Vismed® Gel (Non-Preserved Sodium Hyaluronate eye drops) for the Treatment of Symptoms of Ocular Dryness and Discomfort in Patients with Sjögren's Syndrome.

A Non-Randomised, Patient Completed Questionnaire Report.

Overview.

The sensation of dry eyes is very common and can be quite debilitating for the sufferer.Some medical conditions can affect the quality and integrity of the tear film, amongst these is the autoimmune condition Sjögren's syndrome. Sjögren's syndrome is a chronic inflammatory disorder characterized by exocrine gland dysfunction and a variable systemic course. Lymphocytic infiltration of the lacrimal and salivary glands results in the classic sicca complex characterized by dry eyes (keratitis sicca or keratoconjunctivitis sicca [KCS]) and dry mouth (xerostomia). Among the various unpleasantocular symptoms which can be experienced are a feeling of dryness, grittiness, burning,itchiness or scratchiness of the eyes, a sensitivity to light, blurred vision, and excessive tear flow (caused by an imbalance in the tear film).

These sensations of dryness occur partly as a result of the tear filmbecoming destabilised, breaking down prematurely, and thus no longer lubricating the eye sufficiently. The tear film is a complex structure and has various functions:It lubricates the surface of the eye and keeps the surface tissue of the eye moist, it supplies nutrients and oxygen to the cornea, it hinders bacterial infections, and protects the ocular surface from small dust particles.

Hyaluronic Acid (HA) is a naturally occurring polymer and is ubiquitous throughout the interstitial cellular space in humans. The HA derived Sodium Hyaluronate, a member of the glycosaminoglycan group of recurring poly – saccharides, helps retain moisture in different types of tissue throughout the human body, making it an ideal physiologic tear film substitute.

Sodium Hyaluronate does not alter the normal surface of the eye the way other types of tear substitutes may do. It closely mimics the properties of a normal, healthy tear film, with a longer retention time on the corneal surface than cellulose-based tear substitutes. (1)Vismed® Gel is highly concentrated (0.3%) and hypotonic. Higher concentration hypotonic Sodium Hyaluronate has been shown to be more beneficial than isotonic solutions in patients with Sjögren's Syndrome suffering from Dry Eye.(2)In addition, Vismed® Gel contains no preservatives, so has no toxic or allergenic potential. (3)

The British Sjögren's Syndrome Association (BSSA) was founded in 1986. It is a registered charity which aims to raise awareness of the disease and support research into its cause and treatment. A self-help organisation with more than 2000 members, the BSSA is dedicated to providing mutual support and information to individuals affected by this disabling disease.

Commencing in October 2010, delegates attending the British Sjögren's Society's Annual general meetings (2 data sets 2010, 2011 AGMs), and various other UK Rheumatology/Ophthalmology related congresses where access to the public and non-medical professionals was allowed (3 data sets 2010, 2011), were polled. Non-medical delegates who visited the TRB Chemedica trade exhibition stand were asked if they suffered from symptoms associated with Dry Eye, and whether they regularly used wetting agents or tear substitutes to alleviate their symptoms. Although visitors to the stand were not obliged to reveal any personal details, the vast majority disclosed the fact that they had been diagnosed with Sjögren's Syndrome, that the persistent sensation of dry eyes was considered to be a "Major" problem, and that the instillation of tear substitutes and/or wetting agents was a regular and enduring daily task. All visitors who were prepared to discuss their condition were then asked if they would be willing to take part in a survey to assess whether Vismed Gel™ would offer a greater, lesser or equal amount of ocular relief compared with the eye drops they normally used.

Consenting participants were then given a questionnaire (see appendix 1) and a box of Vismed® Gel (20 mono dose units of 0.45ml Sodium Hyaluronate, preservative free, hypotonic, 0.3% concentration, pH7.3). Participants were asked to note how many times a day, over a period of 2 days, they used their usual eye drops, starting first thing in the morning when they woke up, until last thing at night before sleep. On day 3 participants were asked to switch to using Vismed® Gel instead of their usual eye drops, and to monitor how many times a day, over a period of 2 days, they needed to use Vismed® Gel.

Following each application of eye drops, participants were asked to note the degree of relief, or otherwise, that instilling the eye drops brought about in 5 designated categories. These were; Relief from Dryness / soreness; 0=none, 5= complete, Relief from gritty or burning sensations; 0= none, 5= complete, General ocular comfort after instillation; 0= very uncomfortable, 5= very comfortable, Amount of blurring following instillation; 0=none 5=complete, and Satisfaction; 0= not at all satisfied 5= very satisfied.

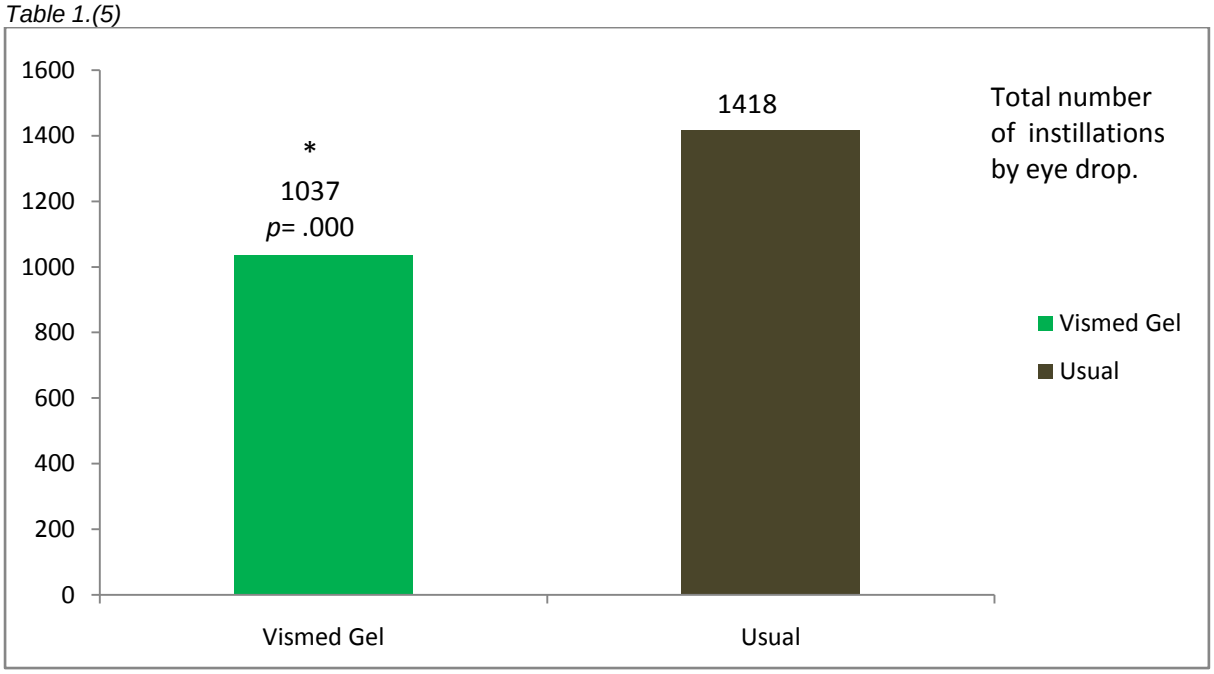
At the end of the 4 day monitoring and reporting period, participants were asked to return their completed questionnaires to TRB Chemedica (UK) Ltd by post, fax or e mail.

Results.

Of the 128 questionnaires distributed, each numbered sequentially by TRB Chemedica staff prior to issue, 84 were returned for analysis (65%). Of these 84, 7 (8%) were rejected, 2 due to defacement of some type, 4 due to incorrect completione.g. written comments instead of a numeric value assigned to a category, and 1 due to the omission of a medical diagnosis, leaving a total of 77 responses. The medical diagnosis was given as Sjögren's Syndrome on 54 questionnaires (70%) and as Dry Eye on 23.

The total number of eye drop instillations by all participants for days 1 & 2 (using their usual eye drops) was 1418 (mean 9.2, Range 5 – 14, S.D. 2.1). The total number of eye drop instillations by all participants for days 3 & 4 (using Vismed® Gel) was 1037 (mean 6.7, Range 4 – 11, S.D. 1.6). The reduction in the mean number of instillations following the switch to Vismed® Gel was statistically significant; (*t* =21.6, *p* .000, 95% C.I. 2.2 – 2.7).*see table 1.*

Table 1.(5)

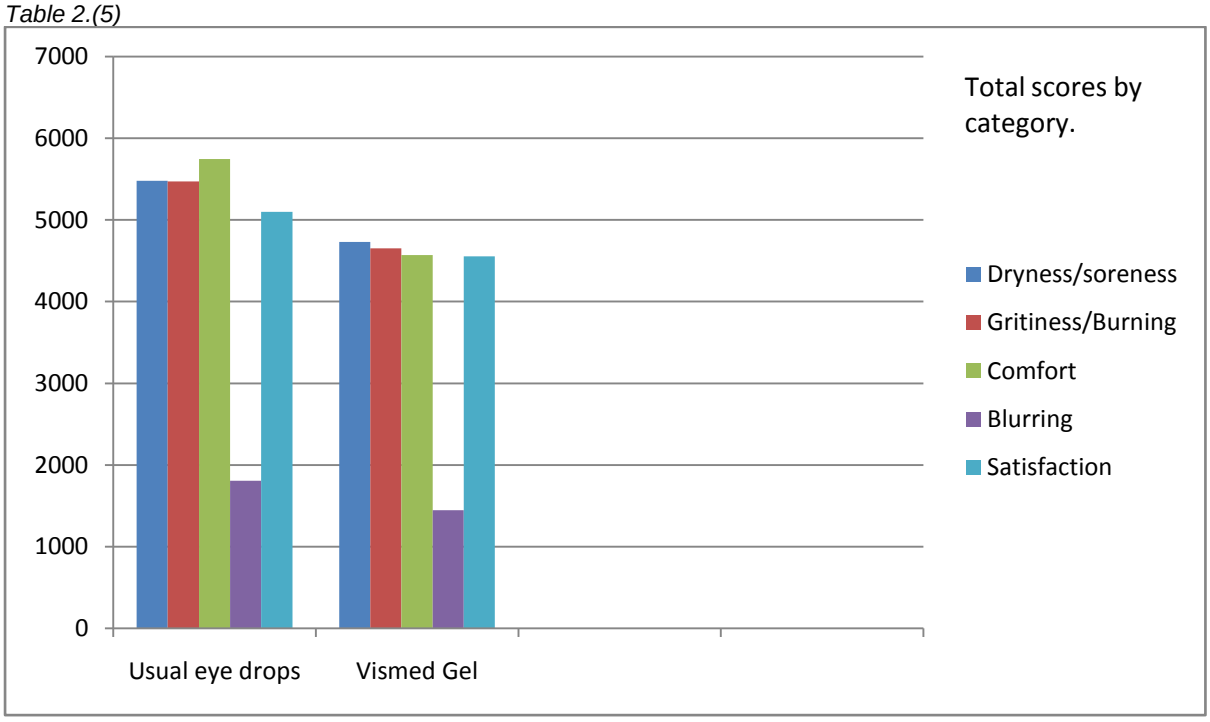


The various subjective measures of symptomatic change were categorised as; 1. Relief from Dryness/soreness, 2. Relief from gritty or burning sensations, 3. General ocular comfort after instillation, 4. Amount of blurring following instillation, and 5. Satisfaction. All but category 4 required a higher mark to demonstrate greater approval rating, whereas category 4 required a lower mark to quantify greater satisfaction, as blurring of vision following instillation is not considered to be a desirable characteristic of eye drops.

Categories 1, 2 and 4 required scores of between 0 (denoting none) and 5 (denoting Complete). Category 3 required scores of between 0 (denoting Very Uncomfortable) and 5 (denoting Very Comfortable), while category 5 required scores of between 0 (denoting Not At All) to 5 (denoting Very Satisfied).

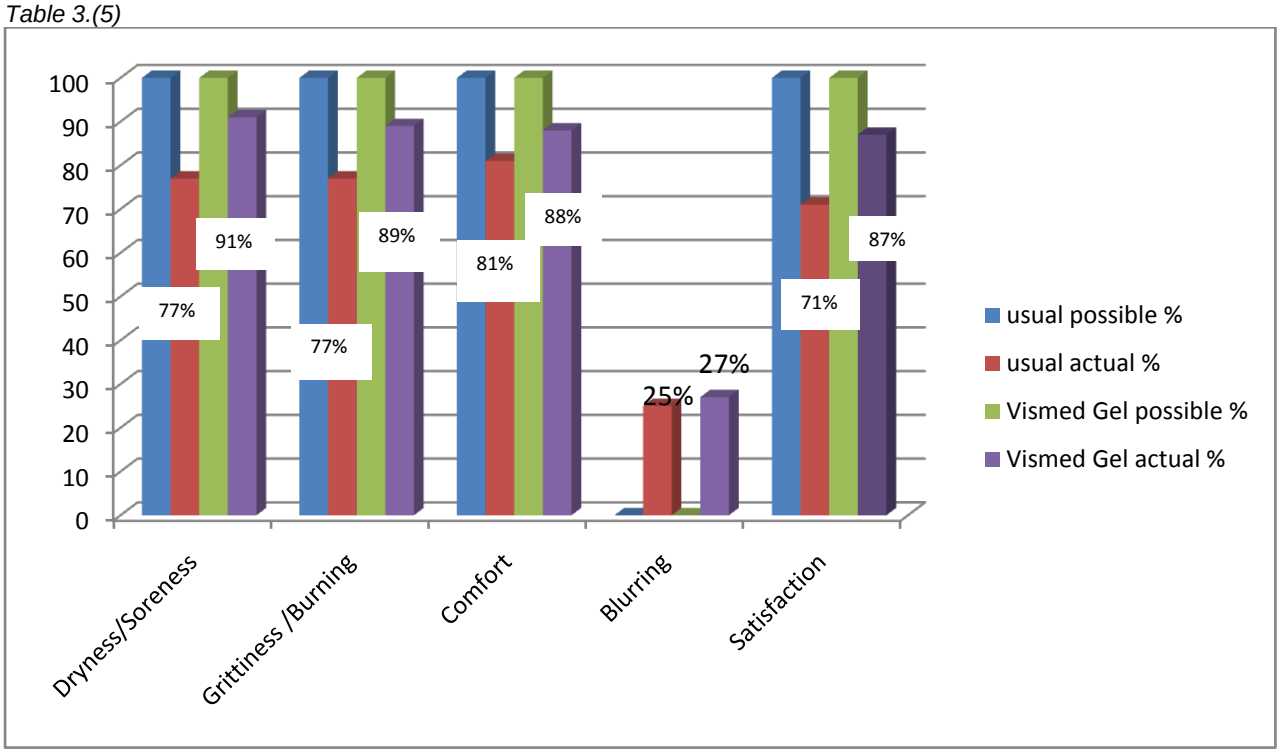
All participants were asked to complete these subjective categorical scores after each instillation of eye drops.There were considerable inter-group variances between total categorical scores due to the differing number of times that participants needed to use their eye drops. Thus, high usage resulted in higher total scores per category than lower usage. Total scores per category for both usual eye drops and Vismed® Gel eye drops are shown in table 2.

Table 2.(5)



In order to explore how participants rated their usual eye drops compared with Vismed® Gel, a calculation of the potential score i.e. the score that each category could have achieved for a 100% approval rating, against the actual score was undertaken. Categories 1,2 3, and 5 required the highest score of 5 in order to demonstrate a 100% approval rating, whereas category 4 required a score of zero to demonstrate total approval. See table 3.

Table 3.(5)



Vismed® Gel required significantly fewer applications over a 2 day period than the usual eye drops used by the participants who returned questionnaires for this report. The necessity for a higher frequency of application of eye drops has been shown to be a source of disruption and annoyance to people suffering from Dry Eye(4). In addition to requiring significantly fewer applications, Vismed® Gel received higher subjective approval ratings in 4 out of 5 categories (relief from Dryness and Soreness, Grittiness and Burning sensations, Improved ocular comfort, and Overall satisfaction). There was a marginally higher score for Vismed® Gel in the blurring category following instillation, indicating marginally lower satisfaction.

Discussion.

Dry eyes are a common symptom experienced by sufferers of Sjögren's Syndrome. The current report sought to identify whether a preservative free, Hypotonic, Sodium Hyaluronate eye drop would prove to be more effective than the participant's usual eye drops. Based on the results garnered, Vismed® Gel offers a more effective option for treating the symptoms of dry eyes than the drops usually used by the participants in this study.

There are, however, a number of limitations to the current study. There was no reporting of what type of eye drops the participants were normally using, therefore no analysis of differing physical properties, side effects, pricing, dispenser presentation, or problems associated with preservatives was possible. Further, more formalised

studies, with higher participant numbers, will help determine whether there are verifiable benefits to using Preservative free, Hypotonic Sodium Hyaluronate as eye drops for patients diagnosed with Sjögren's Syndrome

References.

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