

## Case Report

# Suspected agomelatine-induced tongue temperature perception abnormality: a case report

Li-Lei Lei<sup>1</sup>, Min-Cai Qian<sup>1</sup>, Shi-Liang Wang<sup>2</sup>, Chen-Jie Ge<sup>2</sup>

<sup>1</sup>Department of Neurosis and Psychosomatic Diseases, Huzhou Third Municipal Hospital, The Affiliated Hospital of Huzhou University, Huzhou 313000, Zhejiang, China; <sup>2</sup>Quality Management Division, Huzhou Third Municipal Hospital, The Affiliated Hospital of Huzhou University, Huzhou 313000, Zhejiang, China

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**Abstract:** Tongue temperature perception abnormality typically refers to an alteration in the tongue's ability to sense temperature, which may manifest as diminished or lost perception of heat or cold, or abnormal sensations in the absence of significant temperature changes. This case report describes a 60-year-old female who developed tongue temperature perception abnormality following the use of agomelatine. The patient had a history of good health, with no surgical or chronic disease history, and no family history of mental illness. She presented with symptoms of emotional depression, irritability, and insomnia, and was diagnosed with depression. Initially treated with sertraline and oxazepam, the treatment was changed to agomelatine due to poor sleep quality. One week after starting agomelatine, the patient reported tongue discomfort, which progressed to temperature perception abnormality, leading to burns and blisters. After discontinuing agomelatine and switching to duloxetine treatment, the symptoms rapidly improved. This case suggests a potential adverse drug reaction induced by agomelatine. The report emphasizes the importance of monitoring drug side effects and timely intervention in clinical practice.

**Keywords:** Tongue temperature, Perception abnormality, Case report, Agomelatine

### Introduction

Agomelatine is a “star” drug in antidepressants, which not only has a higher efficiency and cure rate in terms of antidepressant treatment, but also has the characteristics of regulating patients' sleep structure and biological rhythm, improving patients' dynamic fatigue and anhedonia, good tolerance, less influence on sexual function, no influence on weight, and small withdrawal reaction [1]. Therefore, agomelatine has more advantages for patients with depression accompanied by residual sleep rhythm disturbance, lack of motivation, fatigue, anhedonia, etc., and patients who cannot tolerate adverse reactions caused by monoamine antidepressants such as sexual function decline, weight gain, lethargy, gastrointestinal discomfort, etc. [2]. Agomelatine was recommended as a first-line treatment for patients with depression associated with sleep disorders in the 2015 Chinese Guidelines for the Prevention and Treatment of Depressive Disorders (2nd edition) and the 2016 Canadian

Anxiety and Mood Disorders Treatment Network/International Bipolar Society Bipolar Disorder Treatment (CANMAT/ISBD) guidelines [3, 4].

Agomelatine, the first melatonin receptor agonist, activates both the melatonin receptors MT1 and MT2 and antagonizes the 5-HT<sub>2C</sub> receptor [5]. Agomelatine can improve sleep quality and restore biorhythm by activating MT1 and MT2 receptors. By antagonizing the 5-HT<sub>2C</sub> receptor in the postsynaptic membrane, it can increase the release of dopamine (DA) and norepinephrine (NE) in the prefrontal cortex (PFC) and exert an antidepressant effect. When MT activation is combined with 5-HT<sub>2C</sub> receptor antagonism, a unique synergistic effect can be generated [6, 7]. Therefore, agomelatine has promising applications in the treatment of many psychiatric disorders.

The common adverse reaction of agomelatine includes headache, dizziness, excessive sedation, diarrhea, dry mouth, nausea and liver inju-

ry. Among them, liver injury was shown as elevated liver enzymes, which is common in clinic and limited the application of agomelatine [8, 9]. Therefore, agomelatine can only be considered as an alternative drug for patients who do not respond to or cannot tolerate other antidepressant drugs. Here, we report a case of abnormal tongue temperature perception which may be caused by agomelatine. This is rare and has not been reported before. We hope this article could provide some reference for future clinical use of agomelatine.

### Case report

The patient was a 60-year-old Han Chinese female worker who visited the outpatient clinic due to persistent emotional depression, irritability, and insomnia for two months and was diagnosed with depression. She had a history of good health, with no record of surgery or chronic diseases, and there was no family history of mental illness. She had no bad habits such as smoking and drinking. Physical examination and auxiliary tests, including complete blood count, liver and kidney function, blood sugar, blood lipids, and electrocardiogram, showed no significant abnormalities. The initial treatment plan consisted of sertraline 50 mg and oxazepam 15 mg, but the patient still complained of poor sleep quality after one week. Therefore, the treatment was adjusted to agomelatine 25 mg and oxazepam 22.5 mg. After the adjustment, the patient's sleep and mood improved. However, one week after starting agomelatine, the patient reported tongue discomfort, which developed into temperature perception abnormality about two weeks later, unable to perceive the temperature of drinking water, leading to tongue burns and blister formation. Oral examination and neurological examination revealed no obvious abnormalities. Agomelatine was then discontinued, and the patient was switched to duloxetine capsules 60 mg. Two days after the treatment adjustment, the patient's discomfort in the tongue was alleviated, and the symptoms basically disappeared after one week.

### Discussion

Agomelatine is a melatonin receptor agonist (M1/M2) and 5HT<sub>2c</sub> receptor antagonist, used for the treatment of depression [10]. Agomelatine has been shown to significantly

improve sleep in patients with depression in the early stages [11]. Common side effects include headache, somnolence, dizziness, abdominal pain, and diarrhea, as well as temporary increases in transaminase levels. Although agomelatine has a relatively good side effect profile, individual differences during its use require attention [12]. In this case, the patient's tongue temperature perception abnormality may be related to the use of agomelatine. The patient had only emotional and sleep problems before medication, the occurrence of tongue temperature perception abnormality corresponded with the use of agomelatine, and the symptoms rapidly improved after discontinuing agomelatine, further supporting agomelatine as a possible cause. Additionally, the patient was in good health, with no oral diseases, neurological diseases, systemic diseases, or bad habits such as smoking or drinking. Therefore, other related factors causing tongue temperature perception abnormality were excluded. Regarding concurrent medication, common adverse reactions of oxazepam include somnolence, dizziness, and fatigue, with larger doses potentially causing ataxia and tremors. Although individual differences exist, it is unlikely that they caused sensory abnormalities, as the patient continued to use them without affecting the resolution of tongue temperature perception abnormality. Furthermore, there is a possibility that the tongue temperature perception abnormality was a somatic symptom of the patient's depression, which was effectively controlled after using duloxetine capsules. Duloxetine, by acting on norepinephrine, is particularly effective in regulating pain perception and providing relief [13]. However, duloxetine usually takes effect within 1-2 weeks, and despite individual differences, it is unlikely that the symptoms improved within two days after treatment adjustment. Therefore, we believe that the tongue temperature perception abnormality was caused by agomelatine. This serves as a reminder that in clinical practice, physicians should be vigilant about potential adverse drug reactions and adjust treatment plans in a timely manner to alleviate patients' symptoms.

### Conclusion

This case report presents an instance of tongue temperature perception abnormality following

agomelatine treatment. It highlights the need for physicians to closely monitor patients' responses when using agomelatine and other antidepressant medications, and to adjust treatment strategies promptly in the event of adverse reactions. Future research should further explore the safety and tolerability of agomelatine and other antidepressant drugs to optimize treatment plans and reduce the occurrence of adverse reactions.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Chen-Jie Ge, Quality Management Division, Huzhou Third Municipal Hospital, The Affiliated Hospital of Huzhou University, No. 2088, East Campsis Road, Huzhou 313000, Zhejiang, China. E-mail: 18267233183@163.com

### References

- [1] Hong W, Si TM, Li LJ, Xu XF, Gao CG, Li KQ, Shi JF, Jiao ZA, Peng DH, Li Y, Yao ZJ, Qiu CJ, Wang HL, Wang YM, Huang JZ and Fang YR. Argonaut melanesia treatment depression clinical expert advice. Clinical application recommendation on agomelatine in treatment of major depressive disorder. *Chinese J New Drugs* 2018; 37: 601-606.
- [2] Savino R, Polito AN, Marsala G, Ventriglio A, Di Salvatore M, De Stefano MI, Valenzano A, Marinaccio L, Bellomo A, Cibelli G, Monda M, Monda V, Messina A, Polito R, Carotenuto M and Messina G. Agomelatine: a potential multitarget compound for neurodevelopmental disorders. *Brain Sci* 2023; 13: 734.
- [3] Li LJ and Ma X. Chinese guidelines for the prevention and treatment of depression disorder (second edition). China Medical Electronic Audio-Visual Publishing House (Beijing) 2015.
- [4] Lam RW, Kennedy SH, Parikh SV, MacQueen GM, Milev RV and Ravindran AV; CANMAT Depression Work Group. Canadian network for mood and anxiety treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: introduction and methods. *Can J Psychiatry* 2016; 61: 506-509.
- [5] Millan MJ, Marin P, Kamal M, Jockers R, Chanrion B, Labasque M, Bockeaert J and Mannoury la Cour C. The melatonergic agonist and clinically active antidepressant, agomelatine, is a neutral antagonist at 5-HT(2C) receptors. *Int J Neuropsychopharmacol* 2011; 14: 768-783.
- [6] Hickie IB and Rogers NL. Novel melatonin-based therapies: potential advances in the treatment of major depression. *Lancet* 2011; 378: 621-631.
- [7] Yu YM, Gao KR, Yu H, Shen YF and Li HF. Efficacy and safety of agomelatine vs paroxetine hydrochloride in Chinese Han patients with major depressive disorder: a multicentre, double-blind, noninferiority, randomized controlled trial. *J Clin Psychopharmacol* 2018; 38: 226-233.
- [8] Guo P, Xu Y, Lv L, Feng M, Fang Y, Huang WQ, Cheng SF, Qian MC, Yang S, Wang SK and Chen HX. A multicenter, randomized controlled study on the efficacy of agomelatine in ameliorating anhedonia, reduced motivation, and circadian rhythm disruptions in patients with major depressive disorder (MDD). *Ann Gen Psychiatry* 2023; 22: 46.
- [9] Howland RH. A benefit-risk assessment of agomelatine in the treatment of major depression. *Drug Saf* 2011; 34: 709-731.
- [10] Demyttenaere K. Agomelatine: a narrative review. *Eur Neuropsychopharmacol* 2011; 21 Suppl 4: S703-S709.
- [11] Zupancic M and Guilleminault C. Agomelatine: a preliminary review of a new antidepressant. *CNS Drugs* 2006; 20: 981-992.
- [12] MacIsaac SE, Carvalho AF, Cha DS, Mansur RB and McIntyre RS. The mechanism, efficacy, and tolerability profile of agomelatine. *Expert Opin Pharmacother* 2014; 15: 259-274.
- [13] Baldaçara L. Duloxetine: an update. *Research, Society and Development* 2024; 13: e7313345331.