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The Characteristics of Gastroduodenal Perforations in Crack-Heroin Users

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Abstract: *Background:* Crack-heroin has been gaining popularity during recent years in Iran. Unlike crack-cocaine, crack-heroin has not been previously associated with gastroduodenal perforations. This study attempts to report a probable association. *Methods:* This cross-sectional study included 60 patients admitted to a Tehran hospital with a history suggestive of perforated peptic ulcer, whose diagnosis was confirmed postoperatively. They were assigned to two groups on basis of crack-heroin use during the previous 12 hours and compared. *Results:* Crack-heroin use in gastroduodenal perforation patients was associated with lower age, lower incidence of free peritoneal gas, lower white blood cell counts, and absence of a history of previous peptic ulcer. Perforations in crack-heroin users were more prevalent in prepyloric and pyloric areas, while in non-users they were seen more frequently in duodenal and gastric areas. Severe contamination of the peritoneal cavity was significantly higher in the users. *Conclusions:* Crack-heroin related gastroduodenal perforations have distinct characteristics, which may be suggestive of a causative relation or common underlying etiology.

Key words: Crack Cocaine; Heroin; Peptic Ulcer Perforation, Epidemiology; Peptic Ulcer Perforation, Etiology.

INTRODUCTION

The consumption of crack-cocaine, the free-base form of the drug, introduced as an illicit street drug in 1986, has since been linked to perforated peptic ulcers throughout the medical literature (Abramson, D.L., 1991; Kram, H.B., 1992; Schuster, K.M., 2007). The proposed mechanism for crack-cocaine related gastroduodenal perforations has been presumed to be an ischemic process (Arrillaga, A., 1996). The difference in the pathogenesis between these perforations and those unrelated to cocaine, were implied by the difference in the characteristics and manifestations of the perforations (Abramson, D.L., 1991). Crack-cocaine related perforations may be present with extensive contamination despite normal or low white blood cell counts and the absence of pneumoperitoneum on X-rays or previous history of peptic ulcers (Kram, H.B., 1992).

The drug known as “crack” in Iran, however, bears no relation to the widely recognized crack-cocaine and is in fact a compound consisting of concentrated heroin (UN, 2008). The drug has gained tremendous popularity throughout the country during the recent years, to the point that Tehran's Specialist Treatment Addiction Center reported 75% of its patients to have been crack-heroin or crystal heroin users (US, 2007).

A variety of complications have been attributed to heroin, perhaps the most important complication being death, usually due to heroin overdose and acute narcotism (Zador, D., 1996). Other documented complications of heroin use include scarred and/or collapsed veins, bacterial infections of the blood vessels and heart valves, abscesses and other soft-tissue infections, and liver or kidney disease.[8] Many of these complications along with the embolism of non-soluble substances, immune reactions towards these substances, and blood borne infections, such as AIDS and hepatitis B, are the result of intravenous substance use and are not directly linked to heroin per se (US, 2005). In the case of crack-heroin in Iran, which is usually smoked, most of the complications listed do not apply. Heroin use has been linked to stroke, suggested mechanisms including emboli, focal ischemia due to hypoventilation, drug allergy or vessel toxicity (Brust, J.C.M., R.W. Richter, 1976). However, to our knowledge, only one study has documented gastroduodenal perforations in crack-heroin users, and only to a very limited extent (Kahrom, M., H. Kahrom, 2010).

This study was conducted to investigate the characteristics of gastroduodenal perforations in crack-heroin users in order to document the differences of these perforations in comparison to those of patients who did not use crack-heroin previous to the onset of acute abdomen symptoms.

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Methods:

This cross-sectional study included 60 patients admitted to a Tehran hospital during a two year period with a history suggestive of perforated peptic ulcer, whose diagnosis was confirmed post operatively.

Subjects gave informed consent for use of the data for research purposes. The study protocol did not involve any interventions other than those required in the natural course of treatment, and was granted ethical clearance by the University Deputy of Research under research proposal approval number #17837.

Data was recorded by a fourth year surgical resident using patient history, physical examination, diagnostic tests, imaging, and direct observation of the perforations during surgery.

The patients were divided into two groups based on whether they had a history of crack heroin use during the last twelve hours previous to the initial symptoms of acute abdomen. The patients were also asked of their history of alcohol consumption, smoking, and previous peptic ulcer.

Upright chest X-rays were obtained for all patients to assess for free gas in the peritoneum beneath the diaphragm and complete blood cell counts were requested before laparotomy was performed. The X-rays were all taken in the hospital radiology center and the presence or absence of peritoneal gas bubbles was declared by the radiology specialist. The blood cell counts were all performed by the hospital laboratory.

If a perforation was confirmed during surgery, the location of the perforation, and degree of contamination of the peritoneal cavity were recorded. The degree of contamination was considered severe, if pus or fibrin was found in the peritoneal cavity; moderate, if bile was present throughout the entire cavity; and mild, if bile was present only in the upper half of the abdominal cavity.

The perforation site was categorized as duodenal, gastric (located in the antrum, corpus, or fundus), pyloric (situated in the pyloric orifice), or prepyloric (located within 2cm proximal of the pylorus).

Data were analyzed using the chi-square, and Mann-Whitney U test, with the SPSS 13 software package (SPSS Inc., Chicago, IL, USA).

Results:

This study included 60 perforated gastroduodenal ulcer patients, all of which were male except for one. The mean age of the patients was 40.9±16.9 years, the youngest being 14 and the oldest 74. Overall 28 (46.7%) of the patients mentioned a history of substance abuse, 38 (63.3%) were smokers, and 13 (21.7%) reported a history of alcohol abuse. A past medical history of peptic ulcer was positive in 28 (46.7%).

A history of crack-heroin use during the 12 hours preceding the onset of the symptoms of acute abdomen was observed in 21 (35.0%) of the patients.

The mean age of the patients with a history of crack-heroin use was 24.1±7.5 years, compared to a mean age of 50.0±13.3 years in the non-users. This yielded a significant difference ($p<0.001$).

Free peritoneal gas was noted in 76.9% of the non-users, compared to a 47.6% of the crack-heroin users. This difference was also statistically significant ($p=0.023$). The average white blood cell count was 11,500±1,714 for the crack-heroin users, and 14,962±2,561 for the non-users, which was found statistically significant as well ($p<0.001$).

Table 1: Perforation site observed on surgery.

Perforation Site	Crack-heroin users	Non-users	p-value
Gastric	1 (4.8%)	12 (30.8%)	<0.001
Prepyloric	15 (71.4%)	5 (12.8%)	
Pyloric	5 (23.8%)	7 (17.9%)	
Duodenal	0 (0%)	15 (38.5%)	

The perforation site for the crack-heroin users was also significantly different than those of non-users. For crack-heroin users the most common perforation sites in order of frequency were the prepyloric (71.4%), pyloric (23.8%), and gastric regions (4.8%), while the most common sites for the non-users were the duodenal (38.5%), gastric (30.8%), pyloric (17.9%), and prepyloric (12.8%) regions, respectively. This difference was statistically significant (table 1).

The degree of contamination for the two groups is illustrated in table 2. As can be seen, the percent of patients with severe contamination was higher among the crack-heroin users. This difference was also statistically significant ($p<0.001$).

Table 2: Peritoneal contamination observed on surgery.

Contamination	Crack-heroin users	Non-users	p-value
Mild	1 (4.8%)	13 (33.3%)	<0.001
Moderate	7 (33.3%)	23 (58.9%)	
Severe	13 (61.9%)	3 (7.7%)	

Smoking and alcohol consumption did not show a significant association with perforation site, degree of contamination, or free peritoneal gas. A history of previous peptic ulcer showed a relation only with perforation

site ($p<0.001$), and not with the degree of contamination or free peritoneal gas. A positive history was more predictive of a duodenal or gastric perforation, while a negative history was indicative of a prepyloric or pyloric perforation.

The background of the patients revealed no significant difference between crack-heroin users and non-users in terms of smoking and cigarette smoking, but did reveal a significant difference regarding history of previous peptic ulcer: the crack-heroin users were less likely to have had a positive history ($p=0.009$).

The patients were also asked whether they had ever used any drugs other than heroin. Interestingly, a positive history of heroin use was found to be inversely related to the use of other drugs, and this relation was statistically significant ($p=0.005$).

The differences between the two groups are summarized in table 3.

Table 3: Differences observed between the two groups.

	Crack-heroin users	Non-users	P value
Mean Age (yr)	24.1±7.5	50.0±13.3	<0.001
Mean WBC Count	11,500±1,714	14,962±2,561	<0.001
Peritoneal Gas	10 (47.6%)	30 (76.9%)	0.023
History of Smoking	15 (71.4%)	23 (58.9%)	0.252
History of Alcohol Use	3 (14.3%)	10 (25.6%)	0.249
History of Drug Use*	6 (28.6%)	26 (66.7%)	0.005
History of Peptic Ulcer	5 (23.8%)	23 (58.9%)	0.009

* Other than heroin

Ultimately, controlling for co-variance was performed with a logistic regression based on the significant findings of the multiple chi-squares. When logistic regression was performed for severity of disease, taking into account age; history of crack, smoking, alcohol and opium use; and previous history of peptic ulcer disease, only age ($p<0.001$) and history of crack-heroin ($p=0.035$) use were found to be significantly related to the severity of disease. The odds ratio for crack-heroin use was found to be 7.04 for moderate to severe disease, meaning that after taking confounding factors into account, crack-heroin use would be approximately related to a 7-fold increase in the incidence of moderate to severe gastroduodenal perforations compared to mild disease.

Discussion:

The main finding of the study was a striking difference between the characteristics of gastroduodenal perforations in crack-heroin users and non-users. This difference may be suggestive of a causative relation or common underlying etiology.

While less well-known in the rest of the world, crack-heroin has been gaining increasing popularity during the recent years in Iran and neighboring countries Afghanistan and Pakistan. A brief comparison of crack-heroin in this region, with crack-cocaine in other parts of the world demonstrates interesting similarities. A published report by Lee *et al* (1990) revealed that of 27 gastroduodenal perforation patients they had studied, 9 (33.3%) had a history of crack-cocaine use. This is comparable to the percent of patients that mentioned a history of crack-heroin use in the current study, 21 (35%) of the 60 patients.

In this study, the mean age of the patients in the crack-heroin group was significantly lower than the non-users. This has also been shown to be true for crack-cocaine users with gastroduodenal perforations. In 1999, Feliciano *et al* (1999) reported the mean age of crack-cocaine users with gastroduodenal perforations to be 8-10 years younger than non-users. Similar results were also reported by Sharma *et al* (1997), who found crack-cocaine users to be an average of 11 years younger, with a mean age of 37 years compared to the average 48 years of the non-user population. Despite the similarities, the mean age of crack-heroin users in this study was an alarmingly lower 24.1 years.

Another finding analogous to crack-cocaine results was the prevalence of free intraperitoneal gas found on the chest X-ray. This study reported free intraperitoneal gas in only 47.6% of the crack-heroin users, compared to a 76.9% in the non-users. This is in accord with the findings of Sharma *et al*, (1997) who reported a 42% prevalence of free intraperitoneal gas in the X-rays of crack-cocaine users. The same can be said of the white blood cell count, which was found to be significantly lower in crack-heroin users in this study, and has been reportedly lower for crack-cocaine users as well.

The perforation site pattern observed in the present study is particularly suggestive of a causative relation. The most common perforation sites for the crack-heroin users were prepyloric and pyloric regions, as opposed to duodenal and gastric regions which were more prevalent in non-users. Not only are the common perforation sites for crack-heroin related perforations different than those of the general population, but what makes this finding so interesting is that they are also contrary to the age trend. Overall, duodenal perforations are the most common type, but the percent of perforations that occur in the duodenum slightly decrease as age increases (Svanes, C., 1993). The results of this study showed a lower number of duodenal perforations in the crack-heroin users, despite a significantly lower age. This is suggestive of an independent etiology for crack-heroin related perforations.

No significant difference was found between the crack-heroin users and non-users in terms of alcohol consumption and smoking. Smoking has previously been shown to increase the risk of gastroduodenal perforations (Svanes, C., 1997) and further understanding of this pathophysiology may lead to a better understanding of the mechanisms behind crack-heroin smoking related perforations.

Regarding a history of peptic ulcer, a positive history was observed more frequently in non-users. In the general population, perforation is seen without a previous history of peptic ulcer in only 25% of the cases. For the crack-heroin users in this study, 76.2% presented with a perforation without any history of peptic ulcer.

The history of drug use for drugs other than heroin was more frequently found to be positive in the non-users. This finding seems contradictory and not in accord with expected results. In a study by Zador *et al* (1992), most deaths attributed to heroin use were in fact found to be associated with the use of other drugs in combination with heroin, and not heroin alone. One way of explaining this finding is that the crack-heroin users may have concealed information thought to have been irrelevant to their current condition.

Another concern worth mention is the fact that officially, not much is known about the process of manufacturing crack-heroin. Crack-cocaine is generally manufactured by using a base such as baking soda (sodium bicarbonate) or sodium hydroxide (Estroff, T.W., 2001). Crack-heroine, on the other hand, has reportedly been thought to be manufactured uniquely in each laboratory; processes mentioned, range from a simple concentrating of heroin to adding expired drugs such as diazepam, codeine, barbiturates, methamphetamine, corticosteroids, and various sedatives; or substances like ammonia or sodium hydroxide. Considering the different toxicity profiles of cocaine and heroin, and the similarities in gastroduodenal perforations associated with the two drugs in their “crack” form, the gastroduodenal manifestations observed may very well be due to a by-product of the manufacturing process and not the active drug itself.

On the other hand, at least one other study has confirmed a relationship between heroin use and gastric ulcer perforations. The study by Kahrom and Kahrom (2010), which is also from Iran, reported cases of ulcer perforations in opiate users after sudden withdrawal. The interesting point in this study was that 8 of the cases reported were heroin users and 5 others were heroin and opium users. This is to our knowledge the only association made in the literature between heroin use and perforation. However, this association was solely based on an observation of chronological incidents in substance abusers of which, only a small fraction of were heroin users, and could have possibly been confounded by other factors and etiologies.

Overall, gastroduodenal perforations in crack-heroin users were found to occur at a lower age. Intraperitoneal free gas may not be observed on the chest X-rays of these patients and despite higher peritoneal contamination, they may present with lower white blood cell counts. These perforations may occur without a previous history of peptic ulcer.

Since mortality and morbidity rates of gastroduodenal perforations are directly related to the delay in the diagnosis of the patients (Subedi, S.K., 2007), recognizing atypical manifestations of crack-heroin related perforations may help timely diagnosis of such patients. Additionally, the specific manifestations found in these patients may help find the etiology and pathophysiology of the perforations. At last, in order to identify the manifestations precisely, they should be further studied in isolation, with proper matching for confounding factors.

Conflict of Interest:

The authors have no conflicts of interest.

Authors' Contributions:

MRN was responsible for providing the subject of study and remained in charge of directing the study throughout its course. AR provided assistance in the design, statistical analysis, and drafting of the manuscript. AK was the primary consultant for design and statistical analysis. All authors played active parts in each stage of the study and roles overlapped in all domains. The authors have read and approved the content of the manuscript.

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