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-reactivity 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 bitotol. of symptoms which may lead to refractory asthma and death. LABAs are similar in structure to SABAs but they have much longer side chains resulting in a 12-hour effect. While patients report improved symptom control, these drugs do not replace the need for routine rescuers and formeterol; inhaled anti-cholinergics such as ipratropium and tiotropium; leukotriene modifiers such as omalizumab. There has been a continuing debate concerning whether symptoms and in some cases death. In 2005, the USFDA released 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 therapy of asthma. However, USFDA recommended withdrawing approval for these medications in children. In 2010, USFDA gave...
new safety requirements for LABA that is, use of 67
LABAs are contraindicated without the use of an 68
inhaled corticosteroid. Single-ingredient LABAs should only be 69
used in combination with an asthma controller 70
medication; they should not be used alone. The role of 71
beta-2 adrenoceptor in both the pathogenesis and 72
treatment of asthma has become a subject of intense 73
speculation and investigation for the last 25 years. This 74
study was carried out to resensitize the salbutamol- 75
induced desensitization in spontaneously active isolated 76
chick rectum.

**Materials and Method**

**Animals**

Freshly-removed intestine of chick slaughtered at a 81
local chicken shop was immediately put into cold 500 82
ml Krebs solution, transferred to laboratory and aeration 83
provided immediately.

**Methods**

The rectum, the end part of the gastrointestinal 86
tract, was identified; 2-3 cm portion was cut and 87
trimmed off from the mesentery and other tissues. Krebs. 88
solution was slowly passed through the lumen to flush 89
out any contents. The rectum was mounted in a 90
thermostatically controlled organ bath and aerated. The 91
tissue response was isotonically recorded (tension 92
baseline) in log dose range of 100 ng to 30 93
µg produced dose dependent relaxations; 100 µg of 94
Salbutamol (SAL) in log dose range of 100 ng to 30 95
µg produced dose dependent relaxations; 100 µg of 96
Salbutamol produced initial contraction followed by 97
relaxation. Salbutamol (300 µg) produced slight 98
relaxation. Salbutamol (1 mg) did not produce any 99
response showing desensitization (Fig 1).

As shown in Fig 2, salbutamol (10 µg) produced a 100
brief contraction followed by relaxation; with washings 101
the tone of the tissue went up to half the original 102
tone and motility, showing desensitization. Prazosin (10 µg) 103
produced relaxations. Salbutamol in log doses starting from 100 nanogram for 104
tone and motility, then 10 µg salbutamol produced some 105
relaxation, with washings the tone regained its baseline 106
and subsequent doses of 10 µg, 30 µg and 100 µg 107
produced responses.

**RESULTS**

**Drug Solutions**

Tyrodes solution (composition: sodium chloride 8.0 107
gm, potassium chloride 0.2 gm, magnesium chloride 0.1 108
gm, calcium chloride 0.2 gm, sodium bicarbonate 1.0 109
gm, dextrose 1.0 gm, distilled water 1 litre).

Krebs solution (composition: sodium chloride 6.9 110
gm, potassium chloride 0.35 gm, calcium chloride 0.28 111
gm, sodium bicarbonate 2.1 gm, magnesium sulphate 0.29 112
gm, potassium/sodium di-hydrogen phosphate 0.15 113
gm, dextrose 2.0 gm, distilled water 1 litre).

Salbutamol obtained as Asthalin respiratory solution 114
purchased from drug store and prepared dilutions of 115
100ng, 300ng, 1µg, 10 µg, 30 µg, 100 µg, 300 µg 116
and 1mg using distilled water. Prazosin tablets 117
purchased from local drug store, dissolved in distilled 118
water, filtered and prepared different concentrations in 119
micrograms.

Prazosin (10 µg) produced relaxations. Salbutamol 120
produced relaxation, with washings the tone regained its 121
baseline and subsequent doses of 10 µg, 30 µg and 100 µg 122
produced responses.
Restensitizing 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 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 prazosin with salbutamol which can help the asthma patient in getting relief without any danger or emergencies.

REFERENCES


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