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

Asthma, from the Greek (asthma) meaning gasp, is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, increased airway hyper-responsiveness to allergens, poor asthma control, airflow obstruction and bronchial spasm. Symptoms include wheezing, coughing, chest tightness and shortness of breath. Medications used to treat asthma are divided into 2 general classes: long acting beta2 agonists (LABA) such as salmeterol (Albuterol), producing desensitization resulting in an exacerbation of symptoms which may lead to refractory asthma and death.

1. Quick-relief medications used to treat acute range of bronchial constrictor agents. By using these symptoms including Short acting beta-2 agonists medicines too frequently, the efficiency may decline, (SABA) such as salbutamol (Albuterol), producing desensitization resulting in a exacerbation of symptoms which may lead to refractory asthma and death.

2. Long-term, control medications used to prevent further exacerbations including inhaled corticosteroids have much longer side chains resulting in a 12-hour range such as hydrocortisone and beclomethasone; inhaled effect. While patients report improved symptom control, long acting beta-2 agonists (LABA) such as salmeterol these drugs do not replace the need for routine rescers and formoterol; inhaled anti-cholinergics such as and their slow onset means the short acting dilators are ipratropium and tiotropium; leukotriene modifiers such asomalizumab. A health advisory alerting the public to findings that Beta2-adrenoceptor (beta2-AR) agonists are the show the use of LABA could lead to worsening of most commonly used bronchodilators in both the acute and in some cases death. In 2008, members of USFDA recommended withdrawing approval for chronic mono-therapy with long-acting and/or short-acting medicines in children. In 2010, USFDA gave...
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-
induced 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
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
tissue response was isotonically recorded (tension
showing desensitization. Salbutamol produced
relaxation.

Salbutamol (SAL) on in spontaneously active isolated
chick rectum.

**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
mg, 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
transferred into Petri dish containing Krebs solution
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
the tissue response was isotonically recorded (tension
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
showing desensitization. Prazosin (10 μg) produced
salbutamol in log doses starting from 100 nanogram for
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.

Prazosin (10 μg) produced prominent relaxation. 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
dose of prazosin (10 μg) reproduced 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
produced relaxations. Prazosin (30 μg) did
not produce any response, with wash, the tone went up
Resensitizing Salbutamol-Induced Desensitization

![Graph 1](ijpt.iiums.ac.ir)

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

![Graph 2](ijpt.iiums.ac.ir)

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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