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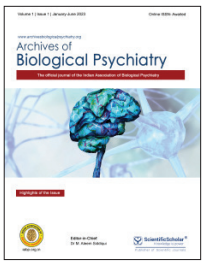

Case Series *Neurophysiology*

Sinus bradycardia as a phenotype in opioid dependence syndrome, acute withdrawal state, a rare case series

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ABSTRACT

Tachycardia is one of the most common physiological phenomena in Opioid withdrawal and is due to the state of transient catecholamine surge. However, till date, no studies have reported bradycardia during opioid withdrawal (acute phase). Hereby, we intend to report rare cases of two young males who developed sinus bradycardia in opioid withdrawal (acute phase). Close electro-clinical monitoring of bradycardia for possible prevention of mortality in opioid withdrawal is proposed.

Keywords: Tachycardia, Electrocardiogram, Smack

INTRODUCTION

Opioid use disorders affect over 16 million people worldwide, and there are over 120,000 deaths worldwide annually attributed to opioids.[1]

Opioid withdrawal develops after the cessation of or reduction in opioid use that has been heavy and prolonged.[2]

It can either be spontaneous (stopping daily use) or precipitated (due to the ingestion of an antagonist or partial agonist). Spontaneous withdrawal starts 6–8 h after the last use of the short-acting opioid, withdrawal severity peak around 36–48 h and resolves after 5–7 days. These patients report symptoms such as tachycardia, sweating, restlessness, mydriasis, joint and body aches, runny nose, lacrimation, gastrointestinal upset, tremors, yawning, irritability, and goosebumps. Among the commonly reported is tachycardia but bradycardia in withdrawal has not been reported. Hereby, we are reporting rare instances of two patients who developed bradycardia during opioid dependence syndrome and the acute withdrawal phase.

CASE SERIES

Case 1

A 30-year-old married male patient presented to the psychiatry outpatient department accompanied by his mother with a history of opioid intake in the form of smack for the past 7 years. There is a history of multiple unsuccessful attempts to quit the substance during these 7 years and the patient had been taking smack continuously for around 3 months when he had presented to us

(was abstained for 1 year previously not on any medications) with last intake being on the day of admission and amount is up to 0.25 g daily chased on a foil paper.

Intake of any other substance was denied. Past medical, surgical, and family histories were insignificant. General and systemic examination revealed no abnormality. Blood investigations including complete blood count (CBC), liver function tests (LFT), kidney function test (KFT), thyroid function test (TFT), and random blood sugar (RBS) were within normal limits. Urine drug screening was not done due to the financial constraints of the patient.

At the time of admission, a baseline heart rate (HR) of 70 bpm and blood pressure (BP) of 120/80 mm of Hg was recorded and the patient was started on symptomatic treatment for opioid withdrawal (non-steroidal anti-inflammatory drugs - a combination of Tab. Ibuprofen 400 mg + Tab. Tizanidine 2 mg given for 6 days, Tab. Lorazepam 2 mg as and when indicated for sleep and Tab. Loperamide as and when indicated for loose motions) while on routine vital monitoring.

Subsequently, after 2–3 h when the patient had shifted to In patient Department (IPD), an electrocardiogram (ECG) [Figure 1] revealed sinus bradycardia with an HR of 57 bpm. Later, during the night after around 4 h when the patient was on routine vital monitoring, HR went down to 46 bpm, while the rest of the vitals were stable and the patient was put on continuous vital monitoring and Inj. Atropine 1 ampule I/v as and when indicated if HR<40 bpm as advised by the medical department. Post-cardiology consultation, 2D Echo was planned which revealed no abnormality [Normal left ventricular [LV] contractility, normal LV function, left ventricular ejection fraction 56%, No mitral regurgitation (MR), aortic regurgitation (AR), tricuspid regurgitation (TR)].

During this time, the patient reported symptoms such as restlessness, sweating, irritability, insomnia, indigestion, tremors, goosebumps, and generalized body ache. The patient's HR fluctuated around (50 ± 4) bpm for the next 2 days of withdrawal and it was on the 4th day of withdrawal his HR started increasing to 68–70 bpm in spite of ongoing administration of Tab. Tizanidine 2 mg + Tab. Ibuprofen 400 mg makes it highly unlikely that the bradycardia could have resulted due to Tizanidine which is known to cause bradycardia infrequently. On the 7th day of withdrawal, the patient was discharged on Tab. Naltrexone 12.5 mg daily and motivational enhancement therapy (MET) sessions were inculcated. ECG done on the day of discharge showed normal sinus rhythm and an HR of 80 bpm.

Case 2

A 21-year-old unmarried male, a hotel management graduate presented to the psychiatry outpatient department accompanied by his mother with a history of opioid intake in the form of smack for the past 5 years and cannabis intake in the form of bhang for the past 5 years. There is a history of multiple unsuccessful attempts to quit smack during these 5 years but cannabis intake has been continuous with the last intake of both substances being 1 day before admission and the amount being up to 0.5 g of smack chased daily on a foil paper, and bhang smoked in a joint, 2–3 joints daily.

Intake of any other substance was denied. Past medical, surgical, and family histories were insignificant. General and systemic examination revealed no abnormality. Blood investigations including CBC, LFT, KFT, TFT, and RBS were within normal limits. Urine drug screening was not done due to the financial constraints of the patient.

At the time of admission, a baseline HR of 62 bpm and BP of 110/70 mm of Hg was recorded and the patient was started on substitution therapy for opioid withdrawal (Tab. Tramadol 50 mg thrice a day, Tab. Lorazepam 2 mg as and when indicated for sleep and Tab. Loperamide as and when indicated for loose motions) while on routine vital monitoring.

Subsequently, when the patient had shifted to IPD, an ECG [Figure 2] was done which revealed Sinus Bradycardia with an HR of 58 bpm. Later, during the night when the patient was on routine vital monitoring, HR went down to 48 bpm,

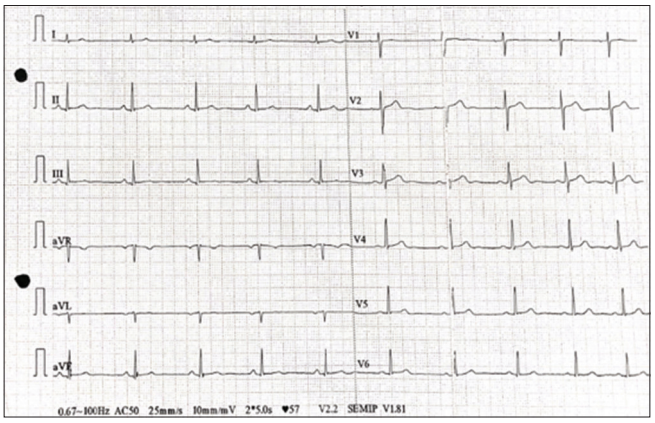

Figure 1: Electrocardiogram of the patient in the first case report.

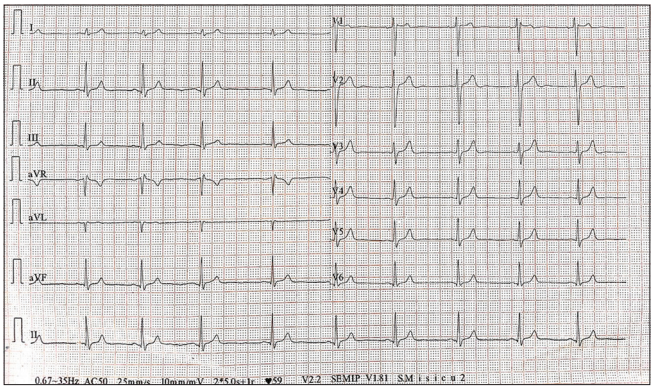

Figure 2: Electrocardiogram of the patient in the second case report.

while rests of the vitals were stable and the patient was put on continuous vital monitoring and Inj. Atropine 1 ampule I/v as and when indicated if HR <40 bpm as advised by the medicine department. Post cardiology consultation, 2D Echo was planned which revealed no abnormality (Normal LV contractility, normal LV function, LVEF 56%, No MR, AR, TR).

During this time, the patient reported symptoms such as restlessness, sweating, irritability, insomnia, indigestion, tremors, goosebumps, and generalized body ache to combat which, the patient was already on opioid substitution therapy, and no sympatholytics were added due to ongoing bradycardia.

The patient's HR fluctuated around (50 ± 10) bpm for the next withdrawal and it was on the 4th day of withdrawal his HR started increasing to 68–70 bpm in spite of an ongoing administration of Tab. Tramadol makes it highly unlikely that the bradycardia could have resulted due to this drug. On the 7th day of withdrawal, the patient was discharged on Tab. Tramadol 50 mg twice a day with a plan to start Naltrexone on subsequent follow-ups and MET sessions were inculcated. ECG done on the day of discharge showed normal sinus rhythm and an HR of 86 bpm.

DISCUSSION

Acute opioid receptor-mediated cardiovascular effects are well-known and include hypotension, orthostasis, bradycardia, and syncope.[3] By contrast, the effects of opioid withdrawal are opposite, representing a manifestation of increased catecholaminergic tone with an abrupt increase in rate pressure product. However, none of the studies have reported bradycardia developing during opioid dependence syndrome and the acute withdrawal phase.

In our first case, a baseline HR of 70 bpm was recorded which went down to 46 bpm, during the initial 3 days of withdrawal and subsequently improved over the next few days. There are few case reports suspecting bradycardia as a result of tizanidine administration. However, in our case, there was a resolution of bradycardia even after an ongoing administration of tizanidine which makes it less likely that bradycardia could have resulted from this drug.

In our second case, the use of cannabis has been continuous for 5 years but the possibility of cannabis-induced bradycardia appears to be highly unlikely as the bradycardia started resolving during the later phase of the withdrawal and complete elimination of Tetrahydrocannabinol (THC) metabolites may take up to 28-day time. Despite us giving reasonable substitution therapy for the acute withdrawal state of opioid dependence syndrome, bradycardia was still prevalent and interestingly resolved over the next few days. All the investigations done were within normal limits.

In both the case reports, monitoring of withdrawal symptoms on objective rating scales like clinical opiate withdrawal scale was not done, which is a limitation of the study.

In all probability, bradycardia developed due to opioid withdrawal, and neurophysiological and neuropathological mechanisms which have to be looked into. Hence, it becomes clinically important for us to closely monitor the vitals of such patients especially when medications like clonidine are prescribed in opioid withdrawal, which can lead to cardiotoxicity.

CONCLUSION

Sinus Bradycardia in opioid withdrawal is a rare but critical phenotype. Clinical suspicion and anticipation is required for the same. Citing conventional use of sympatholytics may inflate mortality risk in this context.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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