properties, such as osmolarity, since a reduction of tear osmolarity could be obtained also by the administration of isotonic solutions. From this perspective, NaHa, for its well known properties such as non-Newtonian characteristics, efficacy on wound healing and anti-inflammatory action,^{8,9} can be considered particularly useful for the treatment of dry eye.

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