Tremor and Paradoxical bronchospasm caused by Terbutaline

Deyan Wang
Dechang People's Hospital https://orcid.org/0009-0007-5548-6449
Jinping Liu
Dechang People's Hospital https://orcid.org/0009-0004-2959-8541
Bin Liang
Dechang People's Hospital https://orcid.org/0009-0002-1960-7171
Jing Zhang
Dechang People's Hospital https://orcid.org/0009-0003-9164-1347
Ya Zhou
Dechang People's Hospital https://orcid.org/0009-0001-4523-4164
Xu Zhang (zhangxuxlws@126.com)
Dechang People's Hospital https://orcid.org/0000-0002-2395-3547

Case Report

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Abstract

Background

Common adverse reactions of terbutaline include skeletal muscle tremor, headache,tachycardia, palpitations, hypokalemia and so on.Bronchospasm caused by terbutaline is rarely reported. This article reports one case of severe bronchospasm caused by nebulized terbutaline sulfate inhalation therapy.

Case presentation

A 51-year-old female patient was admitted to hospital with acute bronchitis.The main complaints were cough, sputum and wheezing. She has no history of drug or food allergies. On the day of admission, terbutaline nebulization treatment immediately caused limb tremor and bronchospasm. After glucocorticoid, aminophylline, non-invasive respiratory support and other symptomatic treatments,the patient improved on the 4th day.

Conclusion

The mechanism of terbutaline leading to bronchospasm is still unclear. The tert-butylline on the chemical structure of terbutaline may bind to proteins to produce IgE-mediated bronchospasm, The excipient ededidine disodium and the osmotic pressure of the nebulized diluent may also lead to bronchospasm. During the clinical treatment, hypotonic nebulizing dilutions should be avoided, and close monitor should be taken in case ofpossible fatal bronchospasm.

Background

Terbutaline is a short-acting β2 -adrenoceptor agonist [1], which has a strong effect on bronchial smooth muscle expansion. The Nebulized inhalation is one of the most common ways to administer terbutaline. Currently, terbutaline is widely used in the clinical practice for the treatment of bronchospasm, such as asthma and chronic bronchitis. Common adverse effects include skeletal muscle tremor, headache, tachycardia, tachycardia, palpitations and hypokalemia.

Elevated plasma levels of lactic acid (lactic acidosis) have also been reported[2–3]. Of concern, bronchospasm may occur in rare cases following inhalation of short-acting beta2 agonists [1, 4].No cases have been reported in the Chinese population.Current literature mentions that the short-acting β2 -adrenoceptor agonists salbutamol, levosalbutamol, terbutaline, ipratropium bromide, salmeterol, and pirbuterol can cause paradoxical bronchospasm [5–10], with salbutamol being more common and terbutaline being rare. In this paper, we report a case of severe bronchospasm caused by nebulizer inhalation treatment with terbutaline sulfate.

Case Presentation

A 51-year-old female patient was admitted to hospital with acute bronchitis. The main complaints were cough, sputum and wheezing. She has no history of drug or food allergies.

On the day of admission (D1),the patient present tremor of the extremities and dyspnea after 9 minutes of nebulised terbutaline inhalation. Immediately hydrocortisone sodium succinate 200mg intravenous bolus was given. The patient's symptoms were sitll not relieved, following loss of consciousnessand unable to respond .Physical examination was pulse 130 /min, respiratory rate of 30 /minute, blood pressure 150/88mmHg and blood oxygen saturation 74% (nasal cannula oxygen 2L/min). 8 minutes after onset of symptoms, the blood gas analysis were PH 7.08, PaCO2 104mmHg, PaO2 70mmHg. After 36 minutes, aminophylline with 5% glucose injection at the speed of per 2ml/h continuous micropumping was given. After treatment, the patient's consciousness was restored, her limbs did not tremble again, and her vital signs were measured with a pulse of 140 /min, respiratory rate of 24/minute, blood pressure of 130/90mmgHg, and blood oxygen saturation of 90% (nasal cannula oxygen 2L/min).2 hours later, her blood gas analysis was PH 7.24, PaCO2 56mmHg and PaO2 54mmHg.

The patient was then admitted to the ICU for further treatment as she was still suffering from hypoxia. After four days, the patient had no dyspnea. Vital signs and blood gas analysis of the patients after the ICU are shown in Table 1.

Discussion And Conclusion

Terbutaline may cause skeletal muscle tremor, but bronchospasm, contrary to its pharmacological effects, is rare. Ayed et al. reported a patient using terbutaline nebulization to cause dyspnea, cough, wheezing, and hypoxia (85% oxygen saturation), tachycardia (110 beats per minute)[1]. All short-acting β2 -adrenoceptor agonists approved by the FDA have warnings about causing paradoxical bronchospasm [4], and the instructions for terbutaline sulfate also suggest that the drug may cause bronchospasm, but the incidence rate the mechanisms are tillunknown.

Some studies suggest that bronchospasm caused by β2 -adrenoceptor agonists may be mediated by IgE, and that salbutamol, terbutaline, and pibuterol share common structural features: a tert-butyl group attached to a nitrogen atom may explain that they can all bind to proteins to produce IgE and cause bronchospasm [11–12]. Other studies have suggested that β2 -adrenoceptor agonists induced bronchospasm may be related to inhalant excipients (propellants and surfactants), preservatives (benzalkonium bromide), osmotic pressure, and/or pH [1,8]. Benzalkonium bromide has been mentioned several times in preservatives [13–15], and edediding disodium has also been reported [16] .In this case, the patient used terbutaline sulfate nebulizate, which does not contain preservatives and excipients, but its excipients contain ededine disodium [1], which may be the cause of bronchospasm. In addition, osmotic pressure of nebulized fluids can cause bronchoconstriction, hypertonic buffers have been shown to cause the release of histamine from normal human basophils and mast lung cells, and both hypotonic or hypertonic saline solutions can induce bronchoconstriction[1]. The 2 ml of sterile water used as a nebulization dilution in this patient may also be related to the hypotonic nature of this nebulization solution.

β2 -adrenoceptor agonists are first-line agents for the treatment of airway spasm diseases such as asthma and chronic obstructive pulmonary disease. However, we should keep vigilance during use. They may lead to paradoxical bronchospasm, a serious adverse reaction, which is extremely rare but fatal. This case shows that terbutaline can rapidly cause bronchospasm after nebulization. The nebulized diluent used at the same time can also cause bronchoconstriction. The use of sterile water for injection should be avoided during the clinical use of terbutaline, and close monitoring is also required.

Abbreviations

ICU: intensive care unit;

PaCO2: Carbon dioxide partial pressure

PaO2: Oxygen partial pressure

K: Serum potassium concentration

PH: Potential of Hydrogen

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

All data are available in the manuscript.

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

DY Wang and B Liang designed and drafted this manuscript. X Zhang and JP Liu researched related articles, drafted and revised manuscript. All authors interpreted and revised the fnal approval of the manuscript to be published. All authors contributed equally in the preparation of this manuscript.

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Table

Table 1: Vital signs and blood gas analysis of the patients

	respiratory rate times/min	pulses times/min	blood pressure mmHg	PH	PaO2 mmHg	PaCO2 mmHg	Lactic acid mmol/L	K mmol/L
D1	22	147	134/88	7.24	54	56	1.0	3.3
D2	20	108	108/60	7.41	87	39	0.3	3.0
D3	21	96	115/64	7.34	111	48	0.6	3.8
D4	20	65	98/59	7.41	110	47	0.5	3.4

Note: D1 means on the day of admission, D2 means second day of admission, D3 means third day of admission, D4 means fourth day of admission.