Surgical complications in parenteral Subutex abusers

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ABSTRACT

Introduction: There were anecdotal reports of an increase in the admissions of parenteral Subutex abusers to our hospital over the past five months. This case study aimed to analyse the surgical complications related to parenteral Subutex abuse and describe the demographics of this group of patients.

Methods: We reviewed all admissions to our hospital between July and November 2005. Only parenteral Subutex abusers were included in this case study.

Results: A total of 53 parenteral Subutex abusers were admitted during this period. 31 had surgical complications, while 22 presented with medical ones. Of the surgical patients, 12 had cellulitis and thrombophlebitis, six developed abscesses of the limbs, ten were patients with ischaemia and gangrene of the digits and limbs, one had septic arthritis, one had necrotising fasciitis, and one had a pseudoaneurysm of the femoral artery. There were no reported mortalities. Only nine patients needed surgical interventions. Most of the patients are young with a mean age of 34.2 years. There was a male predominance of 92.4 percent (49 out of 53). Malays are more frequently affected (72 percent, n=38), followed by Indians (15 percent, n=8), and Chinese (13 percent, n=7).

Conclusion: Parenteral Subutex abuse is a rising concern in Singapore. Many patients present to the surgical and orthopaedic departments for limb and vascular complications. Surgery has a limited role in their management, and most are treated conservatively and expectantly. The solution to this emerging trend requires inter-hospital and ministerial collaboration.

Keywords: buprenorphine, drug abuse, opiate dependence, parenteral injection complications, substance abuse complications, Subutex
abuse. It also hopes to provide a demographical overview of this group of patients. Most of the complications are localised skin infections. However, there are some who develop gangrene of the digits or limbs, severe infections like septic arthritis and necrotising fasciitis, or vascular complications like pseudoaneurysms. While most of the complications are not life threatening, the numbers involved do seem significant – 53 patients over a five-month period admitted to one hospital alone. The management of these patients is challenging because they are often not forthright with the history, tardy in seeking help, demand to be discharged from the hospital against medical advice and are not compliant with treatment. In addition, many are carriers of blood-borne diseases like hepatitis B, C and human immunodeficiency virus (HIV), all of which can pose a threat to the unsuspecting surgeon.

METHODS
All admissions to our hospital between July 2005 and November 2005 were screened. The International Classification of Diseases (ICD) codes for opioid dependence were selected. The electronic medical records of these patients were reviewed and only patients who were parenteral Subutex abusers were included. Abusers of other classes of opioid-like opium or procodin were excluded. The demographics of the Subutex abusers were analysed. Surgical complications and outcome were looked at. In addition, the prevalence of hepatitis B, C and HIV was also examined.

RESULTS
A total of 110 patients with the ICD codes for opioid dependence were admitted between July and November 2005. Of these, 53 were known parenteral Subutex abusers. The other 57 patients were excluded because they abused other classes of opioids like opium, heroin, codeine, or because there were no drugs specified in their records. There was a male predominance of 92.4% (49 out of 53). The distribution by race is as follows: Malay 72% (n=38), Indian 15% (n=8), and Chinese 13% (n=7). The mean age of the patients was 34.5 years and its distribution is shown in Fig. 1.

The patients were admitted for a myriad of conditions (Table I). Superficial skin infection was the commonest presentation. 12 patients presented with either cellulitis or thrombophlebitis after injecting themselves with dirty needles. In one patient, a foreign body lodged in his left arm and precipitated the cellulitis. The anatomical locations of these skin infections ranged from the limbs to the neck and to the groin. Most were treated with parenteral antibiotics and they generally recovered. A few of them had recurrent admissions from repeated parenteral injections of Subutex.

Six patients presented with abscesses affecting both upper and lower limbs. Five out of these six patients underwent drainage and debridement. The remaining patient recovered with intravenous antibiotics alone. Some patients needed more than one operation. The cultures grew a spectrum of organisms that included *Streptococcus milleri*, *Staphalococcus aureus*, *Escherichia coli*, *Klebsiella* species and *Burkholderia cepacia*. The pathogenesis was the unsafe practice of using dirty needles. Digital abscesses were particularly difficult to treat because the defect could not be closed after debridement and secondary healing would result in contractures limiting the range of motion. Moreover, it could be complicated by tenosynovitis, and if the presentation is late, may necessitate digital amputations.
Split skin grafts may be used to close the big wounds but many of these patients are deemed unsuitable for it because they were still abusing drugs. One patient developed a severe infection of his left forearm that eventually turned out to be necrotising fasciitis. He was hospitalised for 18 days, underwent multiple debridements, and was eventually discharged with a view for subsequent skin grafting. One patient injected Subutex into his right knee in desperation, and subsequently developed septic arthritis of that knee, requiring arthrotomy and lavage. The culture grew *Staphylococcus aureus* for which he was given intravenous antibiotics.

Ischaemia and gangrene of the limbs and digits were also a common presentation. There were ten such cases in this study and they were sited in the distal extremities affecting the hands, fingers and feet. Fortunately, most did not require immediate amputation because the limb pulses were present, the ischaemia was incomplete or the gangrene was dry. Hence, nine patients were managed expectantly. They were given non-opioid analgesia for pain, and could be discharged to allow for demarcation and subsequent amputation. In our experience with end arterial embolism, several kinds of medication were tried, ranging from aspirin, heparin, low molecular weight heparin, warfarin, to calcium channel blockers. One patient however developed wet gangrene of the distal phalanx of the right ring finger requiring terminalisation during the same admission.

The addicts often started with injecting into the veins in their limbs. Once these sites were exhausted, they proceeded injecting more proximally to the neck or groin. Often times, they also injected into their arteries, potentially resulting in the formation of pseudoaneurysms. In this study, there was a patient who presented with an inflamed lump at his right groin. Computed tomography confirmed that it was a pseudoaneurysm of the femoral artery. He was referred to the vascular surgeon and underwent a ligation and excision of the femoral artery pseudoaneurysm. He remained well and did not require a major amputation.

In addition to those admitted for surgical complications, there were 22 other parenteral Subutex abusers admitted to the hospital during the study period. These 22 patients were admitted to the medical and cardiology departments for a variety of reasons, ranging from infective endocarditis, to hepatitis, to withdrawal symptoms and even seizures. Of the 31 admitted to surgical departments, nine needed surgery. A fair number of them either absconded, or demanded to be discharged against our advice. The average length of stay for these patients was 6.7 days, with a range of 0 to 55 days (Table II). Most of the patients abused Subutex alone (n=34), while the rest combined it with midazolam (n=19). Only one patients tested positive for hepatitis B but he was negative for hepatitis C. 16 (30%) tested positive for hepatitis C. There was no information on the HIV status of these patients.

**Table II. Outcome parameters of Subutex patients.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of patients</th>
</tr>
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<tbody>
<tr>
<td>Required operation</td>
<td>9</td>
</tr>
<tr>
<td>Conservative treatment</td>
<td>44</td>
</tr>
<tr>
<td>Absconded</td>
<td>2</td>
</tr>
<tr>
<td>Discharged against medical advice</td>
<td>9</td>
</tr>
<tr>
<td>Recurrent admissions</td>
<td>4</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
</tr>
<tr>
<td>Length of stay – average 6.7 days</td>
<td></td>
</tr>
<tr>
<td>&lt;1 day</td>
<td>6</td>
</tr>
<tr>
<td>1-5 days</td>
<td>29</td>
</tr>
<tr>
<td>5-10 days</td>
<td>10</td>
</tr>
<tr>
<td>&gt;10</td>
<td>8</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Subutex has been used for the treatment of opiate dependence for at least 15 years. It was introduced in New Zealand in 1991(3), in France in 1996(4) and was FDA-approved in Oct 2002 for the treatment of opiate addiction in certified physicians’ offices(5). Since then, it has become a popular alternative to methadone for the treatment of opiate dependence in Singapore(3). There was early evidence that it is effective in maintaining abstinence, preventing drug users from seeking illicit drugs, facilitating social and professional rehabilitation, and reducing the number of injections and its related complications(2,3). It has also been found that compared to the other opioid agonists used in maintenance programmes, it has the least potential for abuse(2). In addition, it has a good side-effect profile. Subutex is available in a tablet form meant for sublingual administration. When taken as prescribed, it is effective in preventing withdrawal symptoms. Unfortunately, despite its supposed good profile, many misuse it by injecting it to achieve a “high”. As a result, not only is the opiate dependence not treated, the patients often develop complications related to intravenous drug abuse which are protean and varied(9,10).

In Singapore, the parenteral abuse of Subutex is an area for concern. There is no official published data on the incidence, but there have been anecdotal reports that more patients were seen and admitted to our hospital over the past five months than during the same period in the preceding year. In another local hospital, Loo et al reported four cases of severe upper limb complications from the parenteral abuse...
of Subutex. These patients were admitted in the first three months of 2005 and there was no such case in the preceding three years. They presented with upper limb vascular complications, abscess formation and median nerve injury. They were treated surgically but the outcome was generally poor\(^{31}\). In our series, six patients presented with abscesses affecting both upper and lower limbs.

Ischaemia and gangrene of the limbs and digits were also a common presentation in our series, with ten affected patients. Similar to reports in the literature, despite treatment, the patients in this series did not seem to have any improvement of the ischaemia\(^{31,37}\). The pathogenesis of this complication is thought to be due to microembolism of incompletely dissolved Subutex particles to the distal end arteries. There is also an element of vasoconstriction and thrombosis that contributes to the ischaemia\(^{39}\). In addition, the particulate suspension and the improper cannulation of the artery result in intima injury and thrombus formation. In turn, there is outflow obstruction and downstream ischaemia or gangrene. Mottling is often seen and is postulated to be secondary to local venous stasis\(^{39}\). Limb swelling is commonly seen and is secondary to muscle ischaemia and oedema, and may result in compartment syndrome.

One patient developed a femoral artery pseudoaneurysm that required excision. Pseudoaneurysm formation is a well-documented complication of intravenous drug abuse. The treatment is ligation and excision without any revision. In a case series comprising 26 cases where the superficial femoral artery was simply ligated and the pseudoaneurysm excised, there were no amputations required even without revascularisation\(^{14}\). Some patients described claudication after ligation but were not suitable for revascularisation because they were still abusing drugs. That report concluded that ligation and excision of a femoral pseudoaneurysm is simple, effective and safe, and is recommended for dealing with this group of patients.

Deaths are uncommon but when mixed with midazolam, the outcome can be lethal\(^{15}\). The social and healthcare cost of Subutex abuse is high. In the primary healthcare setting, resources are taxed because many are known to doctor hop to obtain Subutex for abuse. When they develop complications, they are often admitted to hospitals for treatment. Some patients will require surgical resources, with some needing multiple operations. The outcome is usually not favourable and a few patients will be admitted repeatedly for the same problems. As it is with all intravenous drug abusers, the prevalence of blood-borne diseases in these patients is high and healthcare workers should adopt universal precautions when performing procedures on them.

Clearly, the solution to this problem is not a surgical one. In fact, it requires collaboration between hospitals and ministries to control this emerging trend. The new guidelines introduced by the Ministry of Health, Singapore\(^{60}\) will serve to deter the abuse of this drug. There is a possibility that Subutex will be classified as a controlled drug\(^{46}\), making it less easily available. This move needs to be deliberated further because the success of Subutex in treating opiate dependence relied partly on its accessibility\(^{46}\). Allowing trained and licensed physicians to prescribe it in the office-clinic setting encourages intravenous drug abusers to step forward for treatment\(^{46}\). An alternative would be to promote the use of a similar drug, Suboxone, which contains naloxone. It is equally effective when taken sublingually but does not produce a high when injected intravenously due to the opioid antagonist naloxone\(^{47}\).

**REFERENCES**