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Zerrin KAPICIOĞLU[1]
Gamze ÇAN[2]
I. Nuri KALYONCU[3]

Action of Aspirin on Acetylcholine-Stimulated Tear Secretion in Rats

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Departments of [1]Ophthalmology, [2]Pharmacology, [3]Public Heath, Faculty of Medicine, Karadeniz Technical University, 61080 Trabzon-Turkey

Abstract: In this study we investigated the effect of acetylsalicylic acid (ASA) on tear secretion in rats. The animals were anesthetized intraperitoneally (ip) with urethane (1,2g/kg). The treatment was injected subcutaneously (s.c.). Tear samples were collected by folding a 5 mm section of a Schirmer strip over the lower lid margin to absorb tear fluid from the lower conjunctival sac for 5 min. Forty animals were divided into four groups (n=10). Group 1 (control) received 1ml of saline, group 2 received 60mg/kg of ASA, group 3 received 50mg/kg of Acetylcholine (Ach), and group 4 received 60mg/kg of ASA and 30 min later 50mg of Ach. While Ach alone significantly increased tear secretion, ASA reduced it when compared to saline (control) ($p<0.0001$ and $p<0.01$, respectively). Acetylsalicylic acid combined with Ach decreased tear secretion in comparison to Ach alone ($p<0.001$). In conclusion, ASA significantly inhibits Ach-stimulated tear secretion in rats.

Key Words: Aspirin, acetylsalicylic acid, acetylcholine, tear secretion, rat.

Introduction

The activation of phospholipase A_2 which breaks down phospholipids into arachidonic acid produces eicosanoids. Arachidonic acid, is metabolized to prostanoid (prostaglandins) or leukotrienes. In many tissues prostanoids either stimulate secretion or modify the stimulated secretion (1).

Prostaglandins may be involved in regulating electrolyte and water secretion. Prostaglandin PGE_1 stimulates electrolyte and water secretion in vivo. The effect may be a modulatory one, however, as activation of ß-adrenoreceptors is involved in the response. Thus, prostanoids appear to play only a minor role in stimulating lacrimal gland secretion (1).

The effect of acetylsalicylic acid (ASA) as an inhibitor of prostanoid production and lacrimal gland secretion is not clear. Stimulation of lacrimal gland secretion by the classic neurohumoral transmitter acetylcholine (Ach) is well documented (2, 3). Acetylcholine stimulates both fluid (electrolyte and water) and protein secretion via muscarinic receptors (1).

The aim of this study was to investigate the role of ASA in tear secretion in rats.

Material and Methods

Forty male albino rats, each weighing 175-200g, were used in the experiments. The animals were starved for 24 h with free access to water ad libitum. They were then anesthetized intraperitoneally with 1.2g/kg of urethane (Etylcarbamate) (Sigma Chem. Co. USA). The baseline tear secretion was measured before treatment: the following protocol was used 30 min after administration of the treatment. Tear samples were collected by folding a 5 mm section of the Schirmer strip over the lower lid margin to absorb the tear fluid from the lower conjunctival sac for 5 min.(5) Through the utilization of this system neither the researcher nor any other personnel in the laboratory had knowledge of the treatment given to the animals. A fresh solution of ASA (Sigma Chem. Co., St. Louis) was prepared immediately before each test by dissolving 3g of Na HCO_3 (Fisher Sci., St. Louis) and 3g of ASA in 100ml of distilled water, which yielded a stock solution containing 30mg/ml of ASA.[5] The animals were

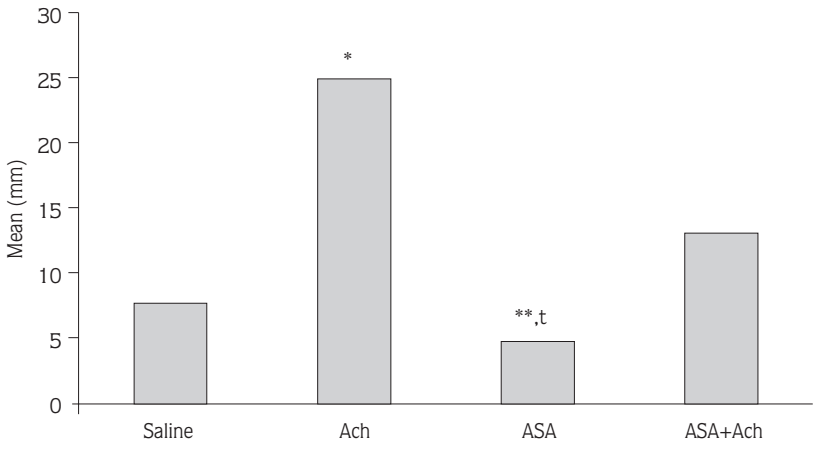

Figure 1. 1: Effect of ASA on tear secretion (mean mm with Schirmer Strip). *p<0.0001, **p<0.01 difference from saline (control) t p<0.0001 difference from Ach alone

divided into four groups (n=10). Group 1 (Control) received 1ml of saline (sc). Group 2 received 60mg/kg of ASA dissolved in 1ml of saline (sc). Group 3 received 50µg/kg of Ach (sc). Group 4 received 60mg/kg of ASA (sc) and 30 min later 50mg/kg of Ach (sc). At t=0~60 µl the local anesthetic proparacain HCL was instilled onto the ocular surface to minimize reflex secretion.

The Mann Whitney U test was used to determine statistical significance.

Results

The mean basal secretion was 7.7±3.2 mm in the control group. In group 3 Ach alone significantly increased lacrimal gland secretion to a mean of 24.8±4.7 mm, while in group 2 ASA alone reduced it to a mean of 4.0±2.3 mm when compared to the control group ($p<0.0001$, $p<0.01$, respectively). In group 4, ASA combined with Ach decreased the secretion considerably to a mean of 13.0±5.5 mm when compared to the Ach group ($p<0.001$), (Figure 1).

Discussion

In this study, we demonstrated that aspirin significantly inhibited Ach-stimulated lacrimal gland secretion in rats, indicating possible PG mediating as the response.

The activation of phospholipase A_2 to break down phospholipids in arachidonic acid produces eicosanoids. Arachidonic acid is metabolized to prostaglandins or leukotrienes. In many tissues, prostaglandins themselves either stimulate secretion or modify stimulated secretion (1). Prostaglandins produce vasodilatation and increase vascular permeability, histamine release, pain, fever and chemotaxis (6).

Aspirin-like drugs (non-steroidal anti-inflammatory drugs, NSAID) inhibit prostaglandin synthesis by lipooxygenase enzyme inhibition (7). Nevertheless, in one study, the ocular anti-inflammatory effects of NSAID (ketoprofen is a NSAID) and ketoprofen-induced prostaglandin synthesis were assessed and compared with indomethacin in rabbit corneal epithelium (8). Ketoprofen inhibited prostaglandin synthesis in both the conjunctiva and iris-ciliary body, but indomethacin was more effective in inhibiting PG synthesis in the conjunctiva than in the iris-ciliary body (8).

In contrast to our results, in another study, it was reported that indomethacin did not alter tear secretion (9). Neither indomethacin (an inhibitor of prostaglandin production), nor dihydroguanetic acid (an inhibitor of leukotriene synthesis) inhibits cholinergic agonist-induced protein secretion (1). Prostaglandins may be involved in regulating electrolyte and water secretion, as prostaglandin E_1 stimulates electrolyte and water secretion in vivo.

The effect may be a modulatory one, however, as activation of ß-adrenoreceptors is involved in the response. Thus, prostaglandins appear to play only a minor role in stimulating lacrimal gland secretion (1). Our study demonstrated that aspirin significantly inhibited Ach stimulated lacrimal gland secretion. Further studies are required to establish the effect of aspirin on lacrimal gland secretion.

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