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, hyper-responsiveness to allergen, poor asthma control and even increased mortality. 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: and provide effective bronchial protection to a wide range of bronchial constrictor agents. By using these symptoms including Short acting beta-2 agonists (SABA) such as salbutamol (Albuterol), producing desensitization resulting in an exacerbation levosalbutamol, terbutaline and bitolterol. of symptoms which may lead to refractory asthma and death. LABAs are similar in structure to SABAs but have much longer side chains resulting in a 12-hour duration to SABAs but 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 terbutaline and formoterol; inhaled anti-cholinergics such as and their slow onset means the short acting dilators are ipratropium and tiotropium; leukotriene modifiers such still be required. However for the past 4 decades, these drugs have much longer side chains resulting in a 12-hour such as theophylline and immunomodulators more harm than good. 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 symptoms and in some cases death. In 2008, members 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 drug; 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 transferred into Petri dish containing Krebs solution, aerated and with washings the tone regained its baseline. As shown in Fig 2, salbutamol (10μg) produced a brief contraction followed by relaxation. Salbutamol (300μg) produced slight relaxation. Salbutamol (1 mg) did not produce any trimmed off from the mesentery and other tissues. Krebs, 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 the tone did not regain its baseline. Salbutamol (100 μg) did not produce any response 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. 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 prazosin (10 μg) reproduced tone and motility, regained the original baseline and motility which can be observed for 5-10 minutes. And subsequent doses of 10 μg, 30 μg and 100 μg resensitized, salbutamol in microgram concentrations salbutamol 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.201. Similarly prazocin in different doses was added and produced tone and motility and in its presence salbutamol-produced relaxations.202. As shown in Fig 4, first dose of 10 μg salbutamol produced relaxation; second dose of salbutamol (10 μg)211. 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)217. 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.

REFERENCES


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