Efficacy of atropine combined with paroxetine in vagus nerve excitatory panic disorder

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Abstract: Panic disorder is often associated with the autonomic nervous system pattern—sympathetic activation and parasympathetic (vagal) withdrawal. However, we present one special case here to show a totally reversed pathogenesis—vagal activation occupying the leading role, which requires atropine to cure the patient’s symptoms. Through this report, it is reasonably proven that panic disorder may be a heterogeneous condition, whose mechanism might be the imbalance between the sympathetic and parasympathetic tone.

Keywords: panic disorder, vagal activation, bradycardia, atropine

Introduction
Anxiety disorders are thought to be the most prevalent psychiatric disorders in the general population. Their somatic expression is often associated with the autonomic nervous system pattern—sympathetic activation and parasympathetic (vagal) withdrawal. Among various anxieties, panic disorder (PD) typifies the occurrence of sudden, recurrent and unexpected panic attacks, reaching a peak in approximately 10 minutes. According to the etiopathogenesis of anxiety disorders, clinicians are used to choosing antidepressants or sedatives to treat PD. The panic attack symptoms of patients, described as palpitations, trembling or shaking, sensations of shortness of breath or smothering, faint, fear of dying, and hot flashes, gradually disappear within the periodic treatment.

However, there are few records on the special modality of PD, which shows a totally reversed pathogenesis—vagal activation occupying the leading role. This case report aims to describe the exceptional condition and discuss the treatment.

Case report
Mrs JYH, a 41-year-old, married, Chinese female, has been suffering from sudden episodes of tingling, numbness, sensations of shortness of breath, and giddiness since the age of 33. She has been treated with many kinds of anxiolytics for a sufficient amount of time but with little effect. Recently, her symptoms were exacerbated with the occurrence of two daily episodes of attacks; she also began to experience the feeling of impending death, and sometimes even fainted, eyes closed. After the attack, she was able to recall the whole process and complained of fatigue and poor sleep with the fear of recurrence which restricted her social functioning markedly. As a result, she came to our hospital. There were no abnormalities on the physical examination and laboratory tests including the tilt-table testing. Her symptoms were reckoned to be common PD according to the diagnostic criteria of the International Classification of Diseases (ICD)-10. Therefore, she began treatment with paroxetine 20 mg/day until the dose was terminated.
increased to 40 mg/day and clonazepam 3 mg/day. However, her symptoms did not improve except for the sleep quality. During her hospitalization, we happened to find her heart rate was 55 beats per minute during a panic attack. After that, it recovered to 70 beats per minute. Based on the variation of her heart rate, we prescribed atropine to control her bradycardia occurring during these episodes. She was treated with atropine 0.6 mg/day, increased to 1.8 mg/day after 1 week. Because of her signs of worry and hopelessness between the intervals of attacks, we did not cease the treatment with paroxetine. Through the treatment for 5 weeks, the patient had remission of PD and her basic heart rate also increased to 76 beats per minute but no obvious somatic discomfort was observed. As a result, she was discharged from hospital. One month later, she visited our outpatient department for follow-up. We were glad to find that she had recovered her normal life with nearly no panic attacks at all.

**Discussion**

PD usually has a lifetime prevalence of 1% to 3% and sudden attacks of fear accompanied by cardiac symptoms such as palpitations, chest pain, and tachycardia. In modern reviews, PD, also the first anxiety disorder to which heart rate variability analysis was applied due to the salience of tachycardia, is dominated by a focus on sympathetic aberrations such as tonic sympathetic nervous system hyperarousal. However, there has been a tendency to emphasize the sympathetic nervous system and neglect the parasympathetic function. According to the report of Massana et al, they also found that some PD patients showed symptoms of bradycardia and generalized sweating, which they called pseudoneurological symptoms. According to their research, they concluded that PD may be a heterogeneous condition and can be sorted into different subtypes. We hypothesize that the reason atropine, used on this specific patient, was effective could be due to the activation of vagus nerve during her panic attack, which was similar to the special subtype of PD mentioned above. As is known to all, the vagus nerve, innervating the sinoatrial and atrioventricular node, could cause a greater reduction in heart rate when stimulated. The patient in this case just showed related inhibitive symptoms such as fainting and bradycardia instead of tachycardia during episodes. Considering this, we assumed that her PD is triggered by the vagus nerve hyperarousal. As a result, we treated her with atropine, a potent cardiac parasympatholytic blocking agent, which could increase the heart rate and is widely used to treat bradycardia. To our delight, the fact demonstrates the efficacy of atropine combined with paroxetine in curing this specific case of PD.

Our case just suggests that the pathogenesis of PD might be the imbalance between the sympathetic and parasympathetic tone, whereas the imbalance could be manifested by the activation of either sympathetic nervous system or parasympathetic nervous system. Hence, when we are confronted with patients with PD, we should pay attention to the variation of their heart rate to differentiate the type of PD and prescribe the pertinent medicine.

**Disclosure**

The authors have no conflicts of interest to disclose in this work.

**References**