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, an increase in airway hyper-reactivity to allergens or other irritants, and a chronic and recurring airway inflammation. The symptoms usually include wheezing, coughing, chest tightness, and chest pain, which are often triggered by factors such as cold air, infections, exercise, or stress. The key feature of asthma is the reversible increase in airflow obstruction and bronchial hyper-responsiveness to a wide 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 an exacerbation levosalbutamol, terbutaline and bitolterol, of symptoms which may lead to refractory asthma and

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 an exacerbation levosalbutamol, terbutaline and bitolterol, of symptoms which may lead to refractory asthma and

2. Long-term control medications used to prevent death. LABAs are similar in structure to SABAs but further exacerbations including inhaled corticosteroids have much longer side chains resulting in a 12-hour 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 rescuers and formoterol; inhaled anti-cholinergics such as salbutamol, terbutaline and bitolterol, of symptoms which may lead to refractory asthma and 3. as montelukast and zafirlukast; mast cell stabilizers such as sodium cromoglicate and nedocromil sodium; methyl 60 regular chronic treatment with these drugs may be doing xanthenes such as theophylline and imunomodulators 61 more harm than good [8]. In 2005, the USFDA released such as omalizumab.

3. Beta2-adrenergceptor (beta2-AR) agonists are the 63 show the use of LABA could lead to worsening of most-commonly used bronchodilators in both the acute 64 symptoms and in some cases death. In 2008, members rescue and maintenance therapy of asthma. However, 65 of USFDA recommended withdrawing approval for chronic mono-therapy with long-acting and/or short- 66 these medications in children. In 2010, USFDA gave
new safety requirements for LABA that is, use of 0
LABAs are contraindicated without the use of an 0
inhaled corticosteroid. Single-ingredient LABAs should only be 0
used in combination with an asthma controller 0
medication; they should not be used alone. The role of 0
beta-2 adrenergic receptor in both the pathogenesis and 0
treatment of asthma has become a subject of intense 0
speculation and investigation for the last 25 years. This 0
study was carried out to resensitize the salbutamol- 0
induced desensitization in spontaneously active isolated 0
chick rectum.

MATERIALS AND METHOD

Animals

Freshly-removed intestine of chick slaughtered at a 0
local chicken shop was immediately put into cold 0
500 ml Krebs solution, transferred to laboratory and aeration 0
provided immediately.

Methods

The rectum, the end part of the gastro-intestinal 0
tract, was identified; 2-3 cm portion was cut and 0
transferred into Petri dish containing Krebs solution. The 0
rectum was mounted in a thermostatically controlled organ bath and aerated. The 0
tone response was isotonically recorded (tension 0
weight 1 gm, magnification 10 times) in non-cumulative 0
and cumulative manner that this tissue invariably had 0
salbutamol (10 μg) did not produce any response 0
spontaneous motility. The rectum was exposed to 0
showing desensitization. Prazosin (10 μg) produced 0
salbutamol in log doses starting from 100 nanogram for 0
1 min each to record the tissue responses, until tissue 0
relaxation, with washings the tone regained its baseline 0
stopped responding which is said to be desensitized. 0
and 10 μg salbutamol produced prominent relaxation.

Continuing further, tissue responses with prazosin 0
(PRA) in different microgram concentrations were 0
observed for 5-10 minutes. Finally, once the tissue 0
dose of prazosin (10 μg) reproduced tone and motility, 0
regained the original baseline and motility which can be 0
resensitized, salbutamol in microgram concentrations 0
produced relaxations. Prazosin (30 μg) did not produce any response, with wash, the tone went up
Resensitizing Salbutamol-Induced Desensitization

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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