Dystonia after Shooting Street Heroin: An Underreported Matter of Concern

Recent World Drug Report mentions opioids as the most harmful drugs in terms of health effects. Neurological sequelae have been reported in a few cases of inhalational heroin use (‘chasing the dragon’). It is conjectured that vapours (pyrolysate) produced after heating black market heroin on aluminium foil, rather than pure pharmaceutical diamorphine, are responsible for the brain damage, although the incriminated adulterant has not been isolated till now. The brain pathology associated with such use is spongiform leukoencephalopathy which can lead to long-term consequences or can even be fatal. Structural brain imaging of these spongiform leukoencephalopathy cases showed the involvement of the posterior fossa, pallidum, corpus callosum and supratentorial white matter tract. In this case series, we shall discuss six patients with acute onset transient dystonia following injection heroin use. To the best of our knowledge, no such cases have been described until date in the literature.

CASE SERIES

Case identification was retrospective and based on the patient self-report and informant description. The patients reported to us in a short span of time, i.e., between July to October 2017 and belonged to the same locality or adjacent districts. Here, we include six cases, of which five were inpatients and one outpatient. All the cases were dependent on injection heroin. We assessed the cases with a thorough general physical examination, including neurological examination, relevant investigations and brain magnetic resonance imaging (MRI). All patients reported experiencing dystonic symptoms within minutes of injecting heroin which developed.
to full in a few hours. All patients reported that the heroin they used had a little effect and instead they developed opioid withdrawals in addition to the dystonic symptoms. All the patients approached medical emergency settings for treatment. Two of the patients reported to our emergency department and were examined thoroughly by the internal medicine team, and consultations were taken from the neurology and psychiatry teams also. Routine emergency tests including serum electrolytes were within normal limits. They were administered injection promethazine 50 mg intravenous which gave complete relief in 10–15 min. The remaining four patients received treatment in the emergency departments of other hospitals. One patient reported being given intravenous calcium without any relief, but later, in another hospital, some intravenous drug was given which gave complete relief. For the rest, treatment details were not available, but they received some intravenous drugs that produced complete relief of dystonia within a few minutes. There was no confusion at the time of dystonia, and patients had sufficient awareness of the symptoms. There was no report of tonic-clonic movement or tremors. All patients developed cervical dystonia with variable involvement of the tongue, face and upper limb. The details of demographics, case description and investigations are provided in Table 1.

None of the patients could produce a sample of the heroin used by them before developing dystonia. As per the patients, they had either finished their dose or discarded it after recovering from dystonia. Despite reassurance of confidentiality and anonymity, inability to provide the sample could also be due to fear of being prosecuted. Three of the patients recalled that the texture and colour of the heroin sample were different from usual. Laboratory investigations included complete blood count (CBC), renal function tests (RFT), liver function tests (LFT), fasting blood sugar (FBS) and lipid profile. Except for the reports mentioned in the table, rest of the values were normal in all subjects. Ultrasonography (USG) whole abdomen, chest X-ray and electrocardiography (ECG) were normal in all patients. 3T MRI brain was also normal in all the patients. All the patients received treatment for opioid dependence in our opioid substitution therapy (OST) clinic. They received individualised doses of Tab buprenorphine/naloxone 2.5 mg combination sublingually.

At the time of writing this case series in October 2017, we have not received any new patients with a dystonic reaction after injection heroin use. All patients are in follow-up at our OST clinic without any recurrence of dystonia, and four of them were drug-free at last follow-up.

**DISCUSSION**

In this cases series, we described acute dystonia in dependent heroin users. There was a clear temporal relationship with the use of injection heroin and the appearance of predominantly localised cervical dystonias. The absence of any other neurological

| Clinical profile, laboratory investigations and clinical features of dystonia of cases |
|----------------------------------|---------------------------------|----------------|----------------|
| Initials, Age (years) | Other substance dependence | Physical illness | Psychiatric illness | Significant reports |
|-------------------|--------------------------|----------------|-----------------|
| M 24 | Tobacco dependence (ST) | HCV+ | None | HCV RNA-TND, LDL-167 IU/L, TG-186 IU/L |
| H 27 | Cannabis and tobacco dependence (ST) | None | None | None |
| I 26 | Tobacco dependence (SLT), alcohol and cannabis dependence currently abstinent | None | None | AST/ALT-86/42 IU/L |
| A 30 | Cannabis, alcohol and tobacco dependence (ST) | Seizure disorder | Bipolar affective disorder | TG-204 IU/L |
| S 20 | Tobacco dependence (ST), cannabis dependence currently abstinent | None | None | None |
| L 20 | Tobacco dependence syndrome (SLT) | None | None | None |

**Clinical features of dystonia as described by patients and informants**

| Initials Age (years) | Heroin amount used (g) | Time to onset of dystonia (minutes) | Duration of symptom (hours) | Retrocollis/torticollis (side) | Tongue protrusion | Grimacing and trismus | Ipsilateral upper limb involvement |
|---------------------|------------------------|-----------------------------------|--------------------------|------------------|----------------|---------------------|---------------------|
| M 24 | ½ | 30 | 3 | Y/Y Right | Y | N | Y, wrist flexion |
| H 27 | 1 | 120 | 2 | Y/Y Right | Y | Y | Y, wrist flexion and locked elbow |
| I 26 | ½ | 20 | 6 | Y/Y Left | Y | N | N |
| A 30 | 3 | 30 | 2 | Y/Y Right | Y | N | N |
| S 20 | ½ | 180 | 1 | Y/N Midline | N | N | N |
| L 20 | ½ | 30 | 3 | Y/Y Right | Y | N | Y, wrist flexion and locked elbow |

Y = Yes, N = No, ST/SLT = Smoked tobacco/smokeless tobacco, HCV = Hepatitis C virus, LDL = Low Density Cholesterol, TND = Target not detected, ALT = Alanine aminotransferase, AST = Aspartate aminotransferase, TG = Triglycerides
abnormalities in the past, at the time of presentation or in subsequent follow-ups rule out the possibility of any underlying neurological disorder. There was no discernible electrolyte abnormality. None of the patients had received any other drug (over the counter or prescription medication) prior to the onset of dystonia. Hence, temporal connection, specificity of presentation and lack of any other apparent cause strongly suggest the role of injection heroin in producing acute dystonias.

Next question is whether dystonias in these patients occurred as a result of direct effect of heroin or due to the adulterants (or cutting agents) mixed with it.

As already mentioned, incidents of acute dystonia following heroin use has never been reported. The reports published so far have described long-lasting features of residual central nervous system (CNS) damage, almost always following inhalational heroin use (rather than injection). Hence, the atypical presentation prompted us to look into the possibility of dystonia induced by adulterants. Reporting of cases in a short span of time, from the same locality, and a similar subjective experience following heroin use too support the adulterant hypothesis. Moreover, being a transit area for South-West Asian heroin, the northern part of India (from where the cases were reported) is no doubt vulnerable to be exposed to the adulterants mixed with it.

On the basis of a review of the literature, we speculate the involvement of a couple of offending agents, namely strychnine and chloroquine. A 2005 report by the United Nations Office on Drugs and Crime (UNODC) listed a range of alkaloidal impurities and adulterants isolated from street heroin samples. A thorough check of the list revealed that a probable candidate could be strychnine, which is a non-opiate cutting agent with pharmacological effects. Strychnine blocks the inhibitory action of glycine at interneuron-motor axon synapses and causes exaggerated motor activity. In 1974, analyses of street heroin samples from Amsterdam were reported to be containing strychnine. Though the samples contained less than the lethal dose, low dose strychnine can produce dystonic reactions. In another UNODC report (2009), chloroquine was identified as one of the cutting agents present in heroin manufactured in Afghanistan. Though chloroquine is considered a non-toxic drug, there are five reported cases of chloroquine-induced extrapyramidal symptoms, including cervical dystonias from India. The exact mechanism of chloroquine-induced dystonia has not been identified, but chloroquine is believed to cause an imbalance in the neurochemical control of psychomotor activity in the basal ganglia. So, chloroquine could be the second candidate which can produce dystonia.

A major limitation is not being able to gather any sample of the used street heroin. Hence, it is impossible to assert about the chemical nature of the adulterant. There are several learning points. In addition to obvious dangers of heroin, the adulterants or cutting agents too are a matter of real concern. We also reiterate the need for improved forensic capacities to identify specific adulterants and periodic monitoring for the level and nature of impurities. Like the United States had a Drug Abuse Warning Network (DAWN) been present in India, a detailed account of the source, nature, cause and extent of these events would have been generated, which in a way would have helped in shaping a public health response.

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Opioids have been abused by humans since ages to obtain pleasure. Repeated use of this group of substances leads to a loss of control and a compulsive pattern of use, which ultimately leads to the development of dependence. The reduction in the usual dose or abstinence from opioids can result in a varying range of withdrawal symptoms, including rhinorrhoea, lacrimation, salivation, body aches, anhedonia, tremors, restlessness, mydriasis, diarrhoea, etc. Dystonia is a movement disorder characterized by sustained or intermittent muscular contraction resulting in either abnormal posturing, movements, or both. They are mainly known to occur as a side-effect to a certain group of medications (antipsychotics, antiemetics, etc.) and are also seen in some neurological conditions. Very few reports of opioid withdrawal-related dystonia are available in the existing literature. We report a case of opioid dependence who presented with acute dystonia during the acute opioid withdrawal phase and discuss the possible neurobiological mechanism to explain the presentation.

A 24-year-old educated, employed, unmarried male was brought to the emergency unit by his mother, with complaints of an involuntary movement of his neck to the right side, along with head tilting, which was associated with a pain in the nape of the neck for the last half an hour. A call was given to the psychiatry department because the history revealed a recent use of brown sugar. The patient could well sense the motor symptom and also reported difficulty in swallowing. A diagnosis of acute dystonia was made, and he was given intramuscular injection of promethazine 1 ampoule (50 mg) that resulted in a dramatic recovery of the motor problem.

A detailed interview revealed daily intake of brown sugar (street heroin or diamorphine), an opioid, for the last 3 years. He was introduced to it by one of his close friends, and he started to chase it as a means to experiment with the substance. He used to buy around 1 g of brown sugar from a drug peddler and would consume it in 2 days. He developed tolerance to its effects, and although he tried to stop chasing, he failed because of withdrawal symptoms like lacrimation, runny nose, low back pain, tremulousness of the whole body, insomnia, anhedonia, and diarrhoea. He last consumed brown sugar 15 h before experiencing the current motor symptom. There was no history of taking any antipsychotic, antiemetic, or any over-the-counter medications prior to this motor problem. He had neither history of any past neurological condition nor any family history of such problems and also no history of taking other substances of abuse. Such symptom never occurred to him in the past. He responded well to promethazine.

On physical examination, he showed signs and symptoms of opioid withdrawal and no focal neurological deficits. Clinical Opiate Withdrawal Scale (COWS) revealed a score of 22, suggestive of