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Effect of Chronic Opium Addiction on Renal Functions in Opium Abusers of Western Rajasthan

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Abstract **Original Research Article**

In traditional medicine, opium has been considered as a remedy for many disorders. This belief along with use of opium as recreation can lead to addiction with this many harmful effects to body. Over the centuries, opium has been the most frequent substance abused in the many parts of the world. In India opium dependence is widely prevalent in certain states of India, especially Rajasthan, Punjab, Haryana, Madhya Pradesh etc. In rural areas of western Rajasthan crude opium is consumed with a social acceptance by adult male population. Later on they become addicted to it. There are many studies about the effects of opium on the various body systems but its chronic abuse effect on autonomic functions is still unclear, therefore this study is undertaken to explore the effect of chronic abuse of opium on renal functions parameters in opium dependent subjects of western Rajasthan and its comparison with normal non - addicted controlled subjects. In this study total 100 male subjects were included, which were further divided in two groups. 50 subjects were from opium addicted population and 50 were healthy subjects. Female subjects were omitted from analysis due to their low numbers. Subjects who fulfilled DSM- IV criteria were chosen as opium dependent subjects. To assess the effect of opium addiction on the renal or kidney functions parameters used are Serum urea, Serum creatinine and Serum uric acid. In our study, we found that in opium addicted subjects, all the three parameters showed statistical highly significant ($P<0.001$) increased values as compared to control group. These observations in our study led to the conclusion that excessive use of opium, with lack of knowledge about its side effect on kidney, would cause structural abnormalities and renal dysfunction. So recognition, treatment, and prevention of this change could be a new step in improving of health and condition of patients.

Keywords: Opium abuse, renal function test, Serum urea, Serum creatinine and Serum uric acid etc.

INTRODUCTION

Opium abuse is a major health problem in developing countries including our country. Despite legal restriction and administrative control, the use of illicit drugs (like opium, heroin etc.) has increased considerably in many parts of North India More than 180 million people around the world have tried illegal drugs at least once, of whom 13.5 million are opium dependent [1].

Opium, in contrast to pure opioid drugs, is a complex and variable mixture of substances. There are however, more than 20 alkaloids [2] and more than 70 components [3] in opium, thus its effect on metabolism and the endocrine system could therefore be different from pure morphine, noscapine and papaverine. Opium is used as the raw material for the synthesis of some medications such as morphine, noscapine and papaverine (10%, 6% and 1%of opium respectively) [4, 5]. It is reported that between 1 and 30 g of opium may be used by an addict, either orally or inhaled. The effects of opium are essentially those of morphine. The major effects of opium are on the central and autonomic nervous system and the bowels; while it also influences other organ systems including the respiratory and cardiovascular systems [1]. Several investigations about the effects of opioid peptides on the cardiovascular system have also been performed [6, 7].

Although there are many studies on various effects of opium in abusers in many parts world, on metabolism like glucose metabolism [8] lipid profile [9] and risk for cardiovascular system [10] and effects on various serum factors like sodium, potassium, calcium, iron, serum proteins and serum

Enzymes like ALT, AST [11], liver function [12] etc. But in India studies related to these effects of opium is very less. The work done is mostly related to its prevalence of abuse in different areas and in different communities [13].

There are very less studies related to effect of chronic abuse of opium on renal function in India. In view of this, the present study is undertaken to show the effects in opium addicted population.

MATERIALS AND METHOD

The present study was conducted in department of Physiology of Dr. S. N. Medical College, Jodhpur. Total 100 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. An informed written consent was obtained from each subject.

All the subjects were then divided into two groups.
Group I: Control - consisted of 50 healthy subjects.

Group II: Opium addicted – 50 subjects (consuming opium about 5-11gm/day for > 2 years), visiting Psychiatric department of MDM Hospital, Jodhpur, for de-addiction and those who fulfill the DSM-IV criteria for opium addiction developed by the American Psychiatric Association (1994) were included in this study.

Exclusion Criteria

Subjects who abused several drugs simultaneously & alcohol abusers, smoker, taking tobacco or any other substance, or having past history of any disease like hypertension, diabetes, dyslipidimeia, heart, kidney or liver diseases, blood related diseases or any special disease like AIDS, before the opium abuse started, were excluded from this study.

Subjects in both the groups (addicted and control) were subjected to assess the renal or kidney functions by parameters: - Serum urea, Serum creatinine and Serum uric acid.

RESULTS

Table 1 shows characteristic changes in Renal function parameters in control (50) and opium addict subjects (50). Data so obtained were expressed as mean ± SD and statistically analyzed by using the Microsoft Excel and Open Epi software (version 2.3.1). Students t‟ (unpaired) was used to analyzed whether the result obtained are significant or not. P value of less than 0.05 will be accepted as significance difference b/w the compared values.

Table no. 1 shows significant rise in S. uric acid, S.urea and S. creatinine in opium addict's subjects compared to that of control subjects.

Table-1: Renal function tests parameters in control and opium addicted group

Parameter	Control Group	Opium addicted group	Students-t test	
			t- *value*	*p- value*
S. uric acid (mg/dl)	5.28± 0.40	5.57±0.79	4.011	< 0.0001***
S. urea (mg/dl)	30.26±7.70	40.47±14.70	7.535	< 0.0001***
S. creatinine (mg/dl)	0.98±0.16	1.12±0.29	5.177	< 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 present study we found that opium addicted group (5.57±0.79) showed a statistical highly significant (P<0.001) increased in uric acid ((mg/dl)) as compared to control group (5.28± 0.40mg/dl). Similarly Serum urea level of opium addicted group subjects (40.47±14.70mg/dl)was significantly more (P<0.0001) than control subjects (30.26±7.70mg/dl) and serum creatinine values also showed highly significant (P<0.0001) rise in opium addicts (1.12±0.29mg/dl) as compared to control (0.98±0.16mg/dl).

The exact reason why these values are higher opium addicted population is unknown. But it may be that the opioids endogenously or exogenously are excreted through the kidney after metabolized in liver.

A metabolite may have higher activity and /or greater toxicity than the original drugs. Metabolites of the drugs that are excreted from kidneys may also cause cellular damage leading to kidneys dysfunction [14]. Morphine, which is commonly used for the treatment of severe pain, is metabolized essentially in the liver, gastronistestinal tract and kidneys [15].

Robert James et al, 2013, in study on arsenic poisoning in opium addicts suggest that that in patients with history of opium abuse and above said complaints should be evaluated for arsenic poisoning. Opium is known to have been adulterated with arsenic in certain parts of north India. Arsenic causes heavy metal poisoning which may also results in damage to liver and kidney with other vital systems. Renal damage results in increase serum/ or blood urea in opium addicts [16].

Our result is agreement with the study done by Atici S etal, 2005 his study found that there was renal tubular vacuolization, mononuclear cell infiltration, focal necrosis and hemorrhage as well as significant

increase in serum urea and S. creatinine in the morphine group compared to control. ($P < 0.05$) [16] Sumathi T, in the year 2009 on rats, observed that long-term consumption of morphine increases creatinine and uric acid level [17] While Divsalar K *et al.* 2010 in his study observed no difference in creatinine level between heroin dependents and controls [18]. Sajad Mami, 2011 find increase serum urea creatinine and uric acid but increase was not satitically significant [19].

Both endogenous and exogenous opioids have a strong influence on the renal functions. Endogenous opioids are known to play a pivotal role in controlling kidney function in normal and pathological states [20]. The endogenous opioid peptides are referred to as 'endorphins' and these bind to mu; delta and kappa receptors localized on the different parts of the kidney [21, 22] Kappa opioid receptors are mostly localized in the renal cortex [23]. Mu and kappa receptors are present on the mesangial cells of the kidney, while delta receptors are barely detectable in mesangial cells [22]. There is considerable variation regarding the presence and localization of these opioid receptors depending on the type of species.

Opioids produce physiological changes in kidney [22, 24] and endorphins along with other opioid peptides participate in the development of uremic syndrome [25]. Studies have also suggested that chronic administration of clinically relevant doses of opioids causes structural abnormalities and renal dysfunction in a murine model of cancer [26]. Overdose of morphine increases the oxidative stress in the renal epithelial which leads to renal injury [27]. Morphine was shown to produce tubular epithelial cell degeneration with cellular casts within the lumen of the tubules in the kidney.

Morphine stimulates the production of superoxide by macrophages and mesangial cells and inhibits the glutathione reductase which leads to increased oxidative stress in cells and renal injury [27]. Morphine has a bimodal effect on glomerular epithelial cells (GEC). At lower concentrations, morphine promotes GEC growth, whereas at higher concentrations, morphine triggers apoptosis of these epithelial cells [28]. The chronic use of morphine leads to structural kidney abnormalities along with up regulation of NOS, COX-2 and HO-1 in a murine model of cancer [26].

Weber and co-workers [29] 2012 suggested that clinically relevant doses (equivalent to approximately 50~301 mg/70 kg human/day) of morphine increases the renal pathology in sickle mice. Light microscopy showed increased number of juxtaglomerular cells and extremely high intraglomerular congestion in morphine treated mice In heroin addicts, the renal disease complication is very common and is associated with membranous nephropathy, nephrotic syndrome, acute glomerulonephritis, focal and segmental glomerulosclerosis (FSGS) amyloidosis, interstitial nephritis, and rhabdomyolysis There is a three-fold increased risk for renal dysfunction in heroin users versus non-drug users[30, 31].

The increased level of these end products of nitrogen metabolism was associated with hepatotoxicity and nephrotoxicity properties of opioids increasing catabolism of purine nucleotides. Therefore, chronic opium addiction may results in electrolyte imbalance.

The aim of the current study was to make awareness among opium addicts and in society about harmful effect of opium addiction and dependence on kidney because long time use of opium may causes permanent damage in kidney which cannot be regenerate again. Less data is available to compare our finding which we have got in our work and a wide scale study is recommended to confirm our findings.

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