Salbutamol-Induced Desensitization and Attempts to Resensitize In Vitro

MOHAMMED SULTAN MOHIDDIN SAJID

ABSTRACT

The study was carried out to desensitize spontaneously active isolated chick rectum with salbutamol in log doses starting from 100 nanogram and resensitize with various drugs as a result to revive the desensitized tissue and respond to Salbutamol. The tissue response after desensitization to alpha, beta adrenergic and muscarinic acetylcholine receptor antagonists was isotonically recorded for 10 minutes using thermostatically-controlled organ bath with aeration. The results with prazosin showed that the tissue recovered from desensitization and exhibited spontaneous motility and responded to salbutamol faster.

Keywords: Salbutamol, Chick rectum, Desensitization, Prazosin, Resensitization
Drug Solutions

Tyrodes solution (composition: sodium chloride 8.0 gm, potassium chloride 0.2 gm, magnesium chloride 0.1 gm, calcium chloride 0.2 gm, sodium bicarbonate 1.0 gm, dextrose 1.0 gm, distilled water 1 litre).

Krebs solution (composition: sodium chloride 6.9 gm, potassium chloride 0.35 gm, calcium chloride 0.28 gm, sodium bicarbonate 2.1 gm, magnesium sulphate 0.29 gm, potassium/sodium di-hydrogen phosphate 0.15 gm, dextrose 2.0 gm, distilled water 1 litre).

Salbutamol obtained as Asthalin respiratory solution purchased from drug store and prepared dilutions of 100ng, 300ng, 1μg, 10 μg, 30 μg, 100 μg, 300 μg and 1mg using distilled water. Prazosin tablets purchased from local drug store, dissolved in distilled water, filtered and prepared different concentrations in micrograms.

Materials and Method

Animals

Freshly-removed intestine of chick slaughtered at a local chicken shop was immediately put into cold 500 ml Krebs solution, transferred to laboratory and aeration provided immediately.

Methods

The rectum, the end part of the gastro-intestinal tract, was identified; 2-3 cm portion was cut and trimmed off from the mesentery and other tissues. Krebs solution was slowly passed through the lumen to flush out any contents. The rectum was mounted in a thermostatically controlled organ bath and aerated. The tone of the tissue went up to half the original baseline. Salbutamol (30 μg) produced relaxation, with washings the tone did not regain its baseline. Salbutamol (100 μg) did not produce any response showing desensitization (Fig 1).

As shown in Fig 2, salbutamol (10 μg) produced a brief contraction followed by relaxation; with washings the tone did not rise and the rectum was exposed to salbutamol in log doses starting from 100 nanogram for 1 min each to record the tissue responses, until tissue regained its baseline. Salbutamol produced relaxations; they should not be resensitized, salbutamol in microgram concentrations produced no response, with wash, the tone went up

Results

Salbutamol (SAL) in log dose range of 100 ng to 30 μg produced dose dependent relaxations; 100 μg of salbutamol produced initial contraction followed by relaxation. Salbutamol (300 μg) produced slight relaxation; salbutamol (1 mg) did not produce any response showing desensitization (Fig 1).

Continuing further, tissue responses with prazosin (PRA) in different microgram concentrations were observed for 5-10 minutes. Finally, the tissue regained the original baseline and motility which can be resensitized, salbutamol produced relaxations. Prazosin (30 μg) did not produce any response, with wash, the tone went up

Published online: January 31, 2013
Resensitizing Salbutamol-Induced Desensitization

Fig 3. Effect of salbutamol (SAL) on isolated chick rectum and influence of various concentration of prazocin (PRA) in vitro

Fig 4. Effect of cumulative doses of salbutamol (SAL) on isolated chick rectum and influence of various concentration of prazocin (PRA) in vitro

Discussions

Salbutamol produced desensitization at beta-2 receptor in Fig 1. Many of our experiments showed that salbutamol is not specific beta-2 adrenergic receptor agonist, it acts on both alpha and beta receptors i.e., producing immediate contraction followed by a slower relaxation and this could be the component which is responsible for sudden deaths in asthma patients [9–14]. Salbutamol produced response by acting on alpha-1 and beta-2 receptors till receptor saturation, Prazosin per se produced tone and motility, and it seems to facilitate relaxation. Combination of salbutamol-prazosin by alternate administration showed beneficial effects. This is fairly satisfactory combination which might help in preventing the desensitization. The numerous experiments are quite supportive that salbutamol and prazosin combination could be a suitable combination in the therapy of asthma. The actual mechanism involved in tissue resensitization is subject of further research.

It is concluded that to certain extent we succeeded in achieving our goal of finding out the possible combination of prazosin with salbutamol which can help the asthma patient in getting relief without any danger or emergencies.

References


**CURRENT AUTHOR ADDRESSES**

Mohammed Sultan Mohiddin Sajid, E-mail: sultanmsajidm@gmail.com