Local complications of pentazocine abuse: Case report and review

Abstract

The skin is the tissue most commonly affected by intravenous drug addiction with pentazocine. The present article attempts to review the adverse effects of injecting drug use along with one case report of cutaneous complications of injection pentazocine abuse underlining the need for early identification, management, and, above all, prevention. It also provides credence to the fact that pentazocine abuse is common in paramedical staff, and easy accessibility of pentazocine injection can easily lead to serious complications.

Keywords: Cutaneous complications, intravenous drug addiction, pentazocine

Pentazocine is a low cost, mixed agonist–antagonist synthetic benzomorphan derivative of morphine, used chiefly for the relief of moderate to severe pain. The analgesic effects of pentazocine are mediated by its agonist action at the k-opioid receptor. The reported data indicate that pentazocine use varies from 0.1% to 21.8% in different parts of India. Pentazocine causes a strong psychological and physical dependence resulting in a severe withdrawal syndrome when the use of the drug is stopped. Addicts prefer the intravenous route of administration as it results in the rapid passage of the drug to the brain. This produces the fastest possible onset of effect, and usually, a “rush” or “buzz” of initial euphoria occurs when a bolus of pentazocine reaches the brain. A time-dependent progression of injection sites has been observed starting with the cubital fossa, followed after 3.5 years by the upper arms and after 4 years, the hands. After 6 years, injection occurs in the neck, foot, and leg and after 10 years in the groin, toes, and fingers. This occurs due to progressive nonaccessibility of the previous vein due to frequent injections. When peripheral veins are sclerosed, the addict injects, by mistake or deliberately, in subcutaneous tissue and muscle. Injecting drug users (IDUs) are prone to suffer from injection-related adverse effects. The process of injecting can give rise to both vascular and soft-tissue injuries and may expose IDUs to pathogens that cause localized or systemic infections. Repeated injections can cause venous or accidental arterial trauma leading to thrombosis, scarring of the vein epithelium and vein...
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Despite the many complications connected with injecting drugs, most injectors do not seek medical assistance due to lack of concern, stigma, preoccupation with drugs or due to severe withdrawal which gets relief with injecting drug itself particularly of the opioid group. We report an adult paramedic who was self-injecting pentazocine-pheniramine combination intravenously for a long time resulting in local complication, after obtaining his informed consent.

CASE REPORT

Index patient is a 32-year-old Hindu married male belonging to a nuclear family, educated up to high secondary school, and works as a private compounding chemist. He presented with a history of injecting pentazocine for 6 years. The patient says that before developing his addiction, he clearly remembers a home visit he made to inject pentazocine to a patient dependent on it. The person was crying due to severe abdominal cramps and body ache along with laceration and restlessness. Shortly after injecting two ampoules of injection pentazocine, symptoms started subsiding. This effect impressed him a lot and one night out of curiosity, he himself injected 1 ml of pentazocine to get relief from his body ache resulting in complete relief and feeling relaxed. He loved the effect so much that he began repeating it once every 3–4 days. Gradually, the frequency and quantity of his use increased, and by 3 months, he was using 5 ml of pentazocine regularly as a lesser dose was ineffective. Subsequently, on the advice of friends, he began to mix 1 ml of pheniramine maleate with 3 ml of pentazocine. This was done to reduce the dose of pentazocine, as he was aware about its addiction potential, and also to increase the pleasurable effect of pentazocine. However, he had to gradually increase the frequency of injection to 4–5 times a day, as he started experiencing withdrawal features 5–6 h after the last dose in the form of intense craving, severe body aches, restlessness, and anxiety. He had to invest a lot of his hard-earned money and time in procuring the drug. He was unable to concentrate on his job being preoccupied with thoughts of drug throughout the day. Many a times, the vein he was injecting developed a counter puncture resulting in extravasations into the tissue with swelling around the site. By 2 years, he was having increasing difficulty in locating veins since most of the veins were blocked. At times after failing to locate a vein, in desperation, he would inject blindly in his forearms. In one or 2 days, erythematous papulonodular lesions would appear at the site of injection which would spontaneously rupture over 2–3 days leaving painless ulcers of 1–2 cm in size. On healing, the ulcers left behind depressed scars. Over the last 4 months due to swelling of his forearms, he started injecting in the legs on a regular basis.

Physical examination revealed that he was an average-build man. There was marked swelling on both forearms and dorsum of the hand, along with ulcers, indurated scar and nodules, hyperpigmented patch, surface atrophy, and muscle fibrosis. Puffy hand syndrome due to lymphoedema caused by the sclerosing action of the drugs was evident [Figures 1 and 2]. The right lower limb was edematous with tense skin and puncture marks [Figure 3]. His general physical and systemic examinations were within normal limits. Routine laboratory investigations including hemogram, blood sugar, liver and kidney function tests, and urine examination were within normal limits. There was no history of needle sharing, syringe reuse, or high-risk sexual behavior. There was no history of use of other opioids or substances, depression, psychotic experiences, head injury, or seizures. He had been detoxified with clonidine twice in the past but relapsed within few weeks due to intense craving. Mental status examination revealed no features of mood disorder or psychosis. He was in the preparation stage of the motivational cycle.

Cessation of injection use was the primary goal of treatment. The related goal was the voluntary retention in the treatment for adequate duration which in future may lead to improvement in socio-occupational functioning. Hence, the patient was put on opiate agonist therapy under which induction was done with sublingual tablet buprenorphine-naloxone, started with 2 tablets of 2 mg and titrated to 5 tablets once daily which was the optimum dose for him. Tablet diazepam was prescribed initially for sleep-related problems which were later tapered off. Supervised feeding by family member was ensured. His acute skin lesions were managed conservatively. After 3 weeks of stabilization, he was referred to surgery department. The plan was chalked out of debriding the fibrous tissue while maintaining the gradual passive stretch of limbs with mobilization exercise of joints involved. He
was given motivational enhancement therapy, and relapse prevention technique was advocated. The patient remained abstinent on regular follow-up for 6 weeks but later was lost to follow-up.

**DISCUSSION**

The case presented has several interesting aspects. It highlights the common occurrence of pentazocine dependence in paramedical staff. The lesions in this patient demonstrate blind dating which is a desperate measure by addict to inject himself blindly in the same area and missing the vein. This occurs late after setting of cutaneous complications. The lesions on the limbs show acute shallow ulcer, punched out ulcer, rim of hyperpigmentation surrounding the ulcer, erythematous papulonodular lesion, skin popping, tense woody fibrosis, and contracture of the joints. The puffy hand syndrome was evident in this case; but, previous literature suggests that the fingers may be spared which are contrary to our finding. The choice of using opiate agonist in this case was obvious as the patient is above 21 years having 6 years of regular intake and previous two unsuccessful attempts to achieve abstinence.

**Skin complications due to injecting drug user**

Cutaneous changes due to pentazocine abuse were first reported by Schlicher et al. and have been found in up to 86% of patients with drug addictions attending medical clinic. The diagnostic signs include tense woody, expansive fibrosis extending beyond the injection sites; irregular scars or deep ulcers with a halo of hyperpigmentation along superficial veins that are not accessible; lack of pain sensation and apparent indifference despite the chronic mutilating process; and puffy hand syndrome. Other lesions reported include lesions resembling morphea, cutaneous sclerosis, panniculitis, limited cutaneous scleroderma, calcific myofibrosis, rhabdomyolysis, tricotropism, toxic epidermal necrolysis, and generalized erythematous desquamative rash with altered hair follicles. Various mechanisms proposed for the cutaneous side effects of pentazocine include trauma of repeated injections, vasoconstriction with tissue ischemia at injection sites, and inflammatory response to precipitated pentazocine in tissues although the exact mechanism remains unknown.

**Skin and soft-tissue infection**

Cutaneous infections are common in IDU. Abscesses and cellulitis occur frequently affecting 22%–65% of IDUs and increase the risk of more serious complications. In a San Francisco-based sample, active injectors had a concurrent abscess (65%), cellulitis (9%), or both (26%). Risk of abscess is more with intramuscular or subcutaneous (skin popping) injection as compared to intravenous injection. The causes of infection are contaminated intradermal injection, the absence of skin asepsis, unsterile equipment, adulterants acting as irritant substances and foreign bodies. Common sites of abscess are, in order of descending frequency, arm, leg, buttocks, deltoid, and head/neck. The most common bacteria isolated were *Staphylococcus aureus*, Group A beta-hemolytic *Streptococcus*, *Actinomyces*, and *Veillonella* species. Anaerobes most commonly isolated from injection-related abscesses were fusobacteria, *Prevotella* species, peptostreptococcus, *Clostridium tetani* and *Clostridium botulinum* are unusual organisms except in IDUs who inject subcutaneously. Necrotizing fasciitis, an uncommon but severe and life-threatening manifestation with a high rate of mortality and amputation, occurs mainly after subcutaneous injection. Necrotizing fasciitis can complicate skin and soft-tissue infections.
Necrotizing ulcers may develop as a result of skin popping, vascular thrombosis, infection, toxicity, and the irritant properties of the drug and adulterants. Some bullous lesions, abscesses, chemical cellulitis, and nodules share identical physiopathology and may precede necrosis and ulceration. Injection at uncommon sites such as penile veins, particularly dorsal vein of the penis may result in necrotizing penile ulcers.

Pyomyositis and multiple sinus tracts
Rarely, pentazocine injection abuse may present as pyomyositis, with minimal overt cutaneous ulcers. The patient had shifted the route of injection from intravenous access in the initial period to repeated injection in the muscle bulk especially in the gluteal area. Such a injection in a circumscribed muscle bulk in desperation when venous access dries up can cause pyomyositis with multiple sinus tracts.

Thrombophlebitis
IDU is a risk factor for deep vein thrombosis due to repeated trauma of venepuncture, local infections, and the irritating qualities of the drugs and adulterants. Jugular vein injection (in the neck) with inflammation may lead to descending cervical cellulitis and mediastinitis with high rate of mortality. IDU is associated with various vasculitic and vasculopathic processes including urticarial vasculitis, Churg–Strauss vasculitis, Raynaud phenomenon, Henoch–Schönlein purpura, necrotizing vasculitis, Buerger’s disease and pseudovasculitis, acute generalized exanthemeutous pustulosis, and Steven Johnson’s syndrome.

Intra-arterial injections
Direct intra-arterial injection of pentazocine may cause severe tissue ischemia and necrosis. Immediately after the injection, the patient develops intense pain and burning sensation, followed after a few hours by marked edema and cyanosis in the area supplied by the artery. This results in peripheral ischemia, edema, and compartment syndrome, which worsen the ischemia. The occurrence of ischemia in an extremity has a multifactorial origin depending on the dose and properties of the injected drug, site of injection, prolonged vasospasm due to local endothelial trauma, thrombosis, embolism due to nondissolvable drug components, or thromboembolism. Management is difficult and consists of analgesia, heparinization, and elevation of the limb. Vasodilators, corticosteroids, and prostaglandin inhibitors have also been used.

Chronic venous insufficiency and ulcers
Clinical evidence of chronic venous insufficiency was found on 88% of people with a history of IDU. Vein trauma, necrotic ulcers, superficial and deep vein thrombosis, blockage of the lymphatic system by repeated infections, and the sclerosing effects of adulterants are the various factors which can contribute to the development of venous insufficiency.

False aneurysm and mycotic aneurysms
These are rare but serious complications. False aneurysm can be caused by vascular injuries after pentazocine injection. S. aureus is the main pathogen in mycotic aneurysms. Most cases involve the femoral artery following groin injection but other locations such as the upper limbs have been described.

Cutaneous nodules, panniculitis, and dermal sclerosis
Although pentazocine is marketed in ampoules, the adulteration with quinine, lactose, lidocaine, caffeine, inositol, dextrose, sucrose, procaine, starch, magnesium silicate (talc), mannitol, and other substances can occur at any stage, and this acts as potential source of irritant. Pentazocine and adulterants can cause a dermal inflammatory reaction which may be a foreign body granuloma or a nonspecific nongranulomatous inflammation with or without detectable foreign bodies. Cutaneous nodules, panniculitis, and dermal sclerosis result from the chronic dermal inflammatory process. These lesions can break down and ulcerate, producing chronic ulcers which may be associated with underlying osteomyelitis.

Leg ulcers and fibrous papules
Pentazocine-induced ulcers can be presented as irregular-shaped deep ulcers with black eschars and surrounding induration, halo of hyperpigmentation around the ulcer, woody induration, needle pricks/thrombophlebitis, fibrous myopathy, and discomfort disproportionately less than the extent of ulcer. Skin biopsy reveals a mixed inflammatory infiltrate with predominance of neutrophils. Neutrophilic septal panniculitis may be observed. Fibrous papules in linear distribution conforming to venous arch of the dorsum of hand, more so in the left hand in a right-handed person, may be seen. Starfish-shaped fibrous papules along the distribution of veins in the dorsum of the hand are reported. Pentazocine-induced ulcers are treated by surgical excision followed by skin grafting.

Pentazocine-induced calcific myofibrosis and fibromyositis
Pentazocine-induced calcific myofibrosis usually involves muscles around the hip, shoulder, elbow, and knee joints following long-standing pentazocine use. The exact mechanism of myofibrosis and fibromyositis condition remains elusive. As pentazocine is acidic in nature and its crystals precipitate easily in a neutral or slightly alkaline
medium, it may be responsible for drug-induced myopathy. The repeated muscle trauma caused by needling and rapid injections of large boluses of drugs, microhemorrhages, and infections may also be contributory factors. It can also cause an atypical myopathy on intramuscular injection. There may be fibrosis and calcification of distant muscle which are not injected with pentazocine. Toe walking due to pentazocine-induced myofibrosis is novel presentation. Although calcific myofibrosis are rare, it can cause significant lifelong disability if it is not detected earlier. There are a few reports of myopathy following chronic pentazocine administration. Its cause remains idiopathic.

**Puffy hand syndrome**

The hands become chronically swollen with repeated injections. This phenomenon is called puffy hand syndrome first described by Abeles, and it seems to be specific to addiction. The puffy hand syndrome is a form of lymphoedema caused by lymphatic obstruction due to the sclerosing action of the drugs. Present as nonpitting edema of the hands and may spare the fingers, but the case reported had involvement of fingers.

**Hypersensitivity reactions**

Opiates can cause itching because of histamine release. The pruritus starts almost immediately after opioids injection and can last 10 min to days. Urticaria was reported in 4% of addicts following opioid injection. Various hypersensitivity reactions can occur, but they remain surprisingly rare given the number and variety of adulterants and drugs possibly because addicts are also mixing antihistaminics such as pheniramine or promethazine with pentazocine injection just like the index patient.

**Hyperpigmentation**

Hyperpigmentation at the site of injection, observed in 54% of individuals, is the most common cutaneous lesion. It is related to scars and tracks along the injected veins and results from a postinflammatory process following repeated skin injuries.

**Scarring**

Scars and needle tracks are prominent stigmata of narcotic abuse found in 76% of IDUs, usually along a vascular distribution, mainly the antecubital area and dorsum of the hand. Scarring remained in 53% of the individuals 5 years after they had stopped IDU. The presence of scarring is related to the duration of drug abuse. Repeated injections in a superficial vein result in superficial venous thrombosis and subsequent fibrosis to form linear cord-like hypopigmented or hyperpigmented scars known as railroad tracks which are pathognomonic of IDU. “Skin popping” results in multiple permanent irregular round or oval atrophic or hypertrophic scars or keloids. Preferred sites for skin popping are extensor aspect of arms, dorsum of hands, abdomen, and thighs; but, they may be seen at any accessible site.

**CONCLUSION**

The abuse of pentazocine is being increasingly reported across the world, especially in developing countries. Many a times, the drug is initially prescribed for a medical indication, and subsequent use by the patient continues without the advice of a physician. Moreover, as in the case reported here, this drug is often abused by medical, paramedical, or nursing staff. Clinicians should be vigilant about the possibility of these compounds being abused, and extra caution should be exercised when dealing with individuals with a history of substance abuse and/or dependence. The spectrum of cutaneous complication due to pentazocine is multiplying. Localized mark over skin can give important clues and alert the physician to the possibility of injection drug use even if history is not volunteered by the patient and therefore can help the physician to take early steps in providing the remedial measures. With free over-the-counter access to these drugs in many developing countries, a great deal of work is needed to control its easy availability. Awareness about its addictive potential, complication of intravenous use, and unwanted side effects should percolate in the society, and a clinician can play a crucial role in disseminating this information.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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