

## **Research Article**

### **A Study on Autonomic Functions in Chronic Opium Abusers**

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**Abstract:** 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 (MP) 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 autonomic functions in opium dependent patients 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 patients were omitted from analysis due to the low numbers of female opium addicts. Subjects who fulfilled DSM- IV criteria were chosen as opium dependent patients (ODP). Various autonomic function test Valsalva Maneuver (VM), Deep Breathing Test (DBT), Lying To Standing Test (LST) were carried out for assessing parasympathetic reactivity and Hand Grip Test for sympathetic reactivity. Our study revealed significant changes in the autonomic functions in addicted population in comparison to normal controlled subjects. In valsalva maneuver, deep breathing test, lying to standing test result were highly significant ( $p < 0.001$ ) and in hand grip test rise in SBP( $p < 0.05$ ) and DBP( $p < 0.001$ ) were significantly lower in addicted group as compared to the control. The risk of dysautonomia in opium addicted subjects was higher than in the non-addicted group. According to this study the longtime use of opium may results in autonomic dysfunction in opium dependent people but more evidence is still needed to completely prove the study. So recognition, treatment, and prevention of this change could be a new step in improving of health and condition of patients.

**Keywords:** Opium abuse, Autonomic function tests, Valsalva maneuver, Deep breathing test, Hand grip test, Lying to standing test.

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#### **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]. Orthostatic hypotension has been reported after opium consumption. 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]. However, we could not find any reports on the effects of chronic abuse of opium on autonomic functions in India and from any part of the world. In view of this, the present study is undertaken to show the effects of opium addiction on autonomic function.

## 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, dyslipidemia, heart, kidney or liver 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 following autonomic function tests.

Parasympathetic functions were assessed by Valsalva maneuver (VM), deep breathing test (DBT) and lying to standing test (LST) [14].

For Valsalva maneuver (VM) subject was asked to blow out or to expire forcefully in rubber tube of mercury manometer to create a pressure of 40 mm Hg and maintain it for 15 sec. Simultaneously an ECG was recorded during VM and 30 sec after finishing it in limb lead II. From the ECG recording, Valsalva ratio was calculated using the formula

Valsalva ratio = longest R-R interval after maneuver / shortest R-R interval during maneuver.

In Deep breathing test (DBT) subjects were asked to breathe deeply at a rate of 6 breaths per minute, allowing 5 sec each for inspiration and expiration. The Parasympathetic activity was measured by calculating E:I (Expiration: Inspiration) ratio using ECG strip.

E:I ratio = average of maximum R-R interval during expiration/average of minimum R-R interval during inspiration.

In Lying to standing test (LST) subject was instructed to stand within 3 seconds from lying position. 30:15 R-R ratio was calculated as the ratio of longest R-R interval around 30th beat and shortest R-R interval around 15th beat from the ECG recording [14].

Sympathetic function was assessed by hand grip test (HGT) [14], for this subjects were asked to grip the dynamometer with his dominant hand at 30% of maximum voluntary capacity for 5 minutes in sitting position. The rise in systolic and diastolic BP at the point just before the release of handgrip is taken as the index of response to HGT.

Data were expressed as mean  $\pm$  SD (standard deviation). For statistical analysis student's t test was used.

## RESULTS

Table 1 and table 2 shows characteristic changes in autonomic functions in control (50) and opium addict subjects (50). Data so obtained were expressed as mean  $\pm$  SD and statistically analyzed by using the Microsoft Excel and Open Epi software (version 2.3.1). Student's 't' (unpaired) was used to analyze 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.

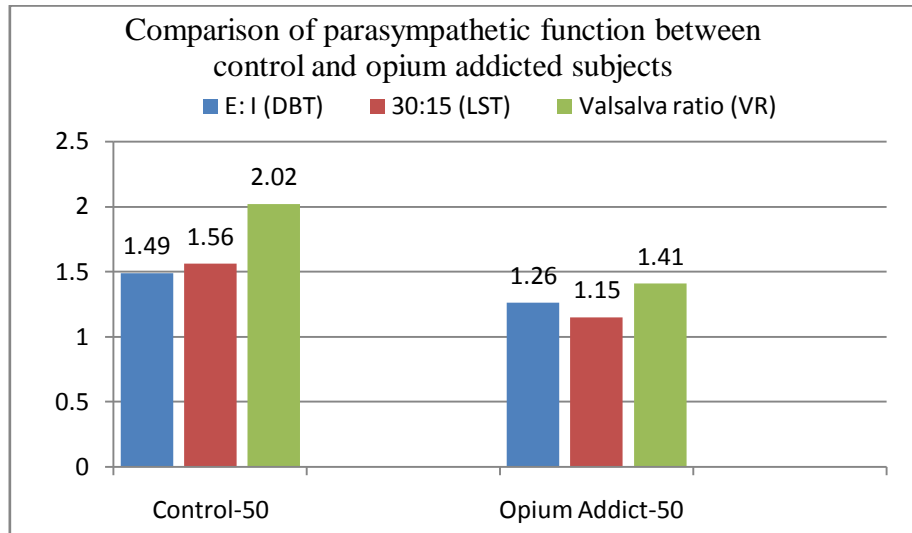
Our result shows a marked difference in all parasympathetic and sympathetic nerve function tests in the addict and non addicted group (control). The values of Valsalva ratio (VR), heart rate response to deep breathing (E: I) and 30:15 ratio were significantly lower ( $p < 0.001$ ) in opium addict group compared to those of control.

The HGT (Sympathetic nerve function test) results indicate that the rise in value of systolic blood pressure was  $20.96 \pm 6.97$  mmHg in control and in opium addicted was  $16.88 \pm 9$  mmHg. While the changes in mean diastolic blood pressure in opium addicted was  $10.65 \pm 5.70$  which was significantly less than that of control  $18.24 \pm 5.18$  ( $p < 0.001$ ).

**Table 1: Comparison of Parasympathetic autonomic functions between control and opium addicted subjects**

Subjects	E: I (DBT)	30:15 (LST)	Valsalva ratio (VR)
Control (50)	1.49±0.17	1.56±0.17	2.02±0.63
Opium Addict (50)	1.26±0.15	1.15±0.20	1.41±0.34
<i>p</i> value	<0.001***	<0.001***	<0.001**

Note – All values are showed as Mean + SD ; *p* value >0.05 (NS) \*, *p*<0.05 (S)\*\*,*p*<0.01 (HS)\*\*\*

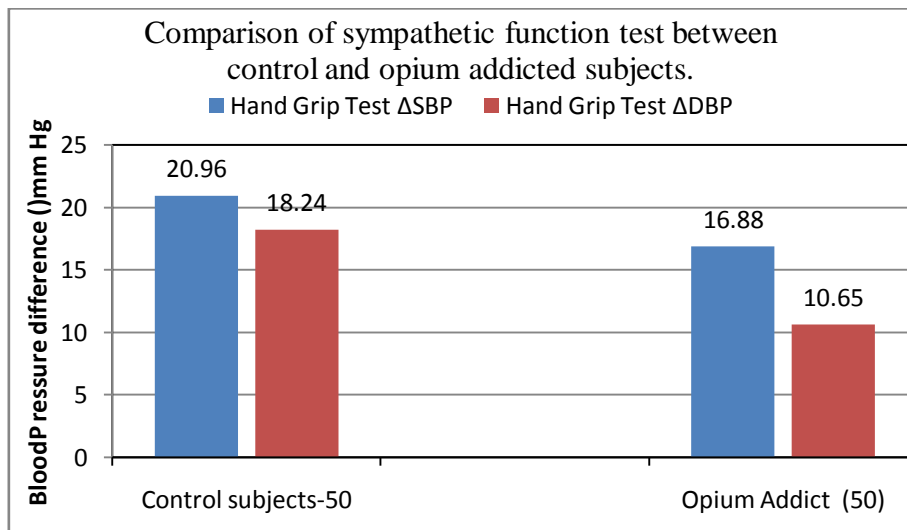


**Fig. 1: Comparison of parasympathetic functions between control and opium addicted subjects**

**Table 2: Comparison of sympathetic autonomic functions between control and opium addicted subjects**

Subjects	Hand Grip Test	
	ΔSBP(mm Hg)	ΔDBP(mm Hg)
Control subjects (50)	20.96±6.97	18.24±5.18
Opium Addict (50)	16.88±9	10.65±5.70
<i>p</i> value	0.013**	<0.001***

Note – All values are showed as Mean + SD ; *p* value >0.05 (NS) \*, *p*<0.05 (S)\*\*,*p*<0.01 (HS)\*\*\*



**Fig. 2: Comparison of sympathetic functions between control and opium addicted subjects**

**DISCUSSION**

In present study to assess parasympathetic activity, heart rate response to deep breathing, lying to standing, and valsalva maneuver (VM) test was measured and blood pressure responses to sustained hand grip was

measured to assess sympathetic activity. No study is available till date in my knowledge to compare the current study result.

The effects of opium are essentially those of morphine. The major effects of opium are on the central and autonomic nervous system [1]. Morphine tends to manipulate the tone of autonomic nervous system in the bodily interacting at various levels. Thus it is autonomically active drug [16].

Autonomic system control many aspects of bodily systems. Autonomic literally means "self-governed". It has two divisions: sympathetic and parasympathetic. Most internal organs are innervated by both branches of the ANS which exhibit antagonistic control. Interaction of sympathetic and parasympathetic nervous system is important in maintaining homeostasis in the body. If antagonistic control of both branches of the ANS disturbed then it results in autonomic dysfunctions which can be assessed by various autonomic function tests. In present study non-invasive function tests as stated above are used to demonstrate the effect of chronic abuse of opium on autonomic functions abusers in western Rajasthan in order to evaluate the presence of any impairment of the autonomic activity.

Dysfunction at any level of ANS (central, preganglionic or postganglionic or at effector organ), results in generalised dysautonomia. Since, the prime function of ANS is to maintain cardiovascular system homeostasis therefore derangement of ANS function at any level is manifested by cardiovascular reflexes integrity evaluation test. The cardiovascular responses dependent not only on intact autonomic function but also on the function of receptor organ, an afferent nerve, the central nervous system and effector organ. A lesion in any part of this nervous chain result in an abnormal autonomic response [15].

The presence of autonomic dysfunction in chronic opium addicts has for long been topic of research. Opiates are among the oldest pharmacological substance known for man; their analgesic, euphoric and addictive effects have been traditionally focal points for research. Without doubt the cardiovascular effects of opiates have been also been apparent to the users and abusers of opiates for several centuries. Person seeking to analgesic, euphoric, or antidiarrheal actions from opiates alkaloids have probably noted dizziness upon sudden standing due to orthostatic hypotension these substance produce.<sup>16</sup>

The result obtained for parasympathetic function tests in the present study as shown in table no 1, deep breathing (E:I ratio), lying to standing (30:15 ratio) and valsalva ratio, were highly significantly lower in opium addicts compare to that of control ( $p < 0.001$ ). While in hand grip test as showed in table no. 2, there was significant difference in systolic blood pressure difference ( $p > 0.05$ ) and statistically highly significant decrease in DBP ( $p < 0.001$ ).

Different investigators suggested that the vagal tone is reduced or loss of vagal tone occur in opium abusers. As a consequence baroreflex activity may be decreased. The reason for decrease in parasympathetic tone in opium addicts could be due its interference to release of neurotransmitter at preganglionic parasympathetic efferent neurons and its peripheral anticholinergic effect [17]. The decrease sympathetic autonomic tone in opium addicts could be that the morphine decrease the central sympathetic outflow and its inhibitory effect on release of neurotransmitter in preganglionic neurons and also its direct antagonize action of sympathetic effect on end organ [17]. HGT test is measure of sympathetic efferent vasoconstrictor function which is chiefly mediated by alpha adrenergic receptors.

This study provides good evidence for autonomic dysfunction following chronic abuse of opium. 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 nervous system mainly autonomic function. No 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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