Clinical Case Report

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Use of low-dose neostigmine intravenously in the treatment of thyroid storm-induced severe tachycardia in patient during huge pelvic mass resection

A case report and review of literature

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Abstract

Rationale: Thyroid storm is a rare and life-threatening metabolic crisis because of an emergent release of excess thyroid hormone. Sinus tachycardia induced by excess thyroid hormone may result in congestive heart failure due to decreased diastolic filling time.

Patient concerns: A controlled hyperthyroidism patient with severe sinus tachycardia.

Diagnoses: A controlled hyperthyroidism patient was induced thyroid storm during huge pelvic mass resection.

Interventions: Application of low-dose neostigmine and β-antagonist esmolol to control the heart rate (HR) avoided hemodynamic collapse.

Outcomes: The patient improved dramatically following application of low-dose neostigmine instead of esmolol to control the HR avoided hemodynamic collapse.

Lessons: Our case suggests that neostigmine, an acetylcholinesterase inhibitor, may warrant further investigation in patients with thyroid storm-induced severe sinus tachycardia.

Abbreviations: ECG = electrocardiogram, $EtCO_2$ = end-tidal carbon dioxide, FT4 = free thyroxine, PTU = propylthiouracil, TT3 = total tri-iodothyronine.

Keywords: acetylcholinesterase inhibitor, neostigmine, sinus tachycardia, thyroid storm

1. Introduction

Neostigmine, as a reversible acetylcholinesterase inhibitor, is routinely used in anesthesia as a muscle relaxants antagonist by inhibiting breakdown of acetylcholine to increase agonist concentration at nicotinic and muscarinic receptors outside the central nervous systerm.[1–3] By interfering with the metabolism of acetylcholine, neostigmine indirectly stimulates both nicotinic and muscarinic receptors.[3] Over 80 years ago, neostigmine was reported to treat supraventricular arrhythmias.[1,2,4] Because of bradycardic arrest and fatality following common neostigmine application, clinical use of neostigmine was largely abandoned to lower heart rate (HR) as an agent.[5,6] However, our report describes a case in which neostigmine was successfully used to reduce thyroid storm-increased HR after other modalities had failed in anesthetized patient.

2. Case descriptions

A 32-year-old, 47 kg, 162 cm, female with controlled hyperthyroidism and huge pelvic mass, presented for huge pelvic mass resection. Her regular medications include propylthiouracil (PTU) and propranolol. Her thyroid function tests showed a suppressed TSH < 0.012 mU/L (normal range, 0.35–4.94 mU/L), with free thyroxine (FT4) 0.68 ng/dL (normal range, 0.70–1.48 ng/dL), and total tri-iodothyronine (TT3) 2.19 nmol/L (normal range, 1.34–2.73 nmol/L).

Physical examinations showed pulse rate (PR) of 63/minute and blood pressure (BP) of 121/71 mmHg. The electrocardiogram (ECG) showed no abnormalities.

The patient was premedicated with injection luminal (0.1 g, i.m.) 30 minutes before entering operation room (OR). The monitoring including pulse oximetry, ECG, noninvasive BP, end-tidal carbon dioxide ($EtCO_2$), bispectral index (BIS) was set up after the patient's presentation in operation room. Invasive BP and nasopharyngeal temperature was achieved after intravenous access. General anesthesia was induced with dexmedetomidine 1 μg/kg, sufentanyl 0.5 μg/kg, and propofol 1.5 mg/kg, and cisatracurium 1.5 mg/kg. Anesthesia was maintained with sevoflurane 1.5% to 3%, remifentanil 0.1 to 0.2 μg/kg/min. During intubation, she was at a rate of 55 to 70 beats/min. After about 5 minutes, she gradually developed sinus tachycardia at a rate of 125

Editor: N/A.

This work was supported by NSFC (No. 81500982).

The authors declare no conflicts of interest.

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Medicine (2018) 97:14(e0300)

Received: 16 December 2017 / Received in final form: 5 March 2018 / Accepted: 7 March 2018

http://dx.doi.org/10.1097/MD.0000000000010300

to 140 beats/min. The value of BIS was 53~60. So attempts to slow the sinus tachycardia with esmolol 0.5 mg/kg resulted in acute hemodynamic deterioration. Esmolol was firstly chosen because only esmolol was available to slow the HR in the operating room. After 1 minute, she had no response but gradually increased the sinus tachycardia at a rate of 165 beats/min. Esmolol 0.5 mg/kg was injected again and failed to lower HR. Esmolol 1 mg/kg was injected again and there was also no effect. It presented exacerbating her hemodynamic deterioration because of inadequate diastolic filling resulting from her rapid HR. The conventional strategy had proven to be ineffective. We decided to attempt to lower the HR with neostigmine, an acetylcholinesterase inhibitor, typically used to reverse neuromuscular blockade in anesthetized patients. Initially, intravenous boluses of neostigmine 2 mg were given. Approximately 2 minutes after the initial bolus, the HR began to fall and remained stable at a rate of 60 to 80 beats/min. The loading dose of neostigmine reduced HR within minutes, associated with improvement in systemic perfusion. This suggested that neostigmine control of tachycardia contributed significantly to a dramatic reversal of cardiogenic shock in this patient. PTU 200 mg and hydrocortisone 200 mg were also administered. Initial laboratory thyroid function analysis showed a suppressed TSH < 0.02 mU/L, with free thyroxine (FT4) 6.1 ng/dL and TT3 7.0 nmol/L.

Surgical procedure lasted for 4 hours, HR and BP were stable with total fluids 2500 mL. Patient was transferred to ward after extubation with a PCA pump when the continuous monitoring shown all her vital signs were stable. She was administered hydrocortisone 100 mg every 8 hours and PTU 200 mg every 6 hours.[7] The patient was continued on hydrocortisone 25 mg every 12 hours and PTU 200 mg every 6 hours and was discharge 7 days later after intensive treatment. Then she was transitioned to oral PTU 80 mg daily.

Ethical approval for this study was approved by the Ethical Committee of Huazhong University of Science and Technology.

3. Discussion

Thyroid storm is an acute exacerbation of hyperthyroidism due to a sudden release of thyroid hormones into the systemic circulation and can be triggered by surgery or anesthesia.[8,9] Commonly reported symptoms of thyrotoxicosis crisis are irritability, dehydration, hyperthermia, tachycardia, rhythm disturbances, and congestive heart failure. The aims of treatment in thyroid storm are to inhibit the central thyroid hormone synthesis and secretion, restrain peripheral thyroxine T4 to triiodothyronine (T3) conversion and avoid target-organ injury by high-level thyroid hormone.[7] Several general therapies for thyrotoxicosis crisis could be considered in this setting:

(1) PTU is standard of treatment in thyroid storm. The preferred treatment is due to its properties of inhibiting peripheral T4 to T3 conversion and therefore achieving rapid control of the thyrotoxicosis.[7,9]
(2) Beta blockers have been proved in preclinical and clinical models to improve heart injury by excessive thyroid.[7] Non-selective β blockers, such as esmolol should be initiated as soon as possible to avoid circulation collapse.[9] However, in this case there was no effect after repeated administration of esmolol.
(3) Hydrocortisone is the preferred treatment for thyroid crisis due to its properties of reducing target-organ damage by high-level thyroid hormone.

In anesthetized patients, the primary physical finding of thyroid crisis is cardiac tachyarrhythmias. During operation, it's difficult to differ from between thyroid storm-induced tachycardia and light anesthesia-induced tachycardia. Thyroid crisis is a dangerous, albeit rare, endocrinological emergency.[7] In anesthetized patient, primary reported finding of light anesthesia also presents as tachycardia, which is the highest in the rate of anesthesia-related complication.[10,11] In this case, the value of BIS showed that the anesthesia was deep enough for the operation. It's primary diagnosed as thyroid crisis because of a gradual increase in HR after anesthesia and a-3-month-history of hyperthyroidism. Early identification and prompt initiation of therapeutic interventions are needed to minimize complications and prevent the mortality associated with this condition that can occur if left untreated.

To the best of our knowledge, this is the first case report of a young patient presented with thyroid storm-induced severe sinus tachycardia, treated by acetylcholinesterase inhibitor neostigmine. A number of clinical reports showed that neostigmine was used to recover severe supraventricular tachycardic when conventional treatments failed.[1,2,4] The mechanisms of acetylcholinesterase inhibitor are to treat tachyarrhythmias by decreasing cardiac stress and increasing the activity of cardiac vagus nerve.[12–14] In our case, neostigmine was successfully used to inhibit the effect of excess thyroid hormone on cardiac tachyarrhythmias.

The use of neostigmine to lower HR should be given by physicians who are extremely familiar with their use. Application of neostigmine can result in a severe side effect of profound bradycardia, even cardiac arrest.[15] It has been reported that neostigmine was routinely used in anesthesia as a muscle relaxants antagonist, resulting in patient death.[1,5,6] Patients being treated with neostigmine should be concurrent administration of muscarinic antagonist atropine to avoid severe bradycardia and inhibit bronchial secretions and the endotracheal intubation and mechanical ventilation were readily available.

The use of neostigmine to decrease HR requires careful patient monitoring and selection.[1] During application of neostigmine, it should be readily available to do the artificially pacing the heart because the severe side effect of bradycardia can occur. Since neostigmine slows the HR by prolonging the role of acetylcholine released from the vagus nerves, intact autonomic innervation of the heart must be available in the patients.[1,16] For example, the intended bradycardic response will not be exhibited in transplant patients because of the completely denervated donor heart.

4. Conclusions

To the best of our knowledge, this is the first case report of a young patient presented with thyroid storm-induced severe sinus tachycardia, treated by acetylcholinesterase inhibitor neostigmine. Conventional treatments with using β-antagonist esmolol was not effective to avoid congestive heart failure. Acetylcholinesterase inhibitor may be considered as an alternative measure to lower the HR in carefully selected patients with refractory supraventricular rhythms in an intensive care setting.

Author contributions

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