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Heroin Abusers: An Immunological Aspect

El-Fiky M.R., Owida M.A., Wilson A.K., and Fahmy M.

Abstract

This immunologic study of 43 intravenous heroin abusers, was carried out to explore the possible existence of pathogenic factors which may trigger the abnormalities. Serum concentrations of immunoglobulins IgM, IgG, and IgA were determined, and compared to those of two control groups. High significant elevations of IgM ($p < 0.01$), and significant increase of IgG and IgA ($p < 0.05$) were detected in parenteral heroin abusers. The associated immunodeficiencies in heroin abusers may be initiated by the action of the drug and adulterants and become aggravated during the course of abuse by malnutrition and infection through needle using and sharing. The data reveal the importance of considering the virological status besides the toxicological investigations of the current abusers of narcotics. Further research is recommended.

Introduction In the past two decades, the effects of psychological and environmental events on immune responses have been investigated. Increased inquiries about the spectrum of morbidity of the abuse of narcotics was partially due to a remarkable increase of death caused by these substances (Staa, 1990). Louria, et al. (1986) and Sapira (1988) recorded that medical complications in chronic heroin abuse may involve multiple organ systems. Immunologic consequences of chronic heroin abuse have been also increasingly recognized. A high prevalence of biologic-false-positive serologic tests for syphilis (Cherubin & Millan, 1978), positive latex fixation tests for rheumatoid factor (Ronald et al 1980) and increased heat stable opsonic antibody activity (Cushman & Grieco, 1973) has been described. However, the most commonly recognized serum immunologic alteration in heroin abusers is polyclonal increase in serum immunoglobulin M (Grieco & Chaung 1983). Brown et al. (1982) also reported that heroin addiction can be accompanied by changes in serum IgG and IgA. The aim of the present work is to demonstrate immunoresponsiveness of heroin abusers as measured by serum immunoglobulins (IgM, IgG, and IgA).

Subjects & Methods Fifty eight male heroin abusers were chosen during the male period July 1990- Oct. 1994 from inpatients of state and private psychiatric hospitals in Egypt, Saudi Arabia, and Kuwait. They were diagnosed according to DSM-III-R (1987) criteria for opioid dependence, (predominantly) and were neither suffering from any relevant medical diseases nor homosexuality. Their mean age was 21.8 ± 6.1 years and exposure time to drug addiction 2.3 ± 2.5 years. They were subdivided into heroin injectors ($n = 43$) (intravenous use of heroin for at least 2 years and syringe promiscuity) and heroin sniffers ($n = 15$). The control group consisted of 15 individuals who never used any drug or complained of any physical disease. They examined for serum concentration levels of immunoglobulins IgM, IgG, and IgA by radial immunodiffusion plates (Partigen plates Behring).

Results Serum immunoglobulin concentrations (Table 1) showed a diffuse increase in level of IgM in 67.4% of heroin injectors and 26.7% of heroin sniffers, and an increase in level of IgG in 39.5% of heroin injectors and 33.3% of sniffers.

Table (1) Serum immunoglobulins levels among the study and control groups

	N	Levels > N		Immunogl. conc.		"p"	Significance
		No.	%	(mg / 100ml.)	Mean \pm SD		
IgM (N = < 280 mg%)							
I.V. heroin abusers	43	29	67.4	282.8	139	<0.01	H. Sig.
Heroin sniffers	15	4	26.7	216.5	97.9		
Controls	15	0	0	180.7	80.4		
IgG (N = < 1.85 mg%)							
I.V. heroin abusers	43	17	39.5	1.74	0.83	0.05	Sig.
Heroin sniffers	15	5	33.5	1.58	0.64		
Controls	15	0	0	1.42	0.65		
IgA (N = < 41 mg5)							
I.V. heroin abusers	43	11	25.6	364.2	157.4	<0.05	Sig.
Heroin sniffers	15	3	20	343.1	156.7		
Controls	15	1	6.7	281.5	130.8		

25.6% of intravenous heroin abusers and 20% of sniffers had an increase in IgA.

Levels of IgM in parenteral heroin dependents were highly significant ($p < 0.01$) greater compared to controls, while levels of IgG and IgA in intravenous heroin addicts were significantly ($p < 0.05$) higher than those of controls.

Discussion Hyperglobulinemia accompanying heroin abuse has been long recognized (Cherubin, 1977, and Louria et al. 1986). The results of the current work that showed elevation of serum immunoglobulins, are in agreement with other studies of Grieco, 1973, Cushman 1974, and Robin, 1983. The most consistent change was an increase in the concentration of IgM. In the present work, the increase of IgM was found in 67.4% of parenteral heroin abusers and 26.7% of heroin sniffers. Nickerson, et al. (1980) reported increased Igm in about two thirds of addicts, though they did not differentiate whether they were syringe-users or sniffers. Comparison of the two groups of abusers between each other and between the group of healthy non-addict persons without inter current diseases could realize that increased IgM detected in heroin abusers seems to be more related to infections than to the drug-addiction itself. Similar

findings were seen in the work of Ramos, et al. (1990) who concluded that immunological disorders detected in needle-using addicts were due to infection by the human immunodeficiency virus and other associated infections. Despite that potential danger of needle-using addiction, Aylett (1982) suggested that those abusers prefer this route due to its rapid effect, and their imagination that they escape danger to the liver, and possible endogenous endorphinencephalin response.

Elevated IgG were notable in the present study in 39.5% of heroin injectors and 33.5% of sniffers. Robin (1983) suggested that increased IgG in active narcotic users is uncommon, while according to Biagini, et al. (1990) elevated IgG levels were present in workers exposed to opiates at a narcotic manufacturing facility, similar to intravenous heroin abusers and they considered these anti-morphine antibodies as biomarkers of exposure. Such findings of increased IgG levels has potentially far-reaching implications for addiction research and drug testing.

Serum IgA levels were high in 25.6% of injectors and 20% of heroin sniffers. Weksler, et al. (1984) had recorded similar findings. Muniz-Diaz, et al. (1993) in their immunologic study of 60 i.o. drug addicts found antiplatelet antibodies in 31% of the patients, of which 50% corresponded to IgG

class, 12% to IgM, 21% to IgG plus IgM, 7% IgM plus IgA, % to IgG plus IgA and 5% IgG plus IgM plus IgA. Our opinion is that these numerous serologic findings in these patients fundamentally express the existence of a chronic polyclonal stimulation of B cells which, maybe initiated by the action of the drug itself and which becomes aggravated during the course of the multiple acquired. Also Shafer et al. (1991) demonstrated that opiates diminish DNA repair capacity and reduce immunoresponsiveness as measured by T-cell, and these interactions of opiates with T-lymphocytes may regulate cell metabolism and could there by be responsible for the sensitivity of from opiate addicts cells to both genotoxic damage and immunological effects. On the contrary, Koster et al. (1990) morphologically examined 66 autopsied drug-related death cases to investigate whether spleens reveal a damage of the immune system, where neither a significant weight changes of the spleen nor an important change of the density of the immunoreactive cells could be registered. Such a quantitative study may be used as a measure to detect any defect in the immune system.

The cause of these immunoglobulin changes in heroin abusers is not clearly known. A number of possible explanations can be proposed. First, pure heroin itself being responsible for these immunoglobulin changes, seems unlikely because IgM elevation has not been produced experimentally (Ryan, et al., 1972). Second, the variability of "started" narcotics is well known. A wide variety of diluents and contaminants may be introduced by the supplier or the user himself during the self-injection procedures, which may contribute to the antigenicity of drug abuse. Therefore, there are a number of possible antigens and /or haptens are expected to be present in chronic heroin addicts according to Cushman & Grieco (1973). Welti, et al (1983) found bacterial contaminants, chiefly bacillus species and coagulate negative staphylococci, in over half of the specimens of street heroin cultures. Third, the usual addict in his haste to "take off" often uses poor injection techniques, with little regard to asepsis and possible infection (Blank, et al. 1980). Fourth, the important role played by needle sharing in the spreading of multiple infections among IV. drug abusers. Patti, et al. (1993) showed high prevalence rates of all

hepatitis viruses and other blood-borne infections in a group of heroin injectors as high as 50.9% for HAV, 65% for HBV, 63.4% for HCV, and 13.3% for HDV.

Mandelli et al (1991) reported that 66.2% of 646 heroin addicts had anti-HIV with concomitant chronic HBV infection in 74.4% of them. Fifth, Mclachlan et al. (1993) referred to the long-term immunosuppression in chronic heroin injectors and said that methadone maintenance as an opioid antagonist- does not significantly impair immune function and possibly even allows some improvement to occur, and it may share the direct and indirect immunoregulatory effects of other opioids. Sixth, hepatic diseases which have been associated with increased serum IgM levels include primary biliary cirrhosis and viral hepatitis (Walker & Doniach, 1978). There were no clinical suggestions of primary biliary cirrhosis obstructive biliary disease, nor chronic aggressive hepatitis in the patients of the present study. Although, hepatitis carrier cases may be present among them (Delfini et al. 1993). Seventh, Cirasino, et al.(1992) pointed to malnutrition in intravenous drug users that can also be present in the first stages of infections and negatively influences the immunodeficiency.

Conclusion The intravenous drug-addicts are considerably and increasingly burdened by infections particularly hepatitis virus, HIV, and other blood borne infections. They show a high risk relating to viral infections transfer to the population because of their rapidly increasing number. From the medical point of view, the virological investigations of the current abusers of narcotics should be considered besides the clinical diagnosis. Serum immunoglobulins and other similar parameters may be advocated as biomarkers with potential implications for addiction research and drug testing.

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Authors

El Fiky, M.R, (MD)

Ass Prof. of Psychiatry, Ain Shams Faculty of Medicine.

Owida, M.A., (MD)

Lecturer of Psychiatry, Al-Azhar Faculty of Medicine.

Effat S. (M.D).

Lecture of Psychiatry, Ain Shams Faculty of Medicine.

Wilson A., (M.D)

Lecturer of Psychiatry, Suez Canal Faculty of Medicine.

Fahmy M. (M.D)

Lecturer of Psychiatry, El-Monofiah Faculty of Medicine.

Address of Correspondence

El Fiky M.R.

Institute of Psychiatry, Ain Shams University, Abbasia, Cairo, Egypt.

الجانب المناعى فى إدمان الهيروين

أجريت الدراسة المناعية لثلاث وأربعين من مدمنى الهيروين عن طريق الحقن بالوريد بهدف الوصول إلى العلاقة المحتملة بالعوامل المرضية الأخرى والتي يمكن أن تحدث تغيرات مناعية. وقد تم تقدير مستويات سائل الدم بالنسبة للجلوبيولين المناعى "م"، "ج"، "أ" فى جميع المرضى وقورنت بممثلاتها فى "أ" و "ب" مجموعتين ضابطين. وأظهرت النتائج وجود إرتفاع ذو دلالة إحصائية عالية بين مستوى الجلوبيولين المناعى "م" وإرتفاع ذو دلالة إحصائية بين مستوى الجلوبيولين المناعى "ج" و "أ" بين المدمنين الذين يستعملون الهيروين بالحقن. وخلصت الدراسة إلى أن هذه التغيرات قد تنشأ بسبب مفعول العقار أو ملوثاته وتزيد خلال فترة سوء الإستخدام بواسطة سوء التغذية وحدث الإلتهابات المتعددة بين مستخدمي الهيروين بالحقن بسبب إستخدام المحاقن أو تبادلها. وكشفت المعلومات أهمية وضع الحالة الفيروسيه فى الإعتبار بجانب الإستقصاءات السمية فى تقدير الحالة الراهنة لمدمنى المخدرات.