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 4 characterized by variable and recurring symptoms, 44 responsiveness to allergen [5], poor asthma control [6] and air flow obstruction and bronchial spasm. Symptoms 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 mainstay for the acute symptomatic treatment of asthma are divided into 2 general classes: 48 and provide effective bronchial protection to a wide range of bronchial constrictor agents. By using these symptoms including Short acting beta-2 agonists 50 medicines too frequently, the efficiency may decline, such as salbutamol (Albuterol), producing desensitization resulting in an exacerbation of symptoms which may lead to refractory asthma and even increased mortality [7]. While patients report improved symptom control, 51 long acting beta-2 agonists (LABA) such as salmeterol these drugs do not replace the need for routine rescuers and formeterol; inhaled anti-cholinergics such as ipratropium and tiotropium; leukotriene modifiers such 58 still be required. However for the past 4 decades, there is 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 chronic management of asthma. However, most commonly used bronchodilators in both the acute 66 these medications in children. In 2010, USFDA gave

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The tone did not rise and further, tissue responses with prazosin μg produced slight relaxation. 100 used alone.

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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 gastrointestinal tract, was identified; 2-3 cm portion was cut and transferred into Petri dish containing Krebs solution, showing desensitization (Fig 1).

As shown in Fig 2, salbutamol (10 μg) produced a brief contraction followed by relaxation. Salbutamol (300 μg) produced slight relaxation. Salbutamol (1 mg) did not produce any trimmed off from the mesentery and other tissues. Krebs response showing desensitization (Fig 1).

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 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 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 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 relaxation. Salbutamol (300 μg) produced slight transferred into Petri dish containing Krebs solution, 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.
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. Similarly 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 relaxations.

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 desensitization 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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