Serious health threats of novel adulterants of the street heroin: a report from India during the COVID-19 pandemic

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Accepted 17 August 2021

To cite: Mahintamani T, Ghosh A, Jain R. *BMJ Case Rep* 2021;**14**:e242239. doi:10.1136/bcr-2021-242239

SUMMARY

The COVID-19 pandemic and a consequent nationwide lockdown in India for several weeks had restricted the access to street heroin and treatment for substance abuse. Use of cutting agents to increase the volume or psychoactive effect has been widely practised under such circumstances. Our patient with opioid use disorder chased heroin with an unknown cutting agent to enhance psychoactive effect from the limited quantities of heroin. He suffered from an abrupt onset sedation, weakness, postural imbalance, slurred speech, cognitive dysfunctions and disinhibited behaviour. Symptoms rapidly reversed following abstinence and initiation of buprenorphine–naloxone. Gas chromatography-mass spectrometric analysis of the adulterant revealed high concentrations of benzodiazepines and barbiturates, alongside the usual cutting agents—caffeine and acetaminophen. Abrupt reduction in availability of 'street drugs' in conjunction with poor healthcare access can lead to the use of novel adulterants with potentially serious clinical and public health implications.

BACKGROUND

The WHO declared COVID-19 outbreak as a pandemic on 12 March 2020. Several countries including India imposed lockdown within borders and partial shutdown across borders to contain the progress of the pandemic. There was a severe limitation in traffic and human movements, outpatient-based medical services were closed down and a strict stay-at-home advisory was issued—all happened within 24 hours of the lockdown announcement.

The United Nations World Drug Report 2020 has discussed the potential impact of COVID-19 and consequent lockdown on the production, supply, availability and use of illicit opium.[1] Harvesting during March–June may have been affected due to lack of labour, whereas trafficking was difficult due to stringent restriction on the air and in land travel. The existing demand was high but there was a disruption on the supply side. Resultantly, the prices of street drugs were likely to go up. Individuals may switch to available and affordable alternatives (like alcohol, benzodiazepine synthetic opioids).[2 3]

There are around 7.7 million harmful or dependent opioid users in India. Heroin is the most commonly used opioids. The second largest population of opioid users in India lives in the Northern state, Punjab.[4] Punjab, like the rest of the country, witnessed a stringent and complete shutdown from end of March to end of May 2020.

In this case report, we described how the limited access to the street heroin has led to the use of an 'unknown substance' as a cutting agent and its subsequent harmful neurological and cognitive effects. We analysed the street sample of this cutting agent and unmasked its composition. A signed informed consent was obtained from the patient.

CASE PRESENTATION

A 28-year-old man from rural Punjab, a state in Northern India, presented to our telemedicine services in July 2020 with acute onset confusion and inability to walk; the duration of symptoms was 1 week. History revealed he had cannabis and tobacco use disorders for 7 years. Heroin use through the inhalation route started in the last 2 years. He transitioned to intravenous heroin use for the last year and shared injection equipment occasionally with friends. During COVID-19-related nationwide lockdown in India, started in the 3rd week of March 2020, his access to heroin was curtailed. It was contributed by the travel restrictions, decreased availability of heroin and a resultant surge in the price of per gram street heroin from $54 to $95. He self-medicated resultant withdrawal symptoms with buprenorphine–naloxone (2–4 mg/day) bought from his friends.

However, the dose was inadequate for withdrawal suppression, and he reinstated heroin use within a month.

He continued to suffer from repeated episodes of severe withdrawal symptoms since the end of June 2020 because of the limited availability of heroin and poor access to buprenorphine. His friends offered him a yellowish powder, known as 'Cut' in common parlance, as an add-on to heroin. He was informed that 'Cut' was a cheaper (costing about $11 per gram) novel drug, which would enhance the effect of street heroin. Persuaded by logic, he chased around half a gram of 'Cut' mixed with around one-tenth gram of heroin on aluminium foil. Within minutes, he reported weakness in both the lower limbs, leading to difficulty in walking. He fell asleep within 30 min of chasing the substances and remained asleep for the next 12–14 hours. These effects were substantially different from that of heroin, which he used to chase earlier. While regularly using the substance for the next 10 days, he remained drowsy for most of the time of the day and had limited interaction with family members. He had difficulty in walking and a stumbling gait. While walking, slippers would often slip off his feet.

Figure 1 MRI of the brain of the patient (sagittal section).

He had slurred speech and frequent dribbling of saliva from the angle of his mouth. He remained delirious during this period. Contrary to his usual self, he would have anger outbursts with minimal provocation. There were instances of breaking household objects during the episodes of anger. The family members persuaded him to seek treatment due to his physical problems and behavioural disturbances. Peers who chased 'Cut' were reported to experience similar symptoms of varying severity. However, we cannot comment on the course and outcomes because the peer group did not seek treatment from this centre.

On a general physical examination (11 July 2020), we observed multiple injection marks and sclerosed veins on his left forearm. Pulse rate was 96/min, regular with normal volume; blood pressure was 126/80 mm Hg. He was poorly oriented to time, place and person; and appeared confused. The Mini Mental State Examination (MMSE) score for orientation was 6 out of 10 (the total score was 23 out of 30). Pupils were constricted and bilaterally symmetrical. There was slurring of speech with saliva drooling from the angle of the mouth. Joint, pressure and vibration senses were intact. Deep tendon reflexes were sluggish in both the upper limbs but were normal in bilateral lower limbs. Plantar reflex was flexor bilaterally. The power in bilateral upper limbs was grade 3/5, and that of lower limbs was grade 4/5. He had a wide-based gait, with frequent staggering and stumbling. He was unable to perform a tandem walk and other cerebellar function tests.

INVESTIGATIONS

Initial urine screen by chromatographic immunoassay revealed morphine and benzodiazepine. Structural MRI of the brain revealed no detectable lesions (figure 1). The initial blood investigations revealed: haemoglobin 147 g/L; total leucocyte count 10.7×10^9/L (differential count: neutrophil 59.8%, lymphocyte 30.5%, monocyte 7.5%, eosinophil 1.3%); platelet count 2.66×10^5/μL; prothrombin time 13 s; international normalisation ratio 1.1; bilirubin 0.7 mg/dL (conjugated 0.3 mg/dL); alanine aminotransferase 271 U/L, aspartate aminotransferase 148 U/L, urea 34 mg/dL, creatinine 0.86 mg/dL, anti-hepatitis C virus (HCV) antibody was negative with hepatitis C viral RNA 7.27000/mm^3. Viral screens for HIV and hepatitis B were negative.

The new substance (or cutting agent)—'Cut'—was analysed by gas chromatography-mass spectrometry (GC-MS) technique. The yellowish powder was dissolved in methanol. Shimadzu GC-MS-QP-2020 NX GC-MS was used for identification of drugs in unknown powder after dissolving it in methanol. The GC was equipped with SH-Rxi-5Sil MS capillary column. The GC was operated in split mode with injector temperature of 250°C. Helium was used as carrier gas with a flow rate of 1 mL/min. The GC oven temperature was raised from 100°C to 280°C at the rate of 15°C/min and then kept hold for 10 min. The MS was operated in electron impact mode with electron energy of 70 eV. The ion source and interface temperature were kept at 200°C and 250°C, respectively. Mass spectra were recorded in full scan mode with a mass range of 50–500 amu. The following drugs were identified in the sample: acetaminophen (8 min), caffeine (10.05 min), methaqualone (12.5 min), oxazepam (13.6 min), ketazolam (14.37 min), nordazepam (15.12 min), pinazepam (18.32 min) and alprazolam (21.26 min) (figure 2).

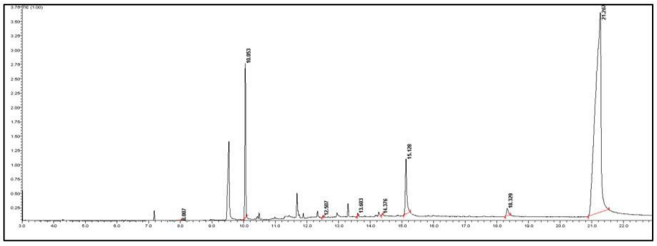

Figure 2 Gas chromatography-mass spectrometry total ion chromatogram of the cutting agent.

DIFFERENTIAL DIAGNOSIS

We considered the walk-in diagnosis of toxic leukoencephalopathy but had to revise it later. The T2 weighted MRI of patients with heroin-induced leukoencephalopathy has consistently revealed symmetric, supratentorial hyperintense signal changes with cortical sparing.[5–7] The reported cases of toxic leukoencephalopathy had a progressively declining course or caused severe disability; death occurred in a quarter to half of all patients.[8 9] Because of a non-significant MRI and rapid recovery from cognitive and neurological dysfunctions, toxic leukoencephalopathy was improbable in our case. Therefore, we implicated the cutting agent ('Cut') for the cognitive–behavioural and neurological symptoms.

TREATMENT

Sublingual buprenorphine–naloxone induction was started. We examined him in the outpatient for the next 5 consecutive days. We monitored mental status, opioid-withdrawal symptoms, and neurological signs and symptoms. We did not prescribe him any antipsychotics for the treatment of delirium but used non-pharmacological treatment and the principle of watchful waiting. We informed the family members about reorientation cues, encouraging normal sleep–wake cycles, and creating a supportive and calm environment. His clinical condition improved rapidly. Opioid-withdrawal symptoms and craving stabilised in the first 48 hours with a buprenorphine–naloxone dose of 6 mg per day. Mood changes also resolved first within 48 hours. Confusion improved on the second day; the orientation score was 10 out of 10 in the orientation item of the MMSE. The overall cognitive function improved over the next 5 days: with MMSE score of 26/30 on day 2, and 30/30 on day 5. He could walk without support from day 3 and gait was normal on day 4. Speech, too, was normal within the first 5 days. Urine screen done on day 7 was negative of illicit opioid, benzodiazepines and barbiturates.

OUTCOME AND FOLLOW-UP

He has been on buprenorphine–naloxone maintenance treatment for the last 7 months. There was no subjective reporting or objective signs of illicit drug use during this period. We did not observe re-emergence of any of the aforementioned cognitive–behavioural and neurological symptoms.

DISCUSSION

The case report presented opportunities to discuss the diagnostic dilemma and the clinical and policy implications of impurities in street heroin during the pandemic.

The points that indicated cutting agent as a possible causative agent were as follows: (a) it comprised of high concentrations of benzodiazepines and barbiturates such as alprazolam, ketazolam, oxazepam, pinazepam, nordazepam and methaqualone. The symptoms experienced by the patient, such as increased sedation, confusion, and altered sensorium, ataxia, and slurring of speech, were characteristically observed in benzodiazepine toxidrome.[10] (b) Irritability and unprovoked aggression might have resulted from methaqualone toxicity[11] and (c) recovery without any residual effect. Nevertheless, concomitant heroin use could have an additive effect.

Reports from Europe and Asia showed caffeine and acetaminophen are the most common types of adulterant and diluent street heroin, respectively.[12–15] Qualitative reviews across several years did not reveal any significant change in the cutting agents for heroin.[12] Reports from the USA showed fentanyl and fentanyl analogues as adulterants of street heroin that had led to the third wave of opioid overdose epidemic.[16] The chromatographic analysis of our sample, too, revealed caffeine and acetaminophen. However, the area% indicated that the concentration of alprazolam was nearly eight times more than caffeine, and concentrations of other benzodiazepines and methaqualone were more than acetaminophen. Methaqualone was used as a cutting agent for heroin in the middle and late 80s.[17] However, recent studies have not listed methaqualone as an adulterant, bulking agent or contaminants of the street heroin.[18] Our report suggested there could be a re-emergence of adulterants that were used in the past.

Our findings have the following clinical and policy implications: (a) use of sedatives in street heroin could increase the odds of opioid overdose and mortality. A study from the USA showed a non-linear increase in benzodiazepine co-involvement in the opioid overdose deaths from 8.7% in 1999 to 21% in 2017.[19] (b) The clinical symptoms resulting from the effects of these cutting agents might be mistaken as toxic leukoencephalopathy, but the course and prognosis are possibly different. (c) Higher impurity in the street heroin was a result of the pandemic-associated disruptions in the supply chain; the type of the cutting agents (or adulterants) might have reflected higher availability of domestically but illegally manufactured benzodiazepines. In recent times, the USA has also witnessed a resurgence of adulteration of cocaine and heroin with locally manufactured fentanyl. The recent press release by the Centers for Disease Control and Prevention attributed the highest number of overdose mortality in a 12-month period to the fentanyl-laced heroin and cocaine.[20] These examples would suggest that a sudden reduction in the supply of street drugs might actually cause more harm than anticipated. (d) Reappearance of methaqualone after more than two decades was an important finding.[11 21] It will be interesting to see whether it is a temporary phenomenon precipitated by the pandemic or will continue to be available in the illicit market even after COVID-19. (e) The public awareness of such adulterations and their health effects and improving the availability and access to treatment could be the keys to address the unanticipated hazards of cutting agents; pandemic-associated poor treatment access has fuelled these problems further.

We would like to add a caveat that testing biological samples such as urine and hair by GC-MS might have helped to detect drugs or metabolites and supplemented the GC-MS analysis of the street sample.

There is a need to study the impurities in street heroin in India systematically. One might also be inclined to examine changes before and after the pandemic and over the years. Until that time, case reports could be an effective modality to inform the clinicians and policymakers in countries like India that do not have an Early Warning Network (European Union) or Drug Abuse Warning Network (USA).

Learning points

- Cutting agents are reasons for health concern, especially during times of restricted availability of drugs.
- These cutting agents may produce different symptoms of intoxication that may be difficult to discern for an unsuspecting clinician.
- Heroin may be laced with unusual benzodiazepines and barbiturates with significant neurocognitive effects.

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Acknowledgements We want to acknowledge Dr S K Jain, Director, Central Forensic Science Laboratory, Chandigarh for allowing us to perform gas chromatography-mass spectrometry analysis of the sample.

Contributors TM prepared the draft. RJ performed the GC-MS analysis and wrote the relevant section. AG supervised the work and edited the final draft.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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