How to Induce Arrhythmias with Salbutamol

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12.1 Introduction

Salbutamol is a selective beta2 adrenoreceptor agonist causing bronchodilation. It is commonly used for the treatment of acute bronchoconstriction episodes such as acute asthmatic crisis or status asthmaticus. It is also used for treatment of chronic obstructive pulmonary disease. Salbutamol is the sulphate salt of the albuterol, a phenethylamine with bronchodilator properties (Fig. 12.1). As a β2 selective agonist, intravenous salbutamol may also serve as a pharmacologic agent for the induction of arrhythmias during electrophysiological study (EPS). At St. Joseph's Heart Center, Rzeszów, salbutamol (Salbutamol WZF, Polfa Warszawa S.A.) is a main drug used during EPS in case of arrhythmia non-inducibility.

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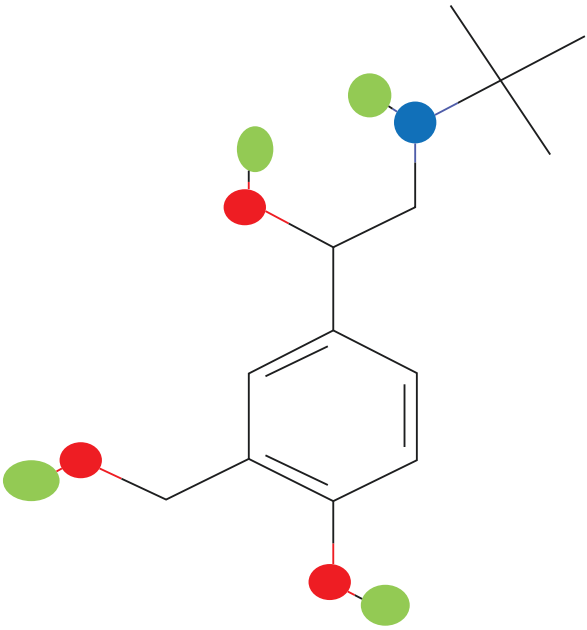

Fig. 12.1 Chemical structure of salbutamol: C13, H21, NO3

12.2 Electrophysiological Effects

Infusion of salbutamol significantly shortens sinus node cycle length and sinus node recovery time. It also shortens effective refractory period of the AV node, significantly shortens AH interval and the Wenckebach point (WP), and decreases atrial and ventricular effective refractory periods [1–5]. Salbutamol is more likely to have impact on sinus node's activity compared to the AV node—it was shown that the presence of β2 adrenoreceptors is more common in the sinoatrial node than in the right atrium [6–8].

12.3 Doses of Salbutamol

At low-infusion rates, salbutamol produces peripheral vasodilatation with a decrease in diastolic blood pressure and reflex increase in norepinephrine plasma concentration and sympathetic cardiac activity.

12.3.1 In Acute Asthmatic Crisis

After *salbutamol's nebulization*, the onset of action is present within 15 min. *Salbutamol's infusion* recommended doses:

– An initial bolus of 15 μg/kg (maximum 250 μg) over 15 min

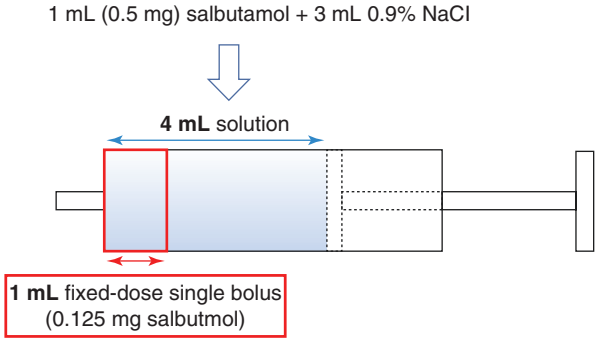

Fig. 12.2 Syringe preparation

– An Intravenous infusion dose of 1–2 μg/kg/min. Intravenous salbutamol can be diluted with 5% glucose or 0.9% sodium chloride.

12.3.2 In the EP Lab

Doses used in the setting of EPS differ from those used during acute asthmatic crisis. A recommended single bolus dose for use in the EP lab equals 0.125 mg of salbutamol.

12.3.2.1 Infusion Preparation

1. The patient preparation should be conducted following standard EP lab procedure regimens. Patient should undergo fasting and IV access should be established prior to induction.
2. An infusion pump is NOT necessary for salbutamol administration.
3. Mix 1 mL (0.5 mg) of salbutamol with 3 mL of 0.9% NaCl into the syringe (Fig. 12.2).
4. A single, fixed dose consists of 1 mL solution (0.125 mg of salbutamol).
5. After a single bolus is administered, the heart rate should increase, usually within 20–60 s programmed stimulation can be performed when heart rate reaches >130% of baseline (Fig. 12.3).
6. Intravenous administration of salbutamol can be repeated when necessary (i.e., in case of limited effect of a single-dose bolus).
7. After ablation, administration of salbutamol can be repeated when appropriate.
8. After the EP study, potassium levels should be checked (as salbutamol induces intracellular increase of potassium with subsequent decrease of potassium levels in blood serum).
9. Half-life elimination of salbutamol ranges from 4 to 6 h.

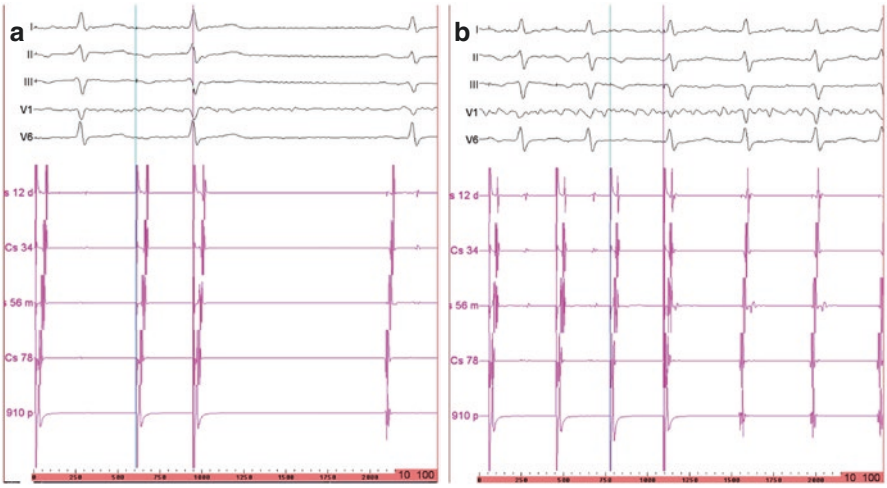

Fig. 12.3 Non-inducibility at baseline (**a**) and induction of typical AVNRT after single fixed dose of intravenous salbutamol (**b**)

12.4 Contraindications and Precautions for Salbutamol Use During EPS

Contraindications

- Intolerance of salbutamol or any of the intravenous ingredients
- Age <6 years

Precautions

- Heart failure
- Ischemic heart disease
- Hemodynamically significant left ventricular outflow tract obstruction
- Hypertension
- Hypokalemia
- Aneurysm
- Hyperthyroidism
- Pheochromocytoma
- Diabetes
- Intolerance of sympathomimetic drugs

12.5 Salbutamol's Possible Side Effects

Most common, minor side effects:

- Tremor
- Anxiety

- Headache
- Muscle cramps, muscle tremors (especially hands)
- Dry mouth
- Palpitation
- Nausea, vomiting
- Agitation, hyperactivity
- Feeling of warmth during bolus administration
- Hypotension caused by peripheral vasodilation
- Hyperglycemia
- Hypophosphatemia

Rare, major side effects
- Angioedema
- Bronchial spasm
- Hypotension
- Shock

12.6 Clinical Use

Literature on the use of salbutamol during EPS is limited. However, in cases of arrhythmia non-inducibility, and when isoprenaline is unavailable, salbutamol can be easily adapted for EP testing. It may also increase the sensitivity of EPS directly after catheter ablation. A few examples of relations between salbutamol use and arrhythmia occurrence were described in the literature.

Al-Hillawi et al. demonstrated that some patients who were treated with salbutamol or serbutaline could later develop arrhythmias such as monomorphic or bifocal ventricular premature contractions and short runs of paroxysmal atrial tachycardia [9]. Trachsel et al. reported two cases of salbutamol-induced supraventricular tachycardia (SVT) successfully converted to sinus rhythm after adenosine administration 0.1 mg/kg, without worsening of asthma symptoms [10].

A case of SVT after standard administration of salbutamol was also reported [11]—an 8-year-old patient receiving salbutamol developed an episode of orthodromic reentrant tachycardia (ORT) of 240 bpm. Two other cases in the pediatric population were also reported by Keller [12] and Cook [13]. The first case was a 19-month-old infant with salbutamol-induced SVT, converted to sinus rhythm after exposure of the infant's face to iced water. The second case was a 4-year-old child with salbutamol-induced SVT, converted to sinus rhythm after intravenous adenosine. Although adenosine has the potential of bronchospasm induction in asthmatic patients and was safely administrated in the presented case, its use requires cautiousness in former patients.

Refractory SVT can also occur as a result of salbutamol toxicity, as previously reported [14].

In patients with Wolf-Parkinson-White syndrome a nebulized salbutamol can induce ORT several minutes after administration [15, 16]. Attempts however to

induce ORT with salbutamol infusion only, without the need of programmed stimulation, may fail [15].

Also other supraventricular arrhythmias can be enhanced by salbutamol. Induction of focal atrial tachycardia was also documented previously [17].

High doses of salbutamol can lead to ventricular fibrillation. Uysal et al. reported a case of 24-year-old female, who developed hypokalemia 2.3 mmol/L and subsequent ventricular fibrillation after suicide attempt with high dose of salbutamol (76 mg) [18].

12.7 How to Induce Arrhythmias in the EP Lab

At St. Joseph's Heart Center, the main indication for administration of salbutamol during EPS is when SVT cannot be induced with programmed stimulation at baseline. When SVT suspicion is high, a single bolus of salbutamol can lead to induction of clinical SVT and subsequent appropriate treatment of arrhythmia. Due to sinus tachycardia, which usually follows a single dose of salbutamol, and due to improvement of conduction properties of atrioventricular node, more aggressive stimulation protocols should be delivered, usually with up to triple extrastimuli on an eight-beat drive train (Fig. 12.3).

Salbutamol can also be used for induction of premature ventricular complexes (PVCs). Activation mapping has a higher value for PVC localization than pacemapping, and this can be facilitated by salbutamol infusion. Induction of PVCs may occur directly after salbutamol infusion, sometimes boosted with programmed ventricular or atrial stimulation, or within minutes after the increase of heart rate was obtained ("the washout" phenomenon) (Fig. 12.4).

Concealed or intermittent preexcitation patterns may also be revealed in patients without visible preexcitation on ECG at rest. After ablation of an accessory pathway, retrograde conduction can also be verified after infusion of salbutamol.

Adverse events of salbutamol administration at the time of EPS may occur very rarely, but have mostly been documented to be palpitations. Sinus tachycardia may last within hours after EPS and can be well controlled with small doses of beta-blockers.

The use of salbutamol for EP testing can be an attractive alternative when other drugs are unavailable. Its electrophysiological utility should be confirmed in future studies.

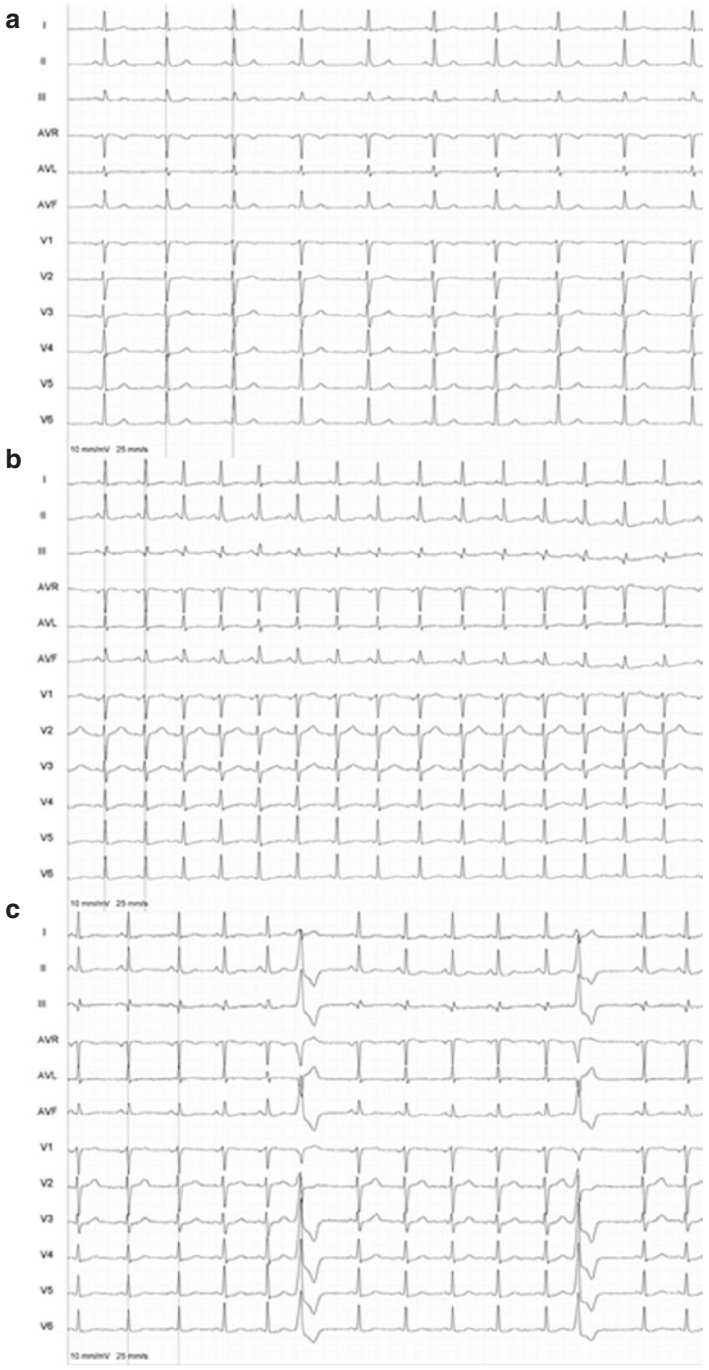

Fig. 12.4 Example of a "washout" phenomenon. Panel **a**: baseline ECG with no PVCs, Panel **b**: sinus tachycardia after single dose of salbutamol, Panel **c**: after heart rate decreases, clinical PVCs show up

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