

## A COMPARATIVE STUDY OF THE EFFECT OF ACETYLCHOLINE AND PROSTAGLANDIN F<sub>2a</sub> ON ISOLATED TRACHEALIS MUSCLE OF GUINEA \*PIG

*Shah. Nawaz, MAJ. Kamran, Qazi Rashid Ahmad and Abdul Rashid*

**Abstract:** Acetylcholine and prostaglandin F<sub>2a</sub>, both produce constriction of the broncheal smooth muscle. In present study, the bronchoconstricting effect of both these drugs was compared by utilizing the isolated trachea of guinea-pig as experimental tissue. Results of the present study have shown that acetylcholine produces more powerful constriction of the isolated trachea of the guinea-pig. At high concentrations, the effect of acetylcholine was more potent than that of prostaglandin F<sub>2a</sub>. But in low concentrations, the bronchoconstricting effect of both the drugs was almost similar.

### INTRODUCTION

Prostaglandins were originally discovered in human seminal fluid, but now they are known to exist in almost every mammalian tissue and have important physiological and pharmacological activities<sup>1</sup>. In vivo they are produced from the phospholipids of the cell wall. Injury to the cell wall results in the formation of long chain polyunsaturated fatty acids known as eicosanoic acids. Cyclization of the centre of the carbon chain of C-20 (eicosanoic) polyunsaturated fatty acids (arachidonic acid) results in the formation of various types of prostaglandins<sup>2</sup>. Prostaglandin F<sub>2a</sub> is a powerful bronchoconstricting agent. Modern research shows that prostaglandins may play important role in the etiology of broncheal asthma<sup>3</sup>. Various studies in the past have been conducted on the bronchoconstricting effects of acetylcholine and prostaglandin F<sub>2a</sub> separately<sup>4,5</sup>. But the review of literature revealed that the comparative study of both the substances has not been carried out. The present study was designed to see the effect of prostaglandin F<sub>2a</sub> on the broncheal smooth muscle and compare its effect with the bronchoconstricting effect of acetylcholine.

### MATERIAL AND METHODS

Experiments were performed on the isolated trachealis muscle of the adult male and female guinea-pigs. After killing the animal by a blow on its head, the chest was opened by a midline incision and trachea was dissected out. It was then transferred to oxygenated Krebs's solution maintained at room temperature. The trachea was cleared of the extraneous tissue and was cut in the form of a spiral from one end to the other<sup>6</sup>. The spiral was cut into two equal pieces. One of the spiral piece was transferred to the

---

From Ayub Medical College, Abbottabad

**SHAH NAWAZ**, MBBS, M. Phil; Asstt. Professor, Department of Pharmacology and Therapeutics

**M.A.J. KAMRAN**, MBBS, M.D. (W.G.), Professor & Head, Department of Pharmacology and Therapeutics

**QAZI RASHID AHMAD**, M.Sc., Pharmaceutical Chemist, Department of Pharmacology and Therapeutics

**ABDUL RASHID**, MBBS, M.Phil.; Associate Professor, Department of Pharmacology and Therapeutics

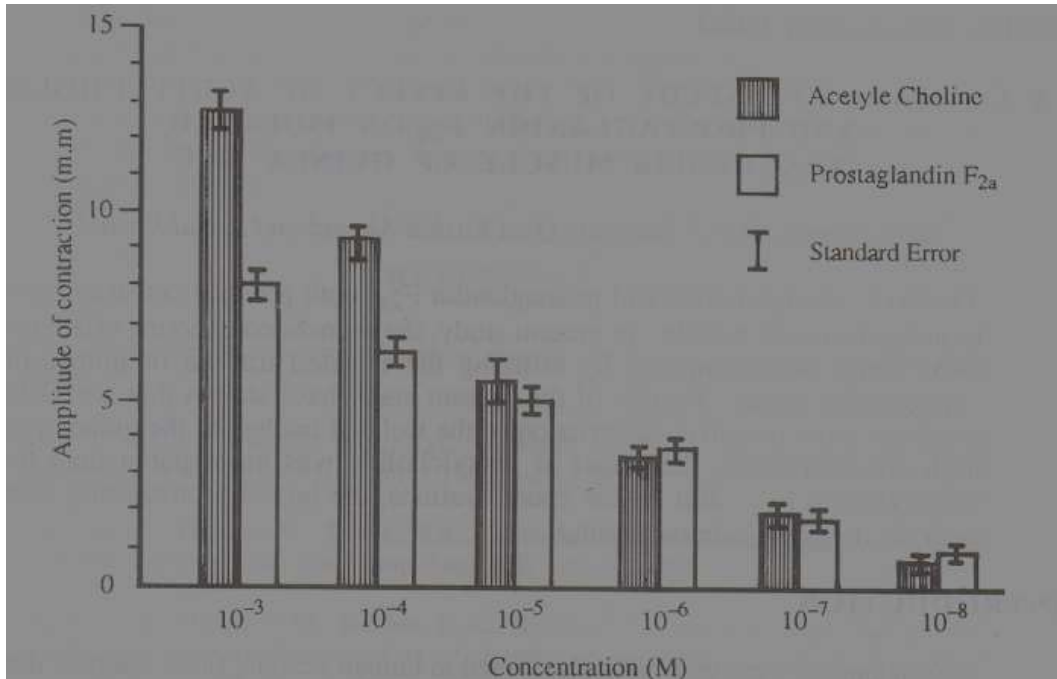


Figure 1: Comparative effect of acetyl choline and Prostaglandin  $F_{2a}$  on trachealis muscle of guinea-pig

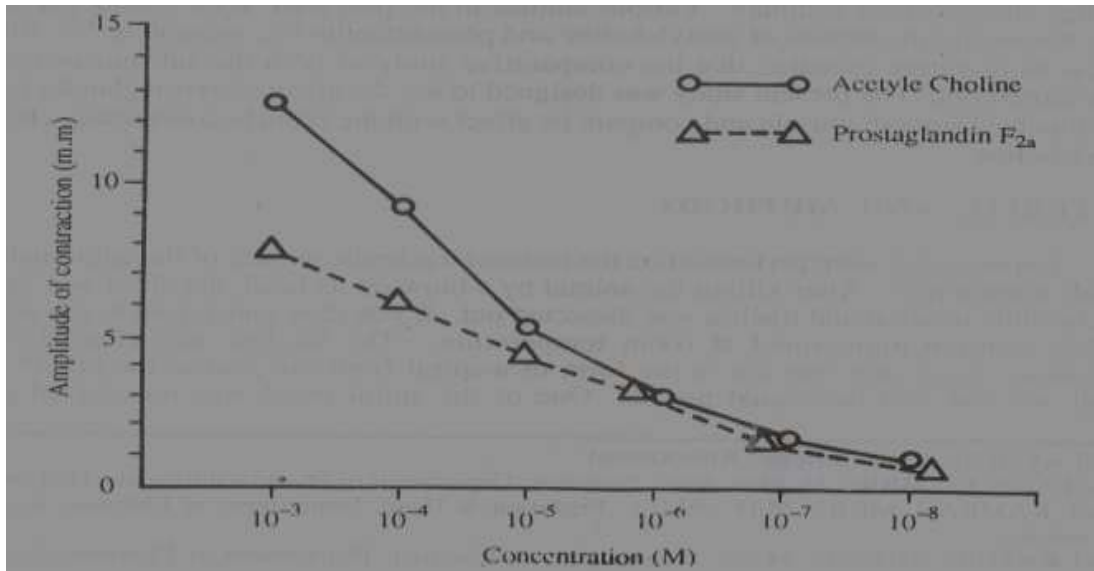


Figure 2: Response of Trachealis muscle on acetyl choline and Prostaglandin  $F_{2a}$ .

isolated tissue bath of 10 ml capacity containing oxygenated Kreb's solution maintained at 37° C. The tissue was connected to the oxygen tube at lower end and the other end was connected to the transducer. The tissue was kept at a tension of 2g. and was allowed to equilibrate for one hour. During the period of equilibration, the nutrient fluid was replaced 3-4 times. The activity of the trachealis muscle was recorded on a polygraph. The tissue was washed 2-3 times with the fresh nutrient solution. After the action of a drug was over, the tissue was kept at rest for 15 minutes before the addition of the next concentration of the drug.

Effects of acetylcholine, in concentrations of  $10^{-8}$ ,  $10^{-7}$ ,  $10^{-6}$ ,  $10^{-5}$ ,  $10^{-4}$ , and  $10^{-3}$  M, were observed on the tissues. Similarly, the effects of prostaglandin F<sub>2a</sub> in the same molar concentrations were observed on the tissues.

## RESULTS

Acetylcholine caused dose-dependent increase in the tone of normal tracheal muscle (Fig.I and II).

The mean values of the magnitude of contraction induced by  $10^{-8}$ ,  $10^{-7}$ ,  $10^{-6}$ ,  $10^{-5}$ ,  $10^{-4}$ , and  $10^{-3}$  M concentrations of acetylcholine were  $0.5 \pm 0.22$ ;  $1.8 \pm 0.32$ ;  $3.3 \pm 0.42$ ;  $5.3 \pm 0.96$ ;  $9.1 \pm 0.96$  and  $12.7 \pm 1.03$  millimeters respectively (Table: I).

**Table -1**

Response of tracheal smooth muscle of guinea-pig to acetylcholine and prostaglandin F<sub>2a</sub>.

Concentration of drug	Effect of Acetylcholine Amplitude of Contraction (m.m S.E.)	Effect of prostaglandin F <sub>2a</sub> Amplitude of Contraction (m.m. S.E.)	'P' Value
$10^{-8}$ M	$0.5 \pm 0.22$	$0.7 \pm 0.26$	> 0.05
$10^{-7}$ M	$1.8 \pm 0.32$	$1.7 \pm 0.30$	> 0.05
$10^{-6}$ M	$3.3 \pm 0.42$	$3.5 \pm 0.45$	> 0.05
$10^{-5}$ M	$5.3 \pm 0.96$	$4.8 \pm 0.46$	> 0.05
$10^{-4}$ M	$9.1 \pm 0.96$	$6.1 \pm 0.74$	< 0.05
$10^{-3}$ M	$12.7 \pm 1.03$	$7.9 \pm 0.78$	< 0.05

P' Value less than 0.05 is significant.

Prostaglandin F<sub>2a</sub> also cause dose-dependent contraction of the normal tracheal muscle. The mean values of the magnitude of contractions with  $10^{-8}$ ,  $10^{-7}$ ,  $10^{-6}$ ,  $10^{-5}$ ,  $10^{-4}$ , and  $10^{-3}$  M concentrations of prostaglandin F<sub>2a</sub> were  $0.7 \pm 0.26$ ,  $1.7 \pm 0.30$ ,  $3.5 \pm 0.45$ ,  $4.8 \pm 0.46$ ,  $6.1 \pm 0.74$  and  $7.9 \pm 0.78$  millimeters respectively (Table: I).

At high concentrations, the effect of acetylcholine was more potent than that of prostaglandin F<sub>2a</sub>. The difference was significant statistically ( $P < 0.05$ ). In low concentrations, the bronchoconstricting effect of both the drugs was almost similar. The difference was non-significant statistically ( $P > 0.05$ ).

## DISCUSSION

The present study shows that both acetylcholine and prostaglandin F<sub>2a</sub> produce a dose-dependent contraction of the isolated trachea of guinea-big. With low concentrations of

acetylcholine and prostaglandin F<sub>2a</sub>, the difference between the effects of two drugs was not significant. While in high concentrations, acetylcholine had more marked bronchoconstricting effect on the tissue than prostaglandin F<sub>2a</sub>: This indicates that acetylcholine is more efficient bronchoconstrictor of the broncheal smooth muscle than prostaglandin F<sub>2a</sub>. Both these chemicals may be implicated in the etiology of broncheal asthma, but the effect of acetylcholine seems to be more dominant. Anticholinergic drugs such as atropine and ipratropium can be used as effective bronchodilators.<sup>2</sup>

Studies in animals have shown that indomethacin is a potent inhibitor of prostaglandins and thromboxane synthesis. As it can block the effects of leukotrienes on airway smooth muscle, suggesting that some actions of leukotrienes may be mediated by the prostaglandins or thromboxane.<sup>7</sup> It has been observed that in human lungs, prostaglandin F<sub>2a</sub> enhances leukotriene production. On the other hand, prostaglandin F<sub>2a</sub> appears to be capable of suppressing leukotriene generation.<sup>7</sup>

In broncheal asthma, damage to lung tissue may occur due to antibody-antigen reaction. This causes the formation of various prostaglandins and leukotrienes. Prostaglandins are responsible for bronchoconstriction by their direct action on the smooth muscle of the lung. In addition, they also increase the production of leukotrienes which are powerful bronchoconstrictors.<sup>8</sup> Mechanism of action of prostaglandin F<sub>2a</sub> on the smooth muscle of broncheal tree is not clear, but a recent study shows that the bronchoconstricting effect of leukotrienes and prostaglandin F<sub>2a</sub> can be effectively blocked by the calcium channel blocker, nifedipine.<sup>9</sup> This suggests that both prostaglandin F<sub>2a</sub> and leukotrienes probably act by increasing the permeability of Ca<sup>++</sup> through the cell membrane of the smooth muscle of the lung.

## REFERENCES

1. Larsen, G.L; and Henson, P.M. Mediators of inflammation. *Annu. Rev. Immunol.*, 1983, I: 335-359.
2. Watanabe, A.M. Acetylcholine receptor stimulants. In: *Basic and Clinical Pharmacology*. (Ed. Katzung, B.G.); New York, Appleton and Lange; 1987,67.
3. Cuthbert, M.F. Prostaglandin and respiratory smooth muscle. In: *The prostaglandins: Pharmacological and therapeutic advances* (Cuthbert, M.A.Ed.). J.B. Lippincott Co. Philadelphia; 1973, pp.253-286.
4. Horton, E.W. Prostaglandin and smooth muscle. *Br. Med. Bull.* 1979, 35: 295.
5. Hyman, A.L. Prostaglandin and the lung. *Med. Clin. North Am.* 1981, 65:789.
6. Constantine, J.W. The spirally cut tracheal strip preparation. *J. Pharm. Pharmacol.*, 1965, 17: 384-385.
7. Sasaki, S. Mechanism of leukotriene induced contraction of isolated guinea-big tracheal smooth muscle. *Lang*; 1984, 162, 369
8. Weichman, B.M; Wasserman, M.A; and Gleason, J.G. A unique Pharmacologic antagonist of bronchoconstriction induced by leukotriene D<sub>4</sub>, Thromboxane, Prostaglandin F<sub>2a</sub> and D<sub>2</sub> invitro. *J. Pharmaco. Exp. Ther*; 1984, 228: 128-132.
9. Kohorogi, H. Nifedipine inhibits human broncheal smooth muscle contractions induced by leukotriene C<sub>4</sub> and D<sub>4</sub>, Prostaglandin F<sub>2a</sub> and potassium. *Am. Rev. Respir. Dis*; 1985, 132: 299.