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, 43 increased airway hyper-responsiveness to allergens [5], poor asthma control [6] and even increased mortality [7]; effects which may be include wheezing, coughing, chest tightness and secondary to beta2-AR desensitization. SABAs are the shortness of breath. Medications used to treat asthma are divided into 2 general classes: and provide effective bronchial protection to a wide range of bronchial constrictor agents. By using these medicines too frequently, the efficiency may decline, producing desensitization resulting in an exacerbation of symptoms which may lead to refractory asthma and death. LABAs are similar in structure to SABAs but 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, these drugs do not replace the need for routine rescuers and formeterol; inhaled anti-cholinergics such as and their slow onset means the short acting dilators are ipratropium and tiotropium; leukotriene modifiers such as still be required. However for the past 4 decades, there as montelukast and zafirlukast; mast cell stabilizers such as has been a continuing debate concerning whether as sodium cromoglicate and nedocromil sodium; methyl 60 regular chronic treatment with these drugs may be doing xanthenes such as theophylline and immunomodulators more harm than good [8]. In 2005, the USFDA released such as omalizumab. a health advisory alerting the public to findings that

Beta2-adrenoceptor (beta2-AR) agonists are the most commonly used bronchodilators in both the acute and in some cases death. In 2008, members 44 rescue and maintenance therapy of asthma. However, 65 of USFDA recommended withdrawing approval for chronic mono-therapy with long-acting and/or short- these medications 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-
duced desensitisation 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 transferred into Petri dish containing Krebs solution, showed no response showing desensitization (Fig 1).

As shown in Fig 2, salbutamol (10 μg) produced a brief contraction followed by relaxation; saltbutamol (300 μg) produced slight relaxation. Salbutamol (1 mg) did not produce any 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. 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. Prazocin (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. and 10 μg salbutamol produced prominent relaxation. Continuing further, tissue responses with prazosin (PRA) in different microgram concentrations were observed for 5-10 minutes. Finally, once the tissue dose of prazocin (10 μg) reproduced tone and motility, regained the original baseline and motility which can be observed. Subsequent doses of 10 μg, 30 μg and 100 μg resensitized, salbutamol in microgram concentrations salbutamol produced relaxations. Prazocin (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 relaxation. Salbutamol (300 μg) produced slight relaxation. Salbutamol (1 mg) did not produce any

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**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 prazocin (PRA) in vitro
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 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 a fairly satisfactory combination which might help in preventing the desensitization. The numerous experiments are quite supportive that salbutamol and prazocin 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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