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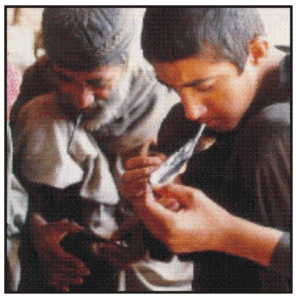

ADDICTIVE DRUGS;
EFFECT ON HAEMATOLOGICAL AND HORMONAL PROFILES IN MEN

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ABSTRACT... sohailali98@hotmail.com. **Background:** The phenomenon of drug abuse and its sequalae affect health of the abuser in multiple ways, e.g. changes in body weight, changes in nutrient metabolism due to the pharmacokinetic and pharmacodynamic effects of the drugs, changes in the endocrine system, etc. There is a paucity of research in this area, in Pakistan. **Objectives:** To study the effects of drugs of abuse on the physiological and biochemical processes of the body, in a Pakistani population of drug addicts; and then to compare these findings with an age and gender matched control group. **Method:** This research study was carried out at the District Headquarters Hospital Faisalabad, at the Model Drug Abuse Treatment and Rehabilitation Centre located in the hospital. It was a cross-sectional, non-interventional, comparative study. Subjects were recruited by a consecutive sampling method. The study group consisted of 100 subjects, consisting of 80 drug addicts and 20 age and sex matched controls. The following measurements were made: Physical parameters, Plasma biochemistry, Liver function tests, Thyroid hormone levels , Plasma electrolytes and trace element levels Statistical analysis was carried out by two way analysis of variance and Student's t test. The threshold for statistical significance was set at a p value equal to or less than 0.05. **Results:** Mean age of drug addicts was 31 years. Most of them were poly-drug addicts and mean duration of addiction was 8 years. The drug addicts had low body weight and high blood pressure and temperature, as compared to the control group. The laboratory tests revealed that the addicts as a group had decreased albumin, globulin and total protein levels; while plasma glucose, SGOT, SGPT, T3 and T4 levels were generally higher in the dug addicts, as compared to the control group. **Conclusion:** Besides the problem of addiction, the effects of drugs of abuse on the physiology and biochemistry of the human body are harmful in their own right. These results are significant because they highlight the importance of holistic assessment and management of drug abusers beyond just managing their addiction.

Key Words: Drug abuse, plasma biochemistry, liver functions, thyroid functions, serum electrolytes.

INTRODUCTION

The problem of drug abuse is centuries old. The variety and pattern of use has varied over time and between geographical regions. In the past; opium, cannabis, and barbiturates were mostly abused; but with time the trend has shifted towards more potent and refined drugs such as cocaine, hallucinogens, heroin, and sedative/hypnotics etc. Patterns of use have also shifted towards multiple drug abuse and increasing use of injectable drugs. The most commonly abused drugs in Pakistan, in the recent years, include heroin, cannabis (as bhang or charas), opium, and tranquillizers[1,2].

The phenomenon of drug abuse and its sequalae affect health of the abuser in multiple ways, e.g. changes in body weight secondary to changes in dietary habits and lifestyle, changes in nutrient metabolism due to the pharmacokinetic and pharmacodynamic effects of the drugs, changes in the endocrine system, etc.

Much research has focused on the effects of heroin and morphine on the body. Heroin addiction can cause hyperkalaemia. Morphine can cause calcium channel inhibition, hypercholesterolemia, hypo or hyperthermia[3]. Serum protein levels in heroin addicts have been reported to be either reduced or normal[4-7]. Thyroid activity is also affected, with tri-iodothyronine (T3) levels reported to be raised in heroin addicts, while thyroxin (T4) and thyroid stimulating hormone (TSH) levels remaining unchanged[8].

Heroin addiction also causes hypertension, weight loss and a decrease in testosterone levels[9]. Inflammatory changes in the liver, with consequent derangement in hepatic enzymes and other liver function measures, are also frequently seen in heroin abusers[10]. Changes in trace elements have also been reported, for example, large doses of morphine have been seen to cause a fall in magnesium content in blood, brain, heart, liver and kidneys in mice[11]. Similarly morphine tends to decrease zinc levels in brain tissue of mice, while increasing zinc levels in the blood[12].

Central nervous system have also been studied in this respect. Intravenous nicotine administration has been seen to cause an elevation in plasma free fatty acids[13]. Nicotine and tobacco also cause hypertension (by increasing the absorption of sodium), hyperkalaemia, and hypothyroidism[14]. Tobacco smoking also increases serum cholesterol while lowering serum selenium and zinc levels[15].Cocaine intake increases blood pressure and pulse rate, as is true of all the CNS stimulants[16].

Alcohol has myriad effects on human physiology. Alcohol intake decreases serum protein, calcium, zinc, magnesium, and phosphate levels by increasing their excretion in urine[17]. While moderate alcohol intake tends to have a protective effect against heart disease, by increasing fibrinolysis and the levels of high density lipoprotein (HDL) cholesterol, excessive intake tends to cause nutritional deficiencies (vitamin deficiencies and protein calorie malnutrition) and alcoholic liver damage, causing derangement of al the liver function tests, and ultimately cirrhosis[14,16,18]. Episodes of hypoglycemia have also been reported in chronic alcoholics[16,19].

Hallucinogenic drugs, such as cannabis, also have complex effects on physiological and biochemical processes in the human body. These effects include high blood pressure, hyperthermia and hyperglycemia, to name a few[14,19]. Opioids have an appetite suppressant effect, ultimately leading to malnutrition and weight loss[14,16].

AIMS & OBJECTIVES

When we conducted a literature search on the subject and explored the clinical scenario in Pakistan, we came up with the following observations:

1. There is a paucity of research in Pakistan, on the physiological and biochemical effects of drugs of abuse on the human body.
2. In our clinical practice, most of the drug abusers were using more than one drug, further complicating the picture.
3 Trends of drug abuse appeared to be changing, with more patients now coming up with intravenous drugs, benzodiazepine, and opiod

analgesic abuse etc; for which the research was deficient, especially in Pakistan.

With this background, we decided to undertake a research project to study the effects of drugs of abuse on the physiological and biochemical processes of the body, in a Pakistani population of drug addicts; and then to compare these findings with an age and gender matched control group.

PATIENTS & METHODS

This research study was carried out at the District Headquarters Hospital Faisalabad, at the Model Drug Abuse Treatment and Rehabilitation Centre located in the hospital. The patients participating in the study were, however, derived from four drug abuse treatment facilities; viz,

- District Headquarter Hospital Faisalabad
- Sunny Trust Bhara Kho
- Nijaat Markaz Rawalpindi
- Rawalpindi General Hospital

It was a cross sectional, non interventional, comparative study. Subjects were recruited for the study by a consecutive sampling method. The following inclusion criteria were used:

1. Age group 16-60 years.
2. A reliable informant was available to corroborate the patient's history pertaining to drug abuse and personal history etc.
3. Subjects gave fully informed consent on a specially prepared form.

Subjects were excluded from the study if:

1. They fell outside the stated age range
2. The subject or informant was deemed unreliable for accurate information, by any of the research team members.
3. Non-consenting subjects
4. Subjects and informants having difficulty communicating with the research team e.g. language differences with the interviewers.
5. Upon physical examination, a medical or surgical condition was suspected that might alter the results of the tests to be carried out e.g. an active infection; or disorders such as diabetes mellitus which were not thought to be secondary phenomena of drug abuse, but which could affect the test results.

The study group consisted of 100 subjects, and the breakup was as follows:

Patient group – 80 subjects

1. Heroin addicts
2. Opium addicts
3. Untreated polydrug addicts
4. Treated polydrug addicts

Control group – 20 subjects (age and gender matched)

Once the groups had been selected, the following measurements were made:

Physical parameters

a. Age in years
b. Body temperature in degrees Fahrenheit
c. Height in feet
d. Weight in kilograms
e. Blood pressure in millimeters of mercury
f. Pulse pressure in mm of mercury
g. Type of addiction
h. Duration of addiction

Plasma biochemistry

a. Plasma glucose level in milligram per deciliter.
b. Plasma total cholesterol level in milligrams per deciliter
c. Plasma protein levels in grams per deciliter;

1. Total plasma protein
2. Plasma albumin level
3. Plasma globulin level
4. Albumin/globulin ratio

Plasma enzymes in Units per milliliter;

a. Glutamate oxalacetate transaminase (GOT)
b. Glutamate pyruvate transaminase (GPT)

Plasma hormones

a. Tri-iodothyronine (T3) in nanogram per milliliter;
b. Thyroxin (T4) in microgram percent

Plasma electrolytes and trace element levels in milligrams per liter;

a. Sodium level (Na)
b. Potassium level (K)
c. Zinc level (Zn)
d. Copper level (Cu)
e. Iron level (Fe)
f. Manganese level (Mn)

Once the data had been collected, statistical analysis was carried out by two way analysis of variance and Student's t test. The threshold for statistical significance was set at a p value equal to or less than 0.05. The SPSS-X software package was used for this purpose[20].

RESULTS

Physical parameters:

These parameters for the various groups are shown in Table I. The results are as follows:

There was no statistically significant difference in age between the various groups. The mean body temperature was significantly higher in all four patient groups as compared to the control group. Mean height didn't differ significantly between the groups.

Table I: Physical Parameters

Groups	Mean age in years	Mean temp in degr. F.	Mean height in feet	Mean weight in Kg	Mean systolic BP in mm hg	Mean diastolic BP in mm hg	Mean pulse pressure in mm hg
Control	32.5a	97.8a	5.6a	66.8a	113a	78a	35a
Poly drug	30.7a	99.2b	5.7a	60.6b	119b	81a	38b
Heroin	31.4a	99.0b	5.5a	52.5c	120b	81a	39b
Opium	31.5a	99.1b	5.6a	60.6b	126c	88b	38b
Poly drug(tr)	31.5a	98.9b	5.5a	55.6c	125c	82a	43c
All four patient group combined	31.3a	99.1b	5.6a	57.3c	122.5b	83a	39.5b

a,b,c :- Similar alphabets within a column indicate that the values mentioned do not differ significantly from each other i.e. p is greater than 0.05. Dissimilar alphabets within a column indicate that the mentioned values have a statistically significant difference from each other i.e. p is equal to or less than 0.05.

Mean weight differed significantly between the groups. It was highest in the control group, intermediate in the polydrug and opium addicts, and lowest in the heroin and treated polydrug addicts. The mean systolic blood pressure also significantly differed between the groups. It was lowest in the control group, intermediate in the polydrug and heroin addicts, and highest in the opium and treated polydrug addicts.

The mean diastolic blood pressure was significantly raised only in the opium addicts, while differing insignificantly across the other groups. The mean pulse pressure differed significantly across the groups; being lowest in the control group, intermediate in all active addict groups, and highest in the treated polydrug addicts.

When all four patient groups were considered together, a statistically significant difference from the control group was seen only for the mean body temperature (higher in the drug abusers), mean body weight (lower in the drug abusers), mean systolic blood pressure (higher in the drug abusers), and mean pulse pressure (greater in the drug abusers).

PLASMA GLUCOSE, CHOLESTEROL AND PROTEIN LEVELS:

These results, shown in Table II below, are as follows:

Mean plasma glucose differed significantly across the groups; being lowest in the control group, intermediate in opium, polydrug and treated polydrug addicts, and highest in the heroin addicts.

The mean plasma cholesterol level also differed significantly across groups; being lowest in the polydrug, opium and heroin addicts, intermediate in the control group, and highest in the treated polydrug addicts.

The mean total plasma protein level differed insignificantly across the groups. The mean plasma albumin level differed significantly across the groups; being lowest in the polydrug addicts, intermediate in the treated polydrug addicts, highest in the opium and heroin addicts and in the control group.

The mean plasma globulin level differed significantly across the groups; being lowest in the heroin and opium addicts, intermediate in the polydrug addicts and control group, and highest in the treated polydrug addicts.

The mean albumin-globulin ratio similarly differed significantly across the groups; being lowest in the treated polydrug addicts, intermediate in the polydrug addicts and control groups, and highest in the heroin and opium addicts.

When all four patient groups were considered together; a statistically significant difference from the control group was seen only for mean plasma glucose (higher in the drug abusers), mean plasma cholesterol (lower in the drug abusers), and mean plasma albumin level (lower in the drug abusers).

Table II: Glucose, cholesterol and protein levels

Groups	Mean plasma glucose in mg/dl	Mean plasma cholesterol in mg/dl	Mean plasma protein in gm/dl	Mean plasma albumin in gm/dl	Mean plasma globulin in gm/dl	Mean albumin/globul in in ratio
Control	96.1a	147.1a	6.2a	4.5a	1.7a	2.7a
Poly drug	129.0b	108.2b	5.5a	3.8b	1.5a	2.5a
Heroin	140.8c	116.9b	5.6a	4.4a	1.3b	3.4b
Opium	121.1d	126.5b	5.7a	4.5a	1.2b	3.8c
Poly drug(tr)	123.8d	177.9c	5.9a	4.0c	2.2c	1.8d
All four patient group combined	128.7b	132.4d	5.7a	4.2c	1.6a	2.9a

a,b,c :- Similar alphabets within a column indicate that the values mentioned do not differ significantly from each other i.e. p is greater than 0.05. Dissimilar alphabets within a column indicate that the mentioned values have a statistically significant difference from each other i.e. p is equal to or less than 0.05.

HEPATIC ENZYMES AND THYROID PROFILE:

These results, shown in Table III below, were as follows:

Mean SGOT differed significantly across the groups;

being lowest in the treated polydrug addicts, heroin and opium addicts, intermediate in the control group, and highest in the polydrug addicts.

Mean SGPT also differed significantly across the groups; being lowest in the control group and treated polydrug addicts, intermediate in the polydrug addicts, and highest in the heroin and opium addicts.

Mean plasma T3 level differed significantly across the groups; being lowest in the control group, intermediate in the polydrug addicts, treated polydrug addicts, and heroin addicts, and highest in the opium addicts.

Mean plasma T4 level also differed significantly across the groups; being lowest in the opium addicts, intermediate in the polydrug addicts, and highest in the control group, heroin addicts and treated polydrug addicts.

Table III: Hepatic enzymes and thyroid profile

Groups	Mean plasma got in u/ml	Mean plasma gpt in u/ml	Mean plasma T3 in ng/ml	Mean plasma T4 in microgm%
Control	90.3a	10.9a	1.8a	14.3a
Poly drug	100.1b	14.1b	3.1b	11.3b
Heroin	75.3c	16.7c	3.7c	13.7a
Opium	80.1c	16.0c	5.5d	9.6c
Poly drug(tr)	68.9d	11.2a	3.0b	13.4a
All four patient group combined	81.1c	14.5b	3.8c	1.2b

a,b,c :- Similar alphabets within a column indicate that the values mentioned do not differ significantly from each other i.e. p is greater than 0.05. Dissimilar alphabets within a column indicate that the mentioned values have a statistically significant difference from each other i.e. p is equal to or less than 0.05.

Table IV: Electrolytes and trace element levels

Groups	Mean plasma sodium in mmol/l	Mean plasma potassium in mmol/l	Mean plasma zinc in mg/l	Mean plasma copper in mg/l	Mean plasma Manganese in mg/l
Control	136.7a	4.3a	1.0a	1.2a	0.06a
Polydrug	143.7a	2.7b	0.6b	0.6b	0.06a
Heroin	137.4a	2.5b	0.6b	0.7b	0.06a
Opium	138.4a	2.8b	0.6b	0.8b	0.07a
Polydrug(tr)	140.3a	2.2b	0.5b	0.7b	0.07a
All four patient group combined	140.0a	2.6b	0.6b	0.7b	0.07a

a,b,c :- Similar alphabets within a column indicate that the values mentioned do not differ significantly from each other i.e. p is greater than 0.05. Dissimilar alphabets within a column indicate that the mentioned values have a statistically significant difference from each other i.e. p is equal to or less than 0.05.

When all four patient groups were considered together, a statistically significant difference from the control group was seen for mean plasma GOT level (lower in the drug abusers), mean plasma GPT level (higher in the drug abusers), mean plasma T3 (higher in the drug abusers), and mean plasma T4 (lower in the drug abusers).

PLASMA ELECTROLYTES AND TRACE ELEMENT LEVELS:

These results, shown in Table IV below, are as follows:

Plasma sodium level differed insignificantly across the groups. Plasma potassium level was significantly lower in all the patient groups, as compared to the control group. Plasma zinc and copper levels were significantly lower in all the patient groups, as compared to the control group. Plasma manganese level differed insignificantly across the groups.

When all four patient groups were considered together, a statistically significant difference from the control group was seen for mean plasma potassium level, plasma zinc level, plasma copper level, and plasma iron level (all lower in the drug abusers).

DISCUSSION

The results of this research project are interesting for a number of reasons;

* Few studies of this nature have been carried out in Pakistan.

* The variables cover a wide range of physical health parameters.

* It is a multicentre study, recruiting subjects for the research from four different institutions caring for such patients.

* Some of the findings echo those of previous research (as shown below), while others show differences from previously published literature, bringing into focus further research questions for future researchers interested in this area.

In the present study, mean body temperature of all addict groups combined was higher than the control group. This is in keeping with previous reports in the literature, such as reports by Isbell and White[21] and Gelder et al[16]. Various mechanism have been proposed to explain this finding, such as the direct effect of drugs on the temperature regulating system of the body, an increase in 5-hydroxytryptamine activity in some parts of the brain, or peripheral mechanisms such as changes in thyroid hormone levels in the body etc.

The mean body weight of dug addicts in our study was lower than the control group. This finding is in line with most previous reports[3,14]. The etiology is probably multifactorial; drugs may affect the central hunger and satiety centers (such as the amphetamines and cocaine etc), may affect the basal metabolic rate, may operate through endocrine and metabolic changes, may reflect dietary neglect or malnutrition due to lifestyle changes seen in drug abusers, or may arise due to complications of drug abuse such as infections or a fall in socioeconomic status etc.

Mean systolic blood pressure and mean pulse pressure was also seen to be significantly higher in the drug addicts as a group. This is also in accordance with previous studies, as reported by Goldman and Bennett[14] and Gelder et al[16]. Different mechanisms could be operating here, e.g. changes in heart activity, peripheral sympathetic activity, direct effects of drugs, endocrine changes, renal pathophysiology, or changes in blood lipid profiles secondary to drug abuse etc[13,14,19]. Further research in this area could reveal more definite explanations.

Mean plasma glucose concentration was found to be higher in the drug addicts as a group. The exact etiology and the clinical implications of this finding are as yet not clear, and warrant further research. Similar findings have been reported by previous authors as well. One possible explanation could be the increased T3 levels seen in the drug addicts. Increased thyroid activity may cause

hyperglycemia by affecting hepatic gluconeogenesis or increased peripheral breakdown of carbohydrates to release glucose into the blood.

Mean plasma cholesterol was seen to be lower in the drug addicts as a group, compared to the control group; but the treated poly drug addicts had a mean cholesterol level actually higher than the control group. These findings pose interesting questions for future research. Varley et al[22] and Tuller[23] reported hypocholesterolemia in heroin addicts and attributed it to malnutrition. Changes in thyroid activity may also have a role in lowering plasma cholesterol levels by affecting the uptake of cholesterol by body tissues.

Mean plasma albumin levels were also significantly lower in the drug abusers, while mean total protein level, mean globulin level and mean albumin/globulin ration showed only non-significant differences from the control group. Previous research to this subject has revealed mixed results; some authors such as Watson and Watzi[17] found hypoproteinemia in alcoholics, Zeb et al[5,6,7] and Sapira[24] reported hypoproteinemia in heroin addicts. Other authors report nonsignificant changes in total serum proteins in drug abusers e.g. Farukh et al[4].

The fall in serum albumin seen in our study could be due to decreased intake (dietary neglect, malnutrition), impaired synthesis (in liver disease due to alcohol or viral hepatitis seen in intravenous drug abusers), or increased excretion (as in nephrotic syndrome). The changes in serum globulin level and A/G ratio seen in individual patient groups may be due to the effects of drug abuse and its complications on the immune status of the patient. Drug abuse, while on the one hand, impairs the immune response, on the other hand stimulates the immune system by continuously introducing pathogens; therefore it comes as no surprise that the effects are varied and complicated. Further research on larger samples of individual drug abuser groups could clarify the situation.

The changes in liver enzymes seen in the drug abusers, especially increased SGPT levels, were expected and most of the previous research supports this finding. The causes of the derangement are complex, ranging from direct toxicity (e.g. alcohol), infections (intravenous drug abusers) or indirect harmful effects on the hepatocytes etc[25,26].

The drug abusers as a group also differed significantly from the control group in serum T3 and T4 levels, although T3 was higher while T4 was lower in the patient group. Previous research has also revealed similarly diverging findings, e.g. Rashid and Tareen[8] reported that plasma T3 concentration increases slightly in drug addicts while plasma T4 concentration remains unchanged. The liver is responsible for metabolism of most of the hormones in the body, and liver damage could be responsible for the increased levels of some hormones in the blood in drug abusers[27]. However this is only one hypothesis, and other explanations may be as likely.

The present study revealed a statistically significant fall in mean plasma potassium concentration in the drug abusers, as compared to the control group, while there was an insignificant change in mean plasma sodium concentration in the combined drug abusers group. Tuller reported wide and rapid fluctuations in serum potassium levels in heroin addicts[23]. The decrease in plasma potassium may either be due to reduced intake and malnutrition, or to increased loss by vomiting and diarrhea (e.g. during alcohol intoxication or heroin withdrawal etc).

On the other hand Pearce and Cox[28] reported hyperkalaemia in heroin dependent patients presenting with an overdose, and attributed it to the leakage of potassium from muscles into the extra cellular fluid. Changes in potassium concentration in the plasma have widespread effects on the body, ranging from changes in muscle tone and motility, to effects on cardiac rhythm[16,27].

Mean plasma zinc concentration was low in drug abusers as compared to the control group. This is in line with previous research. Krause and Mahan[29] reported that alcohol increases urinary excretion of zinc, lowering zinc

levels in the body. Moreover, the fall in zinc levels could also be due to poor nutrition. Mean plasma copper level was also found to be lower in the drug abusers. Frank copper deficiency is very rare in humans, and has mainly been reported in malnourished children[30]. In case of addicts, the copper deficiency may be due to malnutrition, or diseases such as nephrotic syndrome and enteropathies etc.

Our study also revealed a significant iron deficiency in the drug abusers as compared to the control group. In previous research, Abraham[31] and Snapper and Khan[32] observed severe iron deficiency anemia in heroin addicts, and attributed it to poor nutrition and sale of blood to blood banks for money to buy drugs.

CONCLUSION

Besides the problem of addiction, the effects of drugs of abuse on the physiology and biochemistry of the human body are harmful in their own right. These effects are complex and multiple, from general parameters of health, to hematological variables, liver and kidney functions, endocrine system, and even trace element levels. These results are significant because they highlight the importance of holistic assessment and management of drug abusers, beyond just managing their addiction.

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Great minds have purpose; Other have wishes.

Washington Irving