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A BRIEF REVIEW ON SALBUTAMOL THERAPY

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Abstract:

Salbutamol, a selective β2-adrenergic receptor agonist, is one treatment for acute asthmatic bronchospasm episodes and other chronic bronchopulmonary diseases. This article's goal is to make clear in the chemistry, mechanism, pharmacokinetics, indication, dosage, side effect and overall information regarding the salbutamol therapy. The drug is useful for treating symptoms of bronchospasm as well as preventing it due to its potent smooth muscle relaxant properties. Salbutamol, the first selective SABA to be widely utilized in clinical practice, was initially made available in 1968. As a 4-(2-amino-1-hydroxyethyl)-2-(hydroxymethyl) phenol with a tert-butyl group bonded to the nitrogen atom, Salbutamol belongs to the class of phenylethanolamines with molecular weight: 239.31 g/mol. How much salbutamol is prescribed depends on the patient's age, the condition being treated, and the formulation being used. Salbutamol converts cyclic AMP (cAMP) by reversibly binding to β2-receptors. This subsequently sets off a series of intracellular events that block the contraction of the smooth muscle of the bronchi, thus facilitating bronchodilation. Peak plasma salbutamol concentration is seen about two hours following oral dose, which is quickly and well absorbed. But only 50% of the drug's bioavailability is achieved due to the first-pass impact, which is caused by the intestinal mucosa's strong hepatic and pre-systemic metabolism. The drug is used to treat bronchial asthma, bronchospasm, COPD and premature labour. Preterm labour is inhibited and hence pregnancy is prolonged by oral salbutamol, an effective technique. Salbutamol principally induces hypokalaemia by β2-stimulating the skeletal muscle Na+/K+-ATPase pump, which moves potassium intracellularly. Lactic acidosis may potentially result from acute salbutamol poisoning. Headache and muscle cramps are the common side effects associated with salbutamol therapy.

Keywords: Salbutamol, Beta 2 agonist, Asthma drug, Bronchodilator, Albuterol.

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INTRODUCTION:

Salbutamol is a selective β2-adrenergic receptor agonist, used to treat both acute asthmatic bronchospasm episodes and other chronic bronchopulmonary diseases. The medication's strong smooth muscle relaxant qualities make it suitable for both bronchospasm prevention and symptomatic treatment. In 1968, salbutamol was released as the first selective SABA that was widely used in clinical practice [1]. Salbutamol is considered to be among the safest and most effective medications that are vital to healthcare systems by the World Health Organization (WHO) [2]. It eases respiratory issues immediately. The effects remain for three to five hours after it begins to work, usually within a few minutes. Salbutamol is supplied in puffer form. For those who have trouble using an inhaler, it may occasionally be administered as tablets, capsules, or syrup [3]. Oral, intramuscular, subcutaneous, inhalation, and subcutaneous injection are all possible ways to give salbutamol. The administration method now used in daily practice is inhalation due to its higher efficacy at lower doses. For severe acute asthma, IV salbutamol is utilized as a second- or third-line treatment [4]. Whether swallowed or breathed, it absorbs quickly and thoroughly. Humans exposed orally to either syrup or immediate-release tablets had peak plasma concentrations of salbutamol about two hours after exposure; the plasma half-life varied from 2.7 to 5 hours. Anxiety, trembling, headaches, rapid heartbeats, and dizziness are typical adverse effects associated with salbutamol therapy. Low blood potassium levels, an erratic heartbeat, and a development of bronchospasm are examples of serious adverse effects [5].

Chemistry of salbutamol

As a 4-(2-amino-1-hydroxyethyl)-2-(hydroxymethyl) phenol with a tert-butyl group bonded to the nitrogen atom, Salbutamol belongs to the class of phenylethanolamines [6].

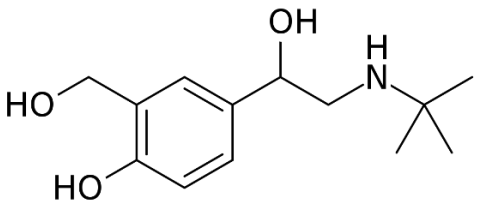

Figure 1: Chemical structure of salbutamol

It is a chiral medication that has isomers for (R) and (S) [7]. Its binding to the human β2-adrenoceptor links its pharmacological activity to the (R)-enantiomer. The (S)-enantiomer's activity is debatable [8][9][10].

Molecular formula: C13H21NO3
Molecular weight: 239.31 g/mol

Dosing of salbutamol

The age of the patient, the ailment being treated, and the formulation being utilised all influence the recommended dosage of salbutamol.

- For asthma symptoms and bronchospasm
  - Salbutamol inhaler 100 micrograms (mcg) per dose:

    Adults- To ease symptoms, use 1-2 puffs every 4 hours up to 4 times (eight puffs) in a 24-hour period. Two puffs fifteen minutes prior to exposure is the recommended dosage to avoid symptoms brought on by exercise or other triggers.
    Children- To relieve symptoms, provide 1 puff (up to 2 puffs if necessary) every 4 hours for a maximum of 4 times (8 puffs) in a 24-hour period. In order to mitigate the effects of exercise or other triggers, it is advised to take 1 puff (15 minutes before exposure; up to 2 puffs if necessary).

  - Salbutamol dry powder inhaler 200 mcg per dose:

    For the relief of symptoms, adults, adolescents 12 years of age and older, and youngsters between the ages of 4 and 11 should inhale once up to four times daily. One inhalation, 10 to 15 minutes prior to exposure, is the suggested dose to prevent symptoms brought on by exercise or other triggers.

  - Salbutamol oral syrup 2 mg/5 ml:

    -Adults (those over 18): Five to twenty millilitres, up to four times a day, is the typical dosage.
    -Children over 12: Three or four times a day, 5 to 10 millilitres is the typical dosage.
    -Children ages 6 to 12: the recommended dosage is 5 millilitres three or four times per day.
    - Children aged between 2 and 6 years: The usual dose is 2.5 ml to 5 ml, 3 or 4 times a day.

  - Salbutamol tablets 2mg and 4mg:

Adults: Three or four times a day, a dose of 4 mg is advised. This could be gradually increased by your doctor to a maximum of 8 mg three or four times per day. It is possible to treat certain people effectively with 2 mg three or four times each day.

For children older than twelve, a dose of two to four milligrams, three or four times a day is advised [11].

- For Severe bronchospasm

  - Salbutamol solution for infusion 5mg/5ml:

    Adults: A gradual injection of 250 micrograms (4 micrograms/kg bodyweight) is the suggested dosage. The dosage can be repeated as required. For a gradual intravenous administration, 250 micrograms in 5 mL (50 micrograms/mL) is an appropriately diluted solution.
  - Salbutamol injection 500 micrograms/ml:

    Adults: 500 micrograms (8 micrograms/kg bodyweight) is the suggested dose for subcutaneous or intramuscular injection, and this should be repeated every 4 hours as needed [11].

Mechanism of salbutamol

Salbutamol converts cyclic AMP (cAMP) by reversibly binding to β2-receptors. This subsequently sets off a series of intracellular events that block the contraction of the smooth muscle of the bronchi, thus facilitating bronchodilation.

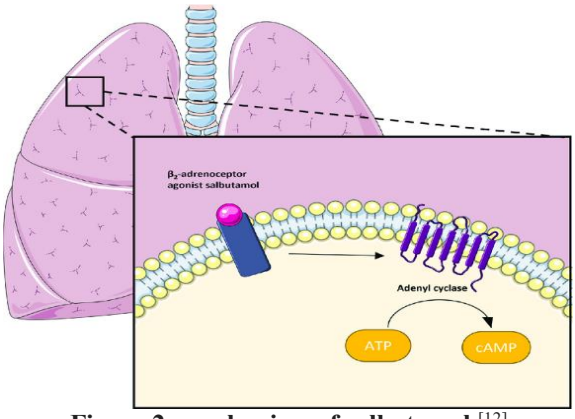

Figure 2: mechanism of salbutamol [12].

The majority of adrenergic receptors in bronchial smooth muscle are beta2 adrenoceptors, while beta1 adrenoceptors are found in the heart. Additionally, 10% to 50% of all beta-adrenoceptors are found in the human heart [13][14].

Pharmacokinetics of salbutamol

Numerous factors affect salbutamol's pharmacokinetics. The amount of medication that enters the airways, absorption, and, ultimately, effectiveness and the profile of side effects are influenced by the formulations and the delivery method (MDI or DPI) that is employed [15].

A study conducted by Kruizinga MD et al. shows the concentration–time curve of mean salbutamol concentration in plasma after intravenous administration of 500µg salbutamol as shown below;

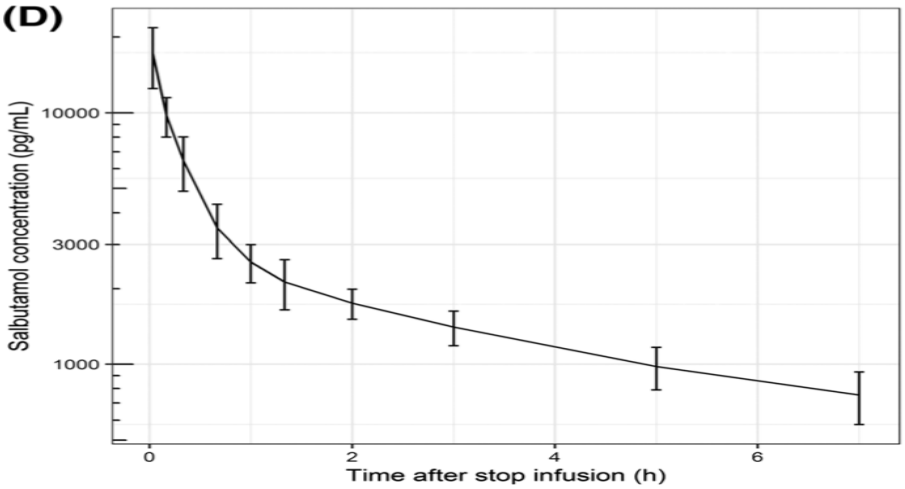

Figure 3: concentration–time curve of mean salbutamol concentration in plasma(±SD) after intravenous administration of 500µg salbutamol (n= 9) [16].

Generally, Peak plasma salbutamol concentration is seen about two hours following oral dose, which is quickly and well absorbed. But only 50% of the drug's bioavailability is achieved due to the first-pass impact, which is caused by the intestinal mucosa's strong hepatic and pre-systemic metabolism [18].

Salbutamol is primarily metabolised into the 4′-O-sulphate ester via sulphate conjugation, which has very little pharmacologic action [17]. Compared to (S)-salbutamol, which metabolises up to ten times more slowly than (R)-salbutamol, the former is eliminated much more quickly [19][20].

Table 1: Pharmacokinetic parameters of salbutamol.

Oral bioavailability	50%
Half life	4 hours
Onset of action	Oral: 30 minutes Inhalations: 5-15 minutes
Duration of action	8-12 hours

Indications of salbutamol

Salbutamol medication is mainly indicated for the treatment of following conditions:

- ✓ Bronchial asthma
- ✓ Bronchospasm
- ✓ COPD
- ✓ Premature labour.

Preterm labour is inhibited and hence pregnancy is prolonged by oral salbutamol, an effective technique [21]. The study's findings by Motazedian S et al. show that, after 48 hours, terbutaline and salbutamol seemed to be equally effective tocolytic drugs [22].

Adverse drug reactions of salbutamol

Salbutamol principally induces hypokalaemia by β2-stimulating the skeletal muscle Na+/K+-ATPase pump, which moves potassium intracellularly [23]. β2-agonist-induced hypokalaemia can be severe enough to induce ECG abnormalities such QT prolongation and U-waves.

Lactic acidosis may potentially result from acute salbutamol poisoning [24]. It is believed that β2-adrenergic stimulation amplifies cAMP-mediated lipolysis and gluconeogenesis [25]. As a result, there is a greater conversion of plasma glucose to lactate and pyruvate. This process is consistent with the observation that salbutamol can also result in momentary hyperglycaemia.

When β2-agonists are used in excess, they can lose their receptor specificity and result in arrhythmias such atrial fibrillation, supraventricular tachycardia, and ventricular tachycardia, as well as tachycardia and cardiac ischemia [26].

Other typical salbutamol side effects include:

- Headache
- muscle cramps
- feeling shaky

Salbutamol's uncommon and extremely uncommon adverse effects include:

- Changes in sleep patterns
- Muscle tension
- Chest pain

A study by P.J. Phillips et al. shows [27] the effect of salbutamol vs rimiterol in pulse rate after infusion of drug as shown below;

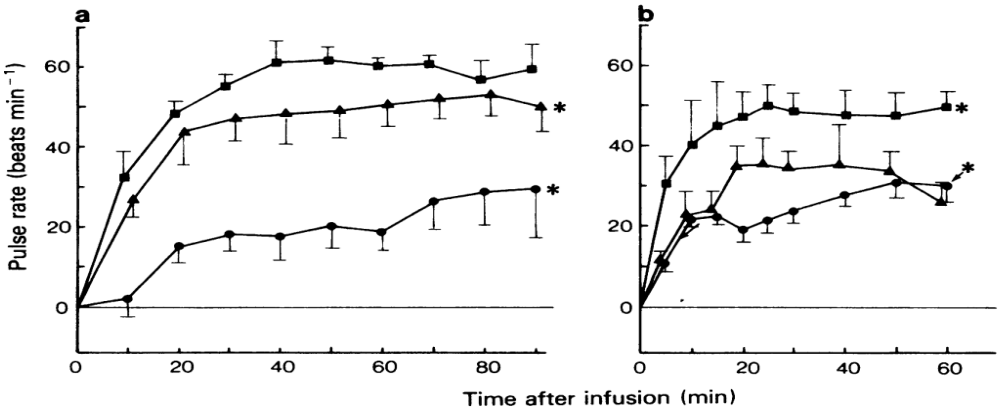

Figure 4: Effect of a) salbutamol (●0.1microgram kg^{-1} min^{-1}, ▲ 0.4microgram kg^{-1} min^{-1}, ■ 0.7microgram kg^{-1} min^{-1}) and b) rimiterol (●0.11microgram kg^{-1} min^{-1}, ▲ 0.22microgram kg^{-1} min^{-1}, ■ 0.44microgram kg^{-1} min^{-1}). [27]

Elevated level of pulse rate associated with salbutamol use have found by the study conducted by P.J. Phillips et al. [27].

CONCLUSION:

In conclusion, Salbutamol, a selective β2-adrenergic receptor agonist, is used to treat chronic bronchopulmonary disorders as well as acute bouts of asthmatic bronchospasm. It instantly relieves respiratory problems. After it starts to act, which normally happens within a few minutes, the benefits last for three to five hours. Salbutamol can be administered orally, intramuscularly, subcutaneously, by inhalation, or by subcutaneous injection. The age of the patient, the ailment being treated, and the formulation being utilised all influence the recommended dosage of salbutamol. Salbutamol binds to β2-receptors reversibly to convert cyclic AMP (cAMP). This then triggers a sequence of intracellular processes that prevent the bronchi's smooth muscle from contracting, allowing for bronchodilation After an oral dose that is rapidly and effectively absorbed, the peak plasma salbutamol concentration is often observed two hours later. However, the intestinal mucosa's robust hepatic and pre-systemic metabolism results in a first-pass impact that only achieves 50% of the drug's bioavailability. The drug is used to treat bronchial asthma, bronchospasm, COPD and premature labour. Salbutamol principally induces hypokalaemia by β2-stimulating the skeletal muscle Na+/K+-ATPase pump, which moves potassium intracellularly. Head ache and muscle cramp are the common side effect of salbutamol. Lactic acidosis may potentially result from acute salbutamol poisoning. Salbutamol can also elevate the pulse rate in the patients.

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