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
new safety requirements for LABA that is, use of
LABAs are contraindicated without the use of an
asthma controller medication such as an inhaled
corticosteroid. Single-ingredient LABAs should only be
used in combination with an asthma controller
medication; they should not be used alone. The role of
beta-2 adrenoceptor in both the pathogenesis and
treatment of asthma has become a subject of intense
speculation and investigation for the last 25 years. This
study was carried out to resensitize the salbutamol-
duced desensitization in spontaneously active isolated
chick rectum.

**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
drilled to Petri dish containing Krebs solution,
transferred into Petri dish containing Krebs solution, and
trimmed off from the mesentery and other tissues. Krebs
response showing desensitization (Fig 1).

**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, 3 µg, 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.

**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).

As shown in Fig 2, salbutamol (10 µg) produced a
brief contraction followed by relaxation; with washings
thermostatically controlled organ bath and aerated. The
tone of the tissue went up to half the original
tissue response was isotonically recorded (tension
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.139
and 10 µg salbutamol produced prominent relaxation.

Continuing further, tissue responses with prazosin
140 With washing, the tone did not rise and finally
(PRA) in different microgram concentrations were
salbutamol 10 µg produced slight relaxation. Second
observed for 5-10 minutes. Finally, once the tissue
142 dose of prazosin (10 µg) reproduced tone and motility,
gained the original baseline and motility which can be
143 and subsequent doses of 10 µg, 30 µg and 100 µg
resensitized, salbutamol in microgram concentrations
144 salbutamol produced relaxations. Prazosin (30 µg) did
produced responses.

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

**Fig 2. Effect of salbutamol (SAL) on isolated chick rectum and influence of prazosin (PRA) in vitro**

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Resensitizing Salbutamol-Induced Desensitization

![Graph](image)

**Fig 3.** Effect of salbutamol (SAL) on isolated chick rectum and influence of various concentration 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 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 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**


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