Salbutamol-Induced Desensitization and Attempts to Resensitize In Vitro

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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
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 transferred into Petri dish containing Krebs solution. Salbutamol (1 mg) did not produce any trimmed off from the mesentery and other tissues. Krebs response showing desensitization (Fig 1).

The 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 tissue response was isotonically recorded (tension) baseline. Salbutamol (30 μg) produced relaxation, with weight 1 gm, magnification 10 times) in non-cumulative and cumulative manner that this tissue invariably had Salbutamol (100 μg) did not produce any response spontaneous motility. The rectum was exposed to showing desensitization. Prazosin (10 μg) produced Salbutamol in log doses starting from 100 nanogram for tone and motility, then 10 μg salbutamol produced some 1 min each to record the tissue responses, until tissue relaxation, with washings the tone regained its baseline stopped responding which is said to be desensitized and 10 μg salbutamol produced prominent relaxation. Continuing further, tissue responses with prazosin (PRA) in different microgram concentrations were initially to produce any tone and motility, regained the original baseline and motility which can be and subsequent doses of 10 μg, 30 μg and 100 μg resensitized, salbutamol in microgram concentrations salbutamol produced relaxations. Prazosin (30 μg) did not produce any 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 300 ng, 1 μg, 10 μg, 30 μg, 100 μg, 300 μg and 1 mg using distilled water. Prazosin tablets purchased from local drug store, dissolved in distilled water, filtered and prepared different concentrations in micrograms.

Figure 1. Effect of various concentrations of salbutamol (SAL) on isolated chick rectum in vitro

Figure 2. Effect of salbutamol (SAL) on isolated chick rectum and influence of prazocin (PRA) in vitro
and finally prazocin 100 μg did not produce any response.

As shown in Fig 3, salbutamol (3 μg) produced relaxation, with washings the tone did not regain to the baseline. Subsequent addition of two doses of salbutamol (10 μg) produced slight relaxations. Prazocin (10 μg) produced tone and motility and in the presence of prazocin, SAL (10 μg) produced relaxations. Similarly prazocin in several fixed doses of 30 μg and a single dose of 10 μg produced tone and motility followed by prominent relaxation with salbutamol (10 μg). Continuing in second tracing in the Fig 3, four doses of salbutamol 30 μg were added with intermittent washings, the first dose did not produce any response, the second dose produced some relaxation, third and fourth doses did not produce any response. Prazocin (30 μg) did not produce any response, a second higher dose of prazocin (100 μg) produced tone and motility and in the presence of 10 μg salbutamol-produced relaxation.

Similarly prazocin in different doses was added and produced tone and motility and in its presence salbutamol-produced relaxations.

As shown in Fig 4, first dose of 10 μg salbutamol produced relaxation; second dose of salbutamol (10 μg) produced slight relaxation. Subsequent three cumulative doses of 10 μg salbutamol did not produce any response could be due to desensitization. Prazocin (100 μg) did not produce any response, second dose of 30 μg prazocin produced contraction. Salbutamol (10 μg) produced relaxation. Subsequent addition of three cumulative fixed doses of 10 μg salbutamol did not produce any response but the tone fell down. Two sets of prazocin and cumulative doses of salbutamol produced contractions followed by relaxations respectively.

**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 prazocin with salbutamol which can help the asthma patient in getting relief without any danger or emergencies.

**REFERENCES**


