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Pain Threshold, C-Reactive Protein and Efficiency of Local Anesthesia in Addictive Drug Abusers with Impacted Lower Third Molar Tooth

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Abstract

Objective: The aim was to assess the pain threshold, C-reactive protein (CRP) level and efficiency of local anesthesia for surgical removal of impacted lower third molar in addictive drugs abuse patients.

Patients and Methods: The study comprised forty male patients indicated for surgical removal of impacted lower third molar. They were 20 addicts with a mean age of 29.7 ± 8.57 years and 20 age matched non addicts who served as control. The visual analogue scale for pain was assessed and CRP measured before and after surgery.

Results: The most common addictive drugs were bango, hashish and pills. Most of the addict patients had medical problems. Addict patients had higher dental affection and poorer dental hygiene. The operation time tended to be longer for addicts. Addicts required two local anesthesia carpules and showed more fear and anxiety. Before surgery the level of CRP in the addict patients was higher than that of control which increased after surgery in both being significant for the non addicts. The VAS significantly reduced after the first injection of local anesthesia in control and second injection in addicts.

Conclusion: Addict patients have a hyperalgesic state and lower pain threshold than non addict patients. They require higher doses of local anesthesia during oral surgical procedures. They are more anxious and irritable and when visiting dental clinics and should be treated cautiously. Care must be taken when dealing with addict patients as they have more co morbidities. Regular visits to dentists are recommended for addicts to avoid dental problems.

Keywords: Pain; C-reactive protein; Local anesthesia; Addiction, Abusers; Impacted lower third molar

Introduction

Drug addiction is a debilitating chronic relapsing disorder characterized by pathological drug taking- and seeking- behaviors with adverse consequences [1]. Poor oral health among addict patients has a substantial impact on the quality of life [2]. Perioperatively, addicts are difficult to manage because of the complex medical and psychosocial factors. Despite these problems, addict patients have a right to receive sufficient perioperative pain therapy and this should not be withheld [3].

Nonmedical (illicit) use of opioid analgesics has skyrocketed among the general population during the past decade. Abuse-disorder patients had a similar physical but worse psychiatric/personality presentation than other chronic-pain patients, which suggests the need for increased psychiatric involvement [4]. Opioid-induced hyperalgesia (OIH) is a state of nociceptive sensitization caused by exposure to opioids and is characterized by a paradoxical response whereby a patient actually becomes more sensitive to certain painful stimuli. Findings of the clinical prevalence of OIH are not available [5]. Indirect support for OIH is the decreased pain thresholds and tolerances in opioid addicts [6]. Whether or not OIH is a clinical reality is an ongoing debate [7]. Hyperalgesic persists for several months in abstinent opiate addicts [8].

A spectrum of local anesthetics is available that permit pain control to be tailored to the specific needs of the patients [9]. Drug addicts need particular anesthetic care due to their co-morbidities and the customized need for analgesics and anesthetics. In spite of the high incidence of addiction worldwide controlled studies and evidence based recommendations for the anaesthesiological management of the patients are missing. The perioperative care for addicts includes the same aspects for chronic diseases. Inadequate analgesic treatment leads to relapses in addiction and should be avoided. This holds true even for those with long term drug abstinence [10].

The visual analogue scale (VAS) is a commonly used outcome measure presented as a 100 mm horizontal line on which the patient's pain intensity is represented by a point between the extremes of "no pain at all" and "worst pain imaginable". Its simplicity, reliability and validity, as well as its ratio scale properties, make the VAS the optimal tool for describing pain severity or intensity [11,12]. Moreover, the VAS was successfully used to assess pain intensity and complication after surgical removal of the lower third molar [13].

It was found that the severity of pain might be associated with high levels C-reactive protein (CRP), a sensitive marker of low grade systemic inflammation, while the intensity of pain assessed by VAS was independently associated in patients with acute rather than chronic pain [14]. In patients with acute lumbosciatic pain, CRP significantly declines in the initial period of treatment and corresponds with a decrease in pain and improvement in function. While in chronic low back pain patients, CRP remains approximately constant throughout

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the whole period with no correlation with pain or function [15]. Surgical trauma during removal of an impacted lower third molar elicits a characteristic metabolic response, including an elevation in the circulating stress hormones and an increase in the synthesis as well as release of various chemical mediators and acute-phase proteins. CRP is the first acute-phase reactant to rise after trauma or surgery and returns to its normal level within 1 week. In some cases its level may reach 2000 times the normal level [16].

The aim of the present study was to assess the pain threshold, C-RP level and efficiency of local anesthesia for surgical removal of impacted lower third molar in addictive drugs abuse patients.

Patients and Methods

The present work included forty male patients with impacted lower third molar tooth requiring surgical removal, 20 were drug abusers and another 20 non-addict age matched serving as control. Patients were recruited from the addiction outpatient clinic of Cairo University hospitals and those attending the outpatient clinic of the Faculty of Oral and Dental Medicine, Cairo University for minor operative procedures. Patients with acute infection, history of recent intake of antibiotics or antihistamines were excluded. The selected patients did not receive any preoperative Non steroidal anti-inflammatory drugs (NSAIDs).

Thorough history taking was carried out for all patients regarding the type of addiction drugs, the systemic and dental conditions. The medical condition of the addict patients was reported from their medical record files. Routine laboratory investigations were performed including complete blood count (CBC), alanine transaminase (ALT) and aspartate transaminase (AST). Dental assessment was performed for all the patients regarding the oral hygiene, presence of gingivitis, caries, missing or fillings. The radiographic assessment of the lower third molar was performed to determine the direction of angulation.

Mandibular nerve block anesthesia was applied to the patients using a local anesthetic (1.8 ml Mepivacaine, HCl 2% with Levonordefrin 1:20000 as vasoconstrictor) (Mepecaine-L, Alexandria Co. for pharmaceuticals, Alexandria, Egypt). Time is allowed for tingling of the lower lip to occur. Supplementary injection was given for the long buccal nerve. Pinprick test with sharp explorer was used to determine the insensitivity of lingual and buccal nerves. Patients showing incomplete analgesia were given another carpule of the same anesthetic solution. The anesthesia onset (latency) was recorded which is the time lapsed from completion of the injection till lower lip numbness. The duration of anesthesia was determined by the time at which numbness completely disappeared from the lower lip. Mandibular third molars were removed using the standard buccal surgical technique. The time of the surgical procedure was recorded.

The visual analogue scale (VAS) of pain was performed before and after administration of the local anesthetic. In those requiring a second carpule, pain was reassessed before and after its administration [11]. C-reactive protein was semiqualitatively measured by latex agglutination method before surgery to exclude the presence of any preexisting inflammatory condition that might interfere with the study. Fresh serum obtained by centrifugation of collected blood was used. The sample was stored at 6°C for 48 hr before performing the test. Latex particles coated with goat anti-human CRP antibodies are agglutinated when mixed with samples containing CRP. Presence of agglutinations indicates a level of CRP in the sample equal or >6 mg/L. The quantitative test was performed using dilutions of the serum in saline. The study was approved by the local ethical committee (Faculty of Medicine and Dentistry, Cairo University Teaching Hospitals ethical board committee) and consents taken from the patients.

Statistical analysis

Analysis of data was performed with a statistical package for the social sciences (SPSS) version 15. Data was presented as mean ± standard deviation. Mann-whitney test was used for analysis of two non parametric quantitative data and Kruskal-Wallis test for one-way ANOVA was used for comparison of three. p value was considered significant if <0.05.

Results

The mean age of the non addict patients was 31.4 ± 6.7 years, while it was 29.7 ± 8.57 years in the addicts with mean addiction duration of 4.53 ± 4.38 years. All drug abusers were regularly smoking cigarettes and ten of them were alcoholic. The most common addictive drugs were bango, hashish and pills (Table 1). There was no clinical or radiographic evidence of infection or inflammation around any of the proposed surgical sites. The non addict patients considered as a control group were systemically free and apparently healthy. All the patients tolerated well the surgical procedure.

All of the addict patients were receiving medications for management of their condition from the psychiatric outpatient clinic. The medications were one or more of the antidepressants and antipsychotics. It was reported that the addict patients are not telling the full truth as described by their psychiatrists.

The time needed in each operation for removal of the lower third molar was 33.25 ± 7.99 minutes for addict and 29.75 ± 9.52 for non addict patients, however, the difference was statistically insignificant. All addict patients required two carpules (3.6 mL) of local anesthesia

Addictive drug abused No (%)	Addict patients (No = 20)	
Bango	15	(75)
Hashish	15	(75)
Pills (Strawberry, cross)	10	(50)
Heroin	4	(25)
Opiates	2	(12.5)
Benzodiazepines	2	(12.5)
Alcohol	10	(50)

Table 1: Addictive drugs used among the addict patients.

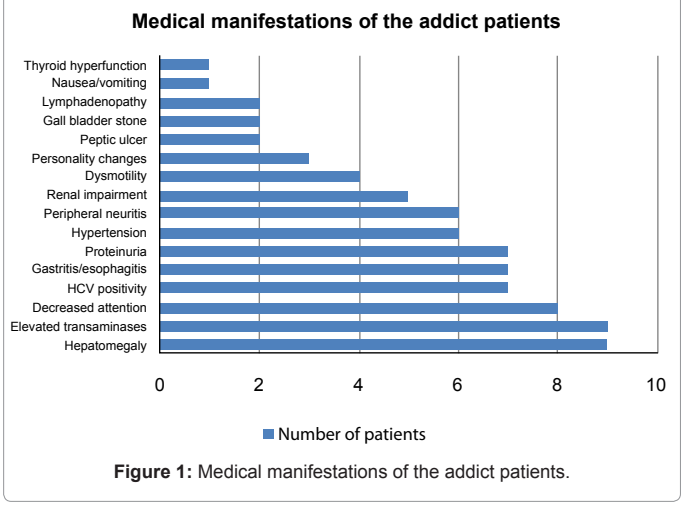

Figure 1: Medical manifestations of the addict patients.

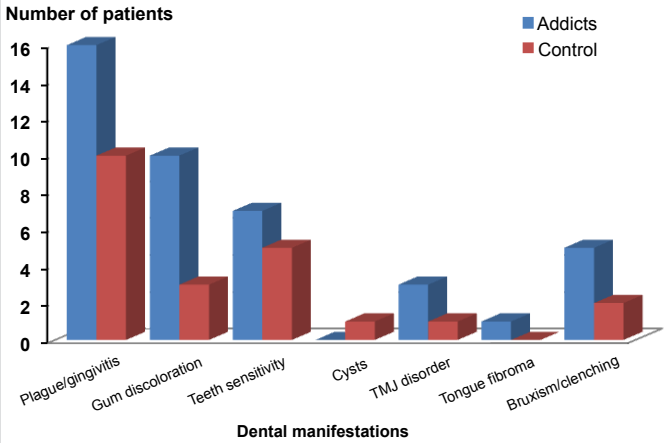

Figure 2: Dental manifestations of the addict patients.

while the control patients received only one carpule (1.8 mL). The mean anesthesia onset time, for all patients was ranged between 1 to 7 minutes with a mean of 4.2 ± 1.54 minutes and the difference between both groups was statistically insignificant. The duration of action anesthesia, was significantly longer in the addicts (101.5 ± 13.77 minutes) than the no addict patients (90.5 ± 12.13 minutes) ($p<0.05$). All addict patients showed more fear and anxiety compared to the control patients.

Fifteen out of the twenty addict patients gave a history of their associated medical conditions (Figure 1). Gastrointestinal manifestations were present in seven 35% of the addict patients in the form of peptic ulcer, gastritis, esophagitis, dysmotility and nausea and vomiting. Nine of the 20 addicted patients had hepatomegaly and elevated liver enzymes. Other patients also had cholecystolithesis and lymphadenopathy. Decreased attention, peripheral neuritis and personality changes were among the neuropsychiatric manifestations presented in eight of the addict patients. Furthermore, hypertension and renal impairment were present in six and five addict patients respectively and hyperthyroidism with goiter was present in one. The cardiac examination of the patients was normal for age of every patient. Secondary hypertension was mostly attributed to the renal involvement. All the non addict patients were healthy without any reported medical condition.

Concerning the dental conditions, all addicts had higher dental affection than the non addict patients (Figure 2). Two of the 20 patients became addict following prolonged toothache problems and using illicit drugs as analgesics for relieving their pain. One of the addict patients developed a tongue fibroma following biting his tongue where he started to be addict to alleviate the pain resultant from the cut tongue. The addicts had poor dental hygiene compared to the non addict patients who were more often proposed crowns and bridges, whereas extraction instead of filling was more often recommended for the addicts. The angulation of the impacted lower third molar of the patients was mostly mesoangular (55%), distoangular (32.5%) and horizontal in 12.5% with no significant difference between addicts and non addicts.

The laboratory investigations results of the addict patients are shown in table 2. Interestingly, the 7 HCV positive patients also had proteinuria. The C-reactive protein (CRP) in addicts was initially higher in the addicts (14.6 ± 15.63 mg/L) compared to the non addicts (5.68 ± 4.92 mg/L) before surgery. After surgery, the level of CRP did not show any remarkable change (17.1 ± 12.51 mg/L) while it significantly increased in the non addicts (21.6 ± 13.12 mg/L) ($p<0.05$).

In addicts the VAS records were 8.3 ± 1.45 cm, 7.85 ± 1.42 cm and 5.9 ± 2.15 cm before surgery, after the first and the second injections respectively. The difference between VAS records before injection and after the first one was statistically insignificant ($p>0.05$). However, the difference between the VAS records before surgery and after second the injection was statistically significant ($p<0.05$). In non addicts the VAS was 7.35 ± 1.87 cm before administration of the LA and significantly reduced to 3.25 ± 1.48 cm after injection of the first carpule ($p<0.05$). The VAS in addicts and non addict patients before and after local anesthesia administration are shown in (Figure 3).

Discussion

The past four decades have witnessed an explosive growth in illicit drug use in many parts of the world [17]. Mortality may occur when these recreational drugs are associated with acute alcohol intoxication [18]. In the present study, the most common addictive drugs were bango and hashish in 75% each, pills in 50% while heroin was used in 25% and opiates in 12.5%. However, a study in Argentina mentioned that the most often drugs used in addict patients are cocaine 90.4%, followed by marihuana 88.3% LSD use is 17.5% and parenteral drug use in 43.1% [19]. The chronic use of opioids leads to lowered pain thresholds and exaggerated pain levels. Several mechanisms have been proposed to explain this heightened sensitivity commonly termed opioid-induced hyperalgesia (OIH). OIH is a state of paradoxically enhanced pain sensitivity observed in patients after chronic exposure

Laboratory investigation mean±SD	Addict patients No=20
RBC count (millions/mm^3)	4.29±0.47
Hemoglobin (g/dl)	13.63±1.19
WBC (thousands/ mm^3)	7.9±2.67
Platelets (thousands/ mm^3)	309.7±76.24
Aspartate transaminase (AST) (U/L)	40.45±21.55
Alanine transaminase (ALT) (U/L)	45.25±27.96
Creatinine (mg/L)	0.85±0.28
Blood Urea Nitrogen (BUN)(mg/L)	29.5±21.97
Fasting blood sugar (mg/L)	101.25±22.86
HCV positivity (No of patients)	7

Table 2: Laboratory investigations of the addict patients.

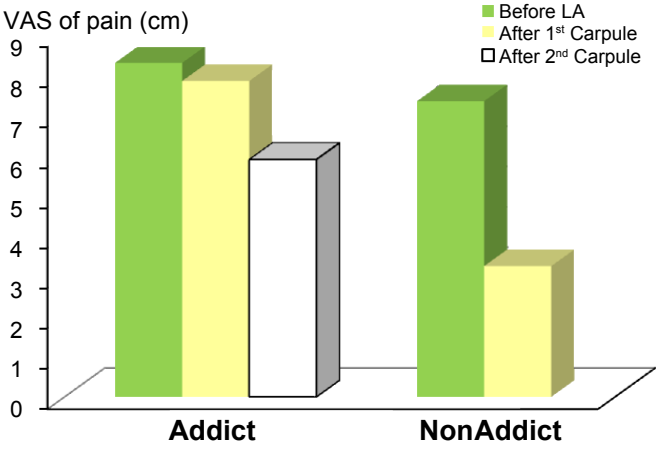

Figure 3: Visual Analogue Scale (VAS) in addict and control patients according to local anesthesia administration.

to opioids including morphine, oxycodone, fentanyl, heroin and others. The mechanisms responsible for the opioid-induced excess in nociceptive sensitization have not been fully explored [20].

Pain control is a major component of patient comfort and safety. Local anesthetics form the backbone of pain control in dentistry. The VAS is considered an effective parameter for evaluation of pain and provides a gross validated and meaningful measurement for anesthetic efficacy, which can be used by both adults and children [21]. Anxiety and pain levels in third molar surgery were successfully assessed by means of VAS [22]. The efficacy of local anesthetic was assessed in several studies [23-27].

In the present study, fifteen out of the twenty addict patients gave a history of their associated medical conditions. Nine of the addict patients (45%) had hepatomegaly and elevated liver enzymes and 7 patients were HCV positive with proteinuria. This is coincidental with the results of Cocozella and coworkers [19], who found liver disease in drug addicts 33.6% and the prevalence was higher for HCV and alcoholism.

Drug addicts frequently have liver diseases for different reasons: alcohol abuse, the drugs themselves, but more often hepatitis B and C infections [19]. Hepatic diseases including hepatitis C virus infection are rather common in intravenous than oral drug addicts especially the needle-sharing abusers. Symptoms of hepatic disorders are found both in the period of active abuse and in abstinence [28-30]. Addict patients going for oral surgery are found to bring a combination of medical problems with them [31].

Concerning the dental conditions, all addict patients had higher dental affection and poorer dental hygiene compared to the non addict patients. This finding maybe because of drug addiction has a rapid, severe and deleterious effect on dental health with tobacco, morphine and alcohol importantly contributing to these changes [32-35]. The addicted group had a high prevalence of orofacial motor behavior (bruxing and clenching) and temporo-mandibular joint (TMJ) disorders (morning headache, joint noises, joint and masticatory muscle tenderness to palpation and tooth wear) compared to the non addict which is in agreement to the result of Winocur et al. [36].

In the present study all addict patients required two carpule (3.6 ml) of local anesthesia while the non addict patients received only one carpule (1.8 ml).

In the current study, before surgery the CRP level in the addict patients was higher than that of non addicts. After surgery the levels of CRP were increased in both groups. In agreement with our results is the study of Housová et al. [37] who found that the serum CRP was markedly higher in the addicts compared to the non addict patients. This could be explained on the basis of addict patients have a clinical pathological profile of immune stimulation with higher ESR, CRP, globulins, globulin:albumin ratio, lymphocyte count, ALT, urea, creatinine and urea:creatinine ratio [38].

Surgical trauma elicits a characteristic metabolic response, including an elevation in the synthesis and release of various chemical mediators and acute-phase proteins. C-reactive protein is the first acute-phase reactant to rise after trauma or surgery. Its concentration increases significantly in the immediate postoperative period [39]. In the study of Marana et al. [40], CRP reached its highest level on the second postoperative day. The CRP showed no significant differences among patients treated by tramadol and ibuprofen in the immediate postoperative samples, whereas a significant increase was recorded 72 hours after treatment [24].

In conclusion, addict patients have a hyperalgesic state and lower pain threshold than non addict patients. They require higher doses of local anesthesia during oral surgical procedures. They are more anxious and irritable and when visiting dental clinics or requiring an oral surgery that should be treated cautiously. Care must be taken when dealing with addict patients as they have more co-morbid diseases such as HCV than non addicts. Lastly, more regular visits to the dentists should be allowed for the addicts to avoid the dental problems. A larger number of patients are recommended to confirm these preliminary results.

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