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ASIAN JOURNAL OF SCIENCE AND TECHNOLOGY

ISSN: 0976-3376

Asian Journal of Science and Technology
Vol. 6, Issue 02, pp. 1041-1043, February, 2015

RESEARCH ARTICLE

STUDY ON HARMFUL EFFECTS OF OPIUM ON LIVER FUNCTIONS IN CHRONIC OPIUM ADDICTS OF WESTERN RAJASTHAN

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ARTICLE INFO

Article History:
Received 28th November, 2014
Received in revised form
08th December, 2014
Accepted 01st January, 2015
Published online 28th February, 2015

Key words:

Aspartate amino transferase (AST),
Alanine amino transferase (ALT),
Alkaline phosphatase

ABSTRACT

Background: Today opium dependence is widely prevalent in certain states of India, especially Rajasthan, Punjab, Haryana, Madhya Pradesh (MP) etc. In rural areas of western Rajasthan crude opium is consumed with a social acceptance by a notable proportion (8.0%) of adult male population. Later on they become addicted to it.
Objective: to observe the changes in liver function parameters in opium addicted subjects in Jodhpur division of Western Rajasthan.
Methods: The present study was conducted in Department of Physiology of Dr. S. N. Medical College, Jodhpur. Total three hundred (300) adult male subjects with age ranged from 25 to 45 years were participated in this study. Among them 150 were opium addicted and were considered as study group (Group B) and another 150 apparently healthy adult male of same age group were designated as control group (Group A). Opium addicts were consuming about 5–11 gm/day opium for >2 years. Then liver function tests were evaluated by estimating total plasma protein, albumin, globulin, serum aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase, serum bilirubin and fasting blood sugar of both the groups.
Results: In this study AST, ALT and alkaline phosphatase levels were found highly significantly ($p<.01$) higher in group B as compared to those of group A. Again, there were significantly ($p<.01$) higher increase in serum bilirubin, blood glucose level and albumin in group B as compared to those of group A. while total protein and globulin was decrease significantly in group B as compared to those of group A.
Conclusion: It is concluded that chronic long term use of opium, increases the risk of hepatic and results in various infectious disease.

INTRODUCTION

Addiction is an alarming issue in all over the world. In India, among the opioid compounds opium has the highest consumption; as India is one of the major opium producing & exporting country. Botanically opium is known as Papaver somniferum which is available in chocolate colored gum form prepared by drying the poppy fruit milk on a cotton cloth in the hot sun. The opium which is extracted from the juice of poppy capsules (Papaver–somniferum) (Kalant, 1997) is used as a raw material for the synthesis of some medicines such as morphine, noscapine and papaverine (10%, 6%, 1% of opium respectively) (Hanson, 1995). Since more than 20 alkaloid (Venturella, 1995) and more than 70 ingredients are present in opium (Buchbauer *et al*., 1994), its impacts can be different in comparison to pure morphine, noscapine & papaverin.

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Since ancient times opium was used by Rajput (warrior) clan of this part of the country particularly in the desert part mainly to reduce bleeding and allay apprehension during war times. It was also used since long as a mind altering drug and as an analgesic on the Indo-Pakisthan Sub – continent (Dwarakanath, 1965). Opium dependence is gradually increasing in certain states of India, especially Rajasthan, Punjab, Haryana, M.P. etc.

In rural areas of Western Rajasthan opium has also being used as ceremonial drink during the vital events, festivals and social functions (Purohit, 1988). In rural areas of western Rajasthan crude opium is consumed with a social acceptance by a notable proportion (8.0%) of adult male population, (Mathur and Bansal, 1991) later on these subjects become addicted to the opium. Today opium addiction is much more common and wide spread in rural areas of western (Thar) Rajasthan. Prevalence rate of opium addiction is higher in Jaisalmer and Barmer District of Jodhpur Divison in western Rajasthan.

In addition, the number of opium addicted subjects is gradually increasing, as there is little is knowledge about the harmful effect of opium. In India total number of registered addicts of opium were 1,10,866 in 2001. So, the present study was done to observe the changes in some liver function parameters in opium addicted subjects of Western Rajasthan. The results of this study would help to create awareness among the clinician to give attention on liver function abnormalities in opium addict's patients and in patients prescribed with different doses of opium.

METHODS

The current study was conducted in Department of Physiology of Dr. S. N. Medical College, Jodhpur. Total 300 male subjects with age ranged from 25 to 45 years were selected from the different areas of Jodhpur region. Before inclusion into the study all ethical consideration for the subjects were taken in account. The purpose and expected outcome of the study were explained to each subject. They were encouraged for voluntary participation. Written informed consent was obtained from each subject. Detailed medical and family history was taken and thorough clinical examination was done. Clinically known case of infections that affect liver & lung like viral hepatitis, HIV, pneumonia, chronic obstructive lung disease, tuberculosis and subjects with history of smoking were excluded from the study.

All the subjects were then divided into two groups 150 healthy subjects designated as control group (Group A) and 150 opium addicts considered as study group (consuming opium about 5-11gm/day for > 2 years visiting Psychiatric department of MDM Hospital, Jodhpur, and those who fulfill the DSM-IV criteria for opium addiction developed by the American Psychiatric Association (1994) were included in this study). The liver function tests were evaluated by estimating Total protein, albumin, globulin, serum aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphates, total bilirubin and blood glucose level. After an overnight fast (5ml), blood samples were taken. Blood sugar level (Bergmeyer, 1974) AST (Bergmeyer and Horder, 1985), ALT (Bergmeyer and Horder, 1985), total bilirubin (Jendrassik *et al*., 1938), Alkaline phosphatase (Henery, 1974) total plasma level (Doumas *et al*., 1971), albumin (Tietz, 1976) were analyzed by commercially available reagents and kits on semi auto-analyzers / fully auto-analyzer.

RESULTS

Subjects of both the groups were matched for age, height and weight. (Table I) In current study there is highly significant decrease in total protein (P<0.001), globulin (P<0.001) in group B as compared to group A while there was a significant increase in albumin and A:G ratio (P<0.01). The mean serum bilirubin level was also increased highly significantly (P<0.001) in opium addicts (group B) as compared to healthy control group (Group A). The serum SGOT (AST), SGPT (ALT), and ALP levels were also increases highly significantly (p<0.001) in opium addicts. Blood sugar level was also higher in group B in comparison to those of group A. (Table No. II)

Table 1. Mean ± SD Anthropometric parameters of both the groups (n=300)

GROUPS	Height (m)	Weight (Kg)	BMI (Kg/m^2)
Group A	1.70±0.06	68.07±7.46	20.00±2.19
Group B	1.68±0.07	65.98±8.74	19.57±2.62
t-value	2.657	2.228	1.542
p value	0.008***	0.0267**	0.1241*

Group A = apparently healthy subjects, Group B= Opium addicts
Note -All values expressed as Mean ± SD; * *p* value > 0.05 (NS) ** *p* value < 0.05(S) *** *p* value < 0.01(HS)

Table 2. Mean ± SD some liver function tests in both the groups (n=300)

Parameter	Group Control Group	Group A (Opium Addicted Group)	Students-t test	
			t- *value*	*p- value*
Total plasma protein (gm/dl)	7.81±0.51	6.98±0.70	11.737	< 0.0001***
Albumin level (gm/dl)	4.29±0.60	4.49±0.50	3.136	0.0019***
Globulin level (gm/dl)	3.52±0.52	2.49±0.75	13.909	< 0.0001***
A:G ratio	1.26±0.35	2.08±1.07	8.921	< 0.000***
S. Bilirubin (mg/dl)	0.73±0.20	1.20±0.44	11.910	< 0.0001***
SGPT (IU/L)	23.87±10.17	35.71±26.07	5.182	< 0.0001***
SGOT (IU/L)	25.71±9.90	79.67±54.07	12.023	< 0.0001***
ALP (IU/L)	140.94±39.62	273.51±77.79	18.599	0.0001***
Blood Glucose (mg/dl)	87.94± 13.67	95.8± 16.74	4.457	< 0.0001***

Note -All values expressed as Mean ± SD; * *p* value > 0.05 (NS) ** *p* value < 0.05(S) *** *p* value < 0.01(HS)

DISCUSSION

In the present study AST, ALT and alkaline phosphatase levels were significantly higher in opium addict group than those of control group. Similar results were observed by other researchers (Wynne, 1983; Bergelleca, 1994 and Nagmastsu and Takahashi, 1988). Generally, long-time use of opioids induces liver injuries. It has been recognized that glutathione increased by morphine is hepatotoxic and causes liver cells death. Gomez-Lechon *et al*., 1987 had observed that culture of human liver cells in proximity of .8–1 ml morphine and 3, 6-diacetyl morphine decreases glycogen. In liver, morphine is biotransformed by hepatic glucoronidation to major but inactive metabolite morphine–3 glucuronide (M3G) and biologically active morphine–6 glucuronide (M6G) (Richard *et al*., ?). These metabolites increase the secretion of enzymes in liver. Continuous and larger dose of opium can impaired the liver functions. Morphine is metabolized mostly in the liver with prolonged clearance because of enter- hepatic circulation which contributes to the maintenance of blood and tissue level of morphine and its metabolites from intestinal hydrolysis of glucuronides (Hank and Aherne, 1985). In current study blood glucose level is increase significantly in chronic opium addicts then control group. There is a considerable controversy about the role of opioids in regulation of glucose homeostasis. That is, while some studies have reported that Opioids induce hyperglycemia (Ipp *et al*., 1980; Karam *et al*., 2008; Feldberg and Gupta, 1974 and Radosevich *et al*., 1984) other studies have claimed that opioids can induce hypoglycaemia (Brase

et al., 1990; Brase *et al*., 1991 and Azod *et al*., 2008). The effect of morphine on serum level of glucose has been demonstrated on animals (Ipp *et al*., 1980; Bossone and Hannon, 1991; Molina *et al*., 1994 and Terner *et al*., 2003). A number of mechanisms, such as elevated plasma adrenalin, noradrenalin, adrenocorticotrophic hormone (ACTH), cortisol (27), and glucagon (28) have been introduced for this effect. These hormones are counter regulatory hormones and increase serum glucose That is, while morphine in low dose (2 mg/h) decreases plasma epinephrine level but causes no change in plasma glucose of intact dog, at high doses, it increases glucose production by liver and decreases glucose clearance by peripheral tissue and, consequently, leads to hyperglycemia (Radosevich *et al*., 1984). Decrease of total protein level in dependents might be due to poor nutrition levels in opium addicted subjects.

Conclusion

From this study it is concluded that chronic long term use of opium, (>2yr) increases the risk of hepatic damage. According to the obtained results of this study we suggest that opium consumption isn't useful in spite of public opinion as, addiction in addition to increasing the risk of infectious diseases (especially HIV), can increase the risk of cardiovascular diseases, osteoporosis, or kidney and hepatic malfunctions. Of course, revealing the involved mechanisms requires more studies.

REFERENCES

Azod L, Rashidi M, Afkhami-Ardekani M, Kiani G, Khoshkam F. Effect of opium addiction on diabetes. *Am J Drug Alcohol Abuse* 2008; 34:383– 388

Bergelleca. Toxicology evaluation of μ-agonist with levo-alpha acetyl methadol- hydrochloride (AMM) and morphine. *J Appl L Toxicol* 1994; 14: 435- 445.

Bergmeyer HU, Horder M. Approved recommendation (1985) on IFCC Method for the measurement of catalytic concentration of enzymes. *J Clin Biochem* 1986; 24:497-510.

Bergmeyer HV. Method of Enzymatic Analysis 1974; 1196: 42-46.

Bossone CA, Hannon JP. Metabolic actions of morphine in conscious chronically instrumented pigs. *Am J Physiol* 1991; 260:R1051–1057.

Brase DA, Singha AK, Estrada U, Lux F, Dewey WL. Hypoglycemia induced by intrathecal opioids in mice: Stereospecificity, drug specificity and effect of fasting. *J Pharmacol Exp Ther* 1990; 253:899–904

Brase DA, Ward CR, Tripathi HL, Dewey WL. An insulin-independent mechanism of intrathecal morphine-induced hypoglycemia in mice: Mediation through a central alpha-2 adrenergic pathway. *J Pharmacol Exp Ther* 1991; 257:587–594.

Buchbauer G, Nikiforov A, Remberg B.Headspace. Constituents of opium. *Planta Med* 1994; 60(2) :181-3

Doumas BT, Watson WA, Biggs HG: Albumin Standards and the Measurement of Serum Albumin With Bromcresol Green. *Clin Chim Acta* 1971;31:87-96.

Dwarakanath C. Use of opium and cannabis in the traditional system of medicine in India. *Bull Narct* 1965; 27: 13-19.

Feldberg W, Gupta KP. Morphine hyperglycaemia. *J Physiol* 1974; 238:487–502.

Gomez-Lechon MJ, Ponsoda X, Jover R. Hepatotoxicity of the opioids morphine, heroin, meperidine, and methadone to cultured human hepatocytes. *Mol Toxicol*. 1987; 1:453–463.

Hank GW and Aherne GW. Morphine metabolism: Lancet 1985; 1 : 221.

Hanson G. Analgesic, antipytretic and anti-inflammatory drugs. In : Gennard AR, Editor. The Science and practice of pharmacy. 19th ed. New York: Mack Publishing Company; 1995. p. 1197-8.

Henery RJ. Enzymes in Clinical chemistry principal and techniques. 2nd ed. New York: Harper & row publisher; 1974. 815 p.

Ipp E, Schusdziarra V, Harris V, Unger RH. Morphine-induced hyperglycemia: role of insulin and glucagon. *Endocrinology* 1980; 107:461–463.

Jendrassik, L.& Grop.P. *Biochem Z* 1938; 297,81.

Kalant H. Opium revisited: a brief review of its nature, composition, non-medical use and relative risks. Addiction 1997; 92(3): 267-77.

Karam GA, Rashidinejad HR, Aghaee MM, Ahmadi J, RahmaniMR, Mahmoodi M, Azin H, Mirzaee MR, Khaksari M. Opium can differently alter blood glucose, sodium and potassium in male and female rats. *Pak J Pharm Sci* 2008; 21:180–184

Mathur ML, Bansal RK. Prevalence of opium consumption in rural population of a desert district, Jodhpur. *Indian J Public Health* 1991; 35(4): 117-8.

Molina PE, Hashiguchi Y, Ajmal M, Mazza M, Abumrad NN. Differential hemodynamic, metabolic and hormonal effects of morphine and morphine- 6-glucuronide. *Brain Res* 1994; 664:126–132.

Nagmastsu K, Takahashi A . Morphine metabolism in isolated rat hepatocytes. Biochem. Pharmacol 1988; 3543-35

Purohit DR. Community approach to opium dependent subjects in rural areas of Rajasthan. *J Comm Psy* 1988; 11(2): 3.

Radosevich PM, Williams PE, Lacy DB, McRae JR, Steiner KE, Cherrington AD, Lacy WW, Abumrad NN. Effects of morphine on glucosehomeostasis in the conscious dog. *J Clin Invest* 1984; 74:1473–1480.

Radosevich PM, Williams PE, Lacy DB, McRae JR, Steiner KE, Cherrington AD, Lacy WW, Abumrad NN. Effects of morphine on glucose homeostasis in the conscious dog. *J Clin Invest* 1984; 74:1473–1480.

Richard KR, Shannon C, Miller,DA, Fiellin RSZ. Princiles of Addiction Medicine .4th ed. Lippincott: Williams and Wikins; p 126-130.

Terner JM, Lomas LM, Smith ES, Barrett AC, Picker MJ. Pharmacogenetic analysis of sex differences in opioid antinociception in rats. *Pain* 2003; 106:381–391.

Tietz N: Fundamentals of clinical chemistry, Philadeiphia, W.B. Saunders, 1976; pp 335-337.

Venturella VS. Natural Product. In: Gennard AR, Editor. The Science and Practice of Pharmacy. 19th ed. New York: Mack Publishing Company; 1995.p.400-2

Wynne AG, M-6-G, An important factor in interpreting morphine radio immunoassays. Lancet 1983; July 27 (I): 210-11.

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