

THE EFFECT OF DESMOPRESSIN ON AQUEOUS SECRETION OF THE LACRIMAL GLANDS

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ABSTRACT

To detect the effect of desmopressin on aqueous secretion of the lacrimal glands.

Sixteen male and sixteen female subjects with no systemic or ocular disease and no current or prior use of systemic or topical medications within 30 days were included into the study. We performed Schirmer test without topical anesthesia to right eyes and Schirmer test with topical anesthesia to left eyes of the subjects. We administered 20 µg desmopressin intranasally after 5 hour rest and performed Schirmer test without topical anesthesia to right eye and Schirmer test with topical anesthesia to left eye again at the end of first hour. Same procedures repeated for three consecutive days and the mean values of pre-desmopressin and post-desmopressin Schirmer test results were compared.

Right eyes pre-desmopressin Schirmer test results ranged between 5-47 mm (mean 18.2 mm) and post-desmopressin results ranged between 2-37 mm (mean 13.7 mm). Left eyes pre-desmopressin Schirmer test results ranged between 3-29 mm (mean 12.7 mm) and post-desmopressin results ranged between 1-30 mm (mean 11.2 mm). Right eyes post-desmopressin Schirmer test results were significantly decreased compared with pre-desmopressin Schirmer test results (-24.7%, p: 0.001). There was no significant difference between left eyes post-desmopressin Schirmer test results and pre-desmopressin Schirmer test results (-11.8%, p: 0.112).

Desmopressin reduced the reflex lacrimal aqueous secretion.

Key Words: *Desmopressin, Aqueous Secretion, Lacrimal Glands.*

ÖZET

Desmopressinin Lakrimal Bezlerin Gözyaşı Salgısı Üzerindeki Etkisi

Desmopressinin lakrimal bezlerin gözyaşı salgısı üzerindeki etkisinin araştırılması.

Çalışmaya sistemik ve göz hastalığı bulunmayan son otuz gün içerisinde sistemik ve/veya topikal ilaç kullanım hikayesi olmayan on altı kadın on altı erkek toplam otuz iki kişi dahil edildi. Katılımcıların sağ gözlerine topikal anestezi uygulanmadan, sol gözlerine topikal anestezi uygulandıktan sonra Schirmer testi yapıldı. Katılımcılar beş saat dinlendirildikten sonra 20 µg desmopressin intranasal yoldan uygulandı ve takiben bir saat sonra Schirmer testleri tekrarlandı. Uygulama üç gün tekrarlandı ve ortalama desmopressin öncesi ve desmopressin sonrası Schirmer test sonuçları karşılaştırıldı.

Sağ göz desmopressin öncesi Schirmer test sonuçları 5-47 mm (ortalama 18,2 mm), desmopressin sonrası Schirmer test sonuçları 2-37 mm (ortalama 13,7 mm) arası değişmekteydi. Sol göz desmopressin öncesi Schirmer test sonuçları 3-29 mm (ortalama 12,7 mm), desmopressin sonrası Schirmer test sonuçları 1-30 mm (ortalama 11,2 mm) arası değişmekteydi. Sağ göz desmopressin sonrası test sonuçlarında, desmopressin öncesi test sonuçlarına göre istatistiksel anlamlı azalma vardı (-24,7%, p: 0.001). Sol göz desmopressin sonrası Schirmer test sonuçlarındaki azalma istatistiksel anlamlı değildi (-11,8%, p: 0.112).

Desmopressin, refleks göz yaşı salgısını azaltmaktadır.

Anahtar Kelimeler: *Desmopressin, Gözyaşı salgısı, Lakrimal bezler.*

INTRODUCTION

Vasopressin (arginine vasopressin), also called antidiuretic hormone, is a nanopeptide synthesized in the hypothalamus and released upon stimulations such as hyperosmolality, hypotension and hypovolemia. It is a major

hormone involved in the regulation of body fluid osmolality and volume (1).

Vasopressin plays an important role in the long-term control of blood pressure through its action on the kidney via V₂ receptors leading to reabsorption of water. Through V₁ receptors

vasopressin also increases the mean arterial pressure (2).

Desmopressin, a synthetic analog of the peptide hormone vasopressin in which the N-terminal -amino group has been removed and L-arginine in position 8 has been replaced by D-arginine, has enhanced antidiuretic potency, markedly diminished pressor activity and a prolonged half-life and duration of action compared to the natural hormone (3) and can be administered either intranasally or parenterally.

The lacrimal glands are the main contributor to the aqueous layer of the tear film. They secrete proteins, electrolytes and water, which helps to nourish and protect the ocular surface.

Vasopressin prevents water loss from the body. Aqueous secretion is also a way of water loss. The purpose of this study is to determine the effect of desmopressin on aqueous secretion of the lacrimal glands.

MATERIAL and METHOD

The study adhered to the Declaration of Helsinki and Good Clinical Practice guidelines. After approval of the study by the Ethics Committee of Firat University School of Medicine, subjects were enrolled. All participants in the study gave their informed consent.

The study was conducted between November 2005 and December 2005. Thirty-two subjects (16 male, 16 female) were recruited from Firat University School of Medicine staff. The inclusion criteria were: no systemic or ocular disease and no current or prior use of systemic or topical medications within 30 days.

We performed Schirmer test without topical anesthesia (4) to right eyes and after 10 minute rest Schirmer test with topical anesthesia (5) (0.5% proparacaine hydrochloride in; Alcaine® Alcon) to left eyes of the subjects. The strip (sno*strips® Chauvin) was placed over the inferior lid margin between the middle third and the lateral third of the eyelid and subjects wanted to close their eyes. In Schirmer test with topical anesthesia the strip was placed 10 minutes after proparacaine hydrochloride instillation. During a 5 minute period, the filter paper becomes soaked with tears and the extent to which the paper is soaked is measured in millimeters. After 5 hour rest we administered 10 µg desmopressin (Minirin® Ferring AB) to each nostril (total 20 µg). After 1 hour (most effective serum

concentration of desmopressin) both Schirmer test without topical anesthesia to right eye and after 10 minute rest Schirmer test with topical anesthesia to left eye were performed again.

We repeated the above procedure for three consecutive days and the mean values of Schirmer tests were taken for statistical analysis. The pre-desmopressin and post-desmopressin results were compared.

Statistical analyses were carried out employing the Statistical Package for Social Sciences soft-ware 11.0 for Windows package software (SPSS, Inc., Chicago, IL). The paired t-test was used and a p value less than 0.05 were considered as statistically significant.

RESULTS

Thirty two subjects aged 18-34 years (mean 25.2 (SD 3.6)) were included in the study. Sixteen subjects were women aged 18-34 years (mean 25.1 (SD 3.7)). Sixteen subjects were men aged 21-34 years (mean 25.3 (SD 3.7)).

Right eyes pre-desmopressin Schirmer test (without topical anesthesia) results ranged between 5-47 mm (mean 18.2 (SD 9.7)) and post-desmopressin results ranged between 2-37 mm (mean 13.7 (SD 9.5)) (Figure).

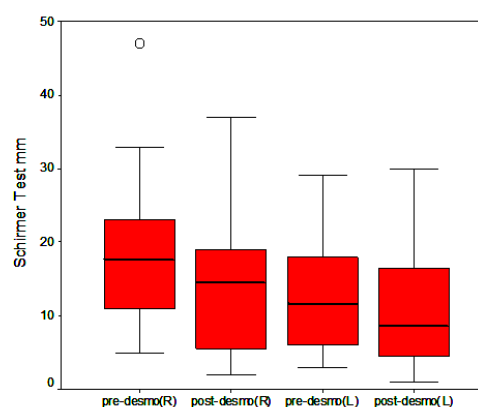


Figure 1. Schirmer test results of right and left eyes before and after desmopressin administration. The black lines in the box plot diagram show the mean values. (o: outlier cases)

Left eyes pre-desmopressin Schirmer test (with topical anesthesia) results ranged between 3-29 mm (mean 12.7 (SD 7.4)) and post-desmopressin results ranged between 1-30 mm (mean 11.2 (SD 8.2)) (Figure).

Kolmogorov-Smirnov test was used to show normal distribution in all groups (Right eyes pre-desmopressin group p:0.695; post-desmopressin group p:0.847; Left eyes pre-desmopressin group p:0.628; post-desmopressin group p:0.331). Paired t-test was used in statistical analysis for comparison of pre-desmopressin and post-desmopressin results. Right eyes post-desmopressin Schirmer test (without topical anesthesia) results were significantly decreased compared with pre-desmopressin Schirmer test (without topical anesthesia) results (-24.7%, p: 0.001). There was no significant difference between left eyes post-desmopressin Schirmer test (with topical anesthesia) results and pre-desmopressin Schirmer test results (-11.8%, p: 0.112).

DISCUSSION

Lacrimal aqueous secretion is divided into basal secretion which is maintained by the accessory exocrine glands of Krause and Wolfring and reflex secretion which is maintained by the main lacrimal gland (5). But recent studies showed that the main and accessory lacrimal glands routinely work simultaneously with one another (6).

The Schirmer test is a test of tear volume and also measures the volume of tear produced during a fixed period of time (4,5). Schirmer test without topical anesthesia measures the reflex secretion mainly maintained by main lacrimal gland. The Schirmer test with topical anesthesia eliminates the reflex tearing produced by irritation from the Schirmer strip and that wetting of the strip represents the basal tear secretion. This basal aqueous secretion mainly maintained by accessory lacrimal glands Krause and Wolfring.

Repeatability of the Schirmer test is more variable (7). So we repeated the Schirmer test measurements for three consecutive days and the mean values of Schirmer tests were taken for statistical analysis.

The results of this study showed that desmopressin reduced the main and accessory

lacrimal glands aqueous secretion but only main lacrimal gland aqueous secretion reduction was statistically significant (p: 0.001).

Lacrimal glands aqueous secretion is controlled by autonomous nervous system and sex hormones. Parasympathetic fibers (8) and β_1 -adrenergic agonists (9) stimulate lacrimal aqueous secretion. The presence of beta 1 receptors in the accessory lacrimal glands had also shown (10). Sex hormones also have important role in secretory function (11) and morphological appearance (12) of the main lacrimal gland. This means lacrimal glands also influenced from the hormonal status. Vasopressin is also hormone so can influence the secretory functions of lacrimal glands.

The presence of vasopressin in the lacrimal gland of the rat has been documented immunohisto-chemically (13). But in the available literature we could not find any knowledge about the effect of vasopressin on human lacrimal gland functions. As a preliminary study we used desmopressin instead of vasopressin because the drug can be administered intranasally without an invasion and it mimics the anti-diuretic properties of vasopressin (3).

Antihistamines, antianxiety agents, and tricyclic antidepressants decrease the lacrimal glands aqueous secretion (14). These drugs cause dry eye symptoms via their anti-cholinergic actions. In sera of primary Sjogren syndrome patients' autoantibodies against muscarinic acetylcholine receptors was found and may be considered among the serum factors implicated in the pathophysiology of the development of dry eyes (15).

In our preliminary study we showed that desmopressin decreases the lacrimal glands aqueous secretion. But further studies are needed to identify the mechanism of vasopressin effect on lacrimal glands. If this mechanism is identified local vasopressin receptor antagonists may have a possible role in the treatment of dry eye.

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