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Effectiveness of Transcranial Direct Current Stimulation (tDCS) on Reducing Craving among Hookah Smokers

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Abstract: The purpose of this study is to analyze the effectiveness of transcranial Direct Current Stimulation (tDCS) on reducing craving among people smoking hookah. The study population included all individuals 25-35 years old hookah smokers in the spring 2015 residing in Mashhad. The 21 students are selected using voluntary sampling and are randomly assigned to experimental and control groups. The experimental group received tDCS treatment at the same level while the control group did not receive any treatment. For data analysis univariate analysis of covariance and SPSS software is used to accelerate obtaining the results. The results showed there is a significant difference in terms of the basic craving and induced craving between the control and experimental of the left and groups at a confidence level of 99% ($p<0.01$). Also, there is a significant difference in terms of the basic craving and induced craving between the control and experimental of the right ande groups at a confidence level of 99% ($p<0.01$). So, it can be said that transcranial direct current stimulation can reduce the basic and induced craving to smoke hookah.

Key words: Direct electrical stimulation, base craving, induced carving, voluntary sampling, covariance

INTRODUCTION

Now a days human society is infected with tobacco use more than ever so that one man dies every 10 sec due to the impact of diseases caused by tobacco (Mohammad *et al*., 2000).

Due to better social acceptance and availability of tobacco than cigarettes, unfortunately hookah smoking has become popular among Asian and African societies, especially the Middle East and Arab countries (Maziak *et al*., 2004). This phenomenon is common among young people and the results of the National Health Project indicate increased hookah smoking in the age group of 15-24 years (Mohammad *et al*., 2000). Also the studies conducted in neighboring countries indicate that 33.9% of young people smoke hookah that is more than the cigarette smokers (Khalil *et al*., 2009).

Due to widespread use of hookah and its harmful effects, it is necessary to follow treatments to prevent the spread of this phenomenon and hookah smoking. So far, few treatments have been done on hookah smokers most of which have been focused on cigarette smokers and few studies are conducted on smoking hookah. One of the new treatments that its effectiveness is confirmed is transcranial Direct Current Stimulation (tDCS) that is used as a noninvasive, cheap and safe method to change the excitability of the cerebral cortex (Knotkova and Cruciani, 2010). Addiction is a chronic disease that is affected by a variety of biological, psychological and social factors. One of the important aspects of the phenomenon of drug addiction and smoking is carving.

Research findings have shown that craving plays an important role in returning after treatment and continuing consumption (Abrams, 2000). Craving is an uncontrollable desire for consumption, this desire if not satisfied, can cause psychological and physical sufferings such as fatigue, anorexia, anxiety, insomnia, aggression and depression.

Craving actually refers to motivation that is associated with a penchant for using drugs. In terms of physiology, behaviors such as eating when hungry, drinking when thirsty and having sexual intercourse are under the control of the emotional motivational system leading the general situation of appetite, desire or interest to carry out activities to respond to a biological drives but in the process of drug abuse, due to drugs' bio neurological effects on the brain reward system, this system finds another physiological orientation. This orientation includes appetite and tendency to abuse drugs added to the drug abuser. In fact drug abuse disorder starts when the tendency is so intense that overcomes spatio-temporal and moral considerations and requirements.

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Craving is an uncontrollable desire for consumption of drugs that if not satisfied, it is followed by psychological sufferings such as weakness, lack of appetite, anxiety, insomnia, aggression and depression (Tiffany and Carter, 1998). Craving is a poor motivation for drug abuse formed in the cognitive organization of the addicts and it is the main factor to continue and relapse after treatment.

Studies have shown that a visual or non-visual, sound or smell sign in the external environment or an endogenous imagination can induce craving (Ekhtiari *et al*., 2006). Drummond (Rahmanian *et al*., 2006) has considered craving as desire, impulses, need or compulsion to consume. World Health Organization defines craving as the foundation for starting drug dependency, loss of control and relapse and argue that it is created in the face of symptoms associated with experiences or the patients' imaginations under the drug abuse conditions.

Craving plays an important role in the phenomenon of relapse after treatment and maintaining consumption dependence. In the treatment of addicts after reaching a state of avoidance, there is a penchant to have the experience of drug abuse. This feeling may last for a few hours after the start of treatment until days and months later. The frequency and intensity of craving slowly declines but disappears rarely; thus, diagnosis and treatment of this clinical phenomenon is important as one of the factors for treatment failure (Abrams, 2000).

After reaching a state of avoidance, there is a penchant to have the experience of drug abuse. This feeling may last for a few hours after the start of treatment until days and months later. This detoxification phenomenon happens in the first month. Then its frequency and severity is decreased but disappears rarely. Dopaminergic brain systems that mediate pleasure plays a vital role in the mechanisms related to drug abuse. The craving for the avoidance mode gabanergic and glutamatergic systems are involved while craving is related to memory and rewarding effects possibly associated with dopaminergic and opioid mechanisms. Craving that occurs in stressful situations might be associated with serotonergic mechanisms that act in cooperation with the mechanisms mentioned above.

Studies have shown that a visual or non-visual, sound or smell sign in the external environment or an endogenous imagination can induce craving (Ekhtiari *et al*., 2006). Given that different medications and methods are associated with environmental conditions and special psychological states, the carving signs created in the consumers are different based on the method of consumption. The basic premise of open activation investigations indicates that the pattern of responses to stimuli that induce craving is influenced by early experiences of each person of the stimulus and will develop differently. Differences in response to drug-related stimuli are likely to emanate from conditioned experiences, thus it is assumed that the amount of reactivation and the type of stimulus are caused by the history of drug abuse. In fact, the presentation of the signs to induce craving is possible in various aspects and these aspects include image, smell, taste, touch, hearing and imagination (Garavan *et al*., 2000).

Although, the deployment of a multidimensional sign (like a glass of wine or the real image of smoking opium) includes smell, hearing and visual aspects, it complicates the measurement and analysis of findings and it is associated with legal and ethical problems. The visual signs provide a dimension that is largely close to the conditioned experiments but it lacks the intensity and fragility in confrontation with the real environment, especially for people who are at risk of return. Surveys conducted in Iran in the field of visual signs inducing craving in addicts injecting heroin have shown that among the possible signs that cause craving in drug among these people are the packed or ready for use drug, unpacked syringes or needles especially in situations filled with drugs, preparing the injection material or the act of injection are the most effective visual inducers of craving (Ekhtiari *et al*., 2006).

The studies also have shown that demographic factors such as age, gender, education, type of drug, method of consumption and history of previous treatments could affect craving and subsequent successful treatment. Also the female methamphetamine addicts have higher craving during the treatment than men that use the same drug (Culbertson *et al*., 2010). Neuroscience psychology has widely used the emergence of brain imaging techniques such as fMR, ERP and brain-stimulation techniques such as TMS. Recently a number of new brain stimulation techniques have become popular. The key drawbacks of some of these techniques are being expensive and invasive. As a result advances in brain imaging our knowledge about the brain regions involved in motor, sensory, cognitive and excitement functions is increased during the past two decades. As a result, simpler and cheaper neurostimulation techniques can improve our understanding of Neuropsychological functions in normal or clinical subjects. A very promising approach in this area is tDCS (Nitsche *et al*., 2008). tDCS method has a long history. Volta and Galvanic experiments in 1791 and 1792 on animal and human led to the birth of clinical use of direct current stimulation in 1804. In the same year Aldini treated the patients with melancholia successfully with this technique. However, the discovery of Electric Shock Therapy (EST) by Bini and

Sarlati led to sudden loss of interest in the tDCS techniques. This technique is revived in the 1960s and its effects are investigated systematically. At that time, it is shown that tDCS can affect brain functions through changes in cortical excitability. Albert in two studies published in 1966 showed that electrical cathode stimulation of the medial cortex in mice destroyed memory and anode stimulation of the medial cortex accelerates memory consolidation. Despite this temporary interest tDCS technique is forgot due to the treatment of psychological disorders through the medication (Utz *et al*., 2010). Probably a deeper insight into the basic mechanisms of tDCSis effective in recent years to increase the popularity of this method. Increased understanding of the method is facilitated by the study of brain mechanisms such as TMS and fMRI and led to the development of using clinical applications. Another important is steps to increase safety standards along with evidence of a lack of serious harmful effects. These developments made tDCS a promising method to study of brain stimulation on cognitive functions in boh healthy subjects and patients with damage to the central nervous system (Utz, 2010).

Nitsche and Paulus (2000) found that the least 17 micro-amp current density per square meter is required on stimulate the motor neurons. Studies conducted on other parts of the brain also suggests 20-25 micro ampere per square meter is necessary to stimulate neurons under electrode. Iyer *et al*. (2005) found that stimulating the left prefrontal cortex with a current of 1 mA has no impact on verbal fluency but with the 2 mA current a significant improvement has been created.

Direct stimulation of the brain's electrical system can change the systems of GABA (Nitsche *et al*., 2004a; Stagg and Nitsche, 2011), glutamate), acetylcholine (Thirugnanasambandam *et al*., 2011), serotonin (Nitsche *et al*., 2004b; Brunoni *et al*., 2013) and dopamine (Monte-Silva *et al*., 2010; Kuo *et al*., 2008). These moderators might have been effective on formation processes and cause the electrical stimulation of the brain to be used as an important tool for clinical treatment.

Considering the above mentioned points and given that so far no studies have examined the effectiveness of tDCS to reduce the craving of hookah smokers, the purpose of the study is to analyze whether tDCS is able to reduce craving of hookah smokers or not.

Research hypotheses:

- The tDCS method reduces basic craving in hookah smokers
- The tDCS method reduces induces craving in hookah smokers

MATERIALS AND METHODS

The present study is applied and experimental using pre-test and post-test design. The study population included all individuals 25-35 years old hookah smokers in the spring 2015 residing in Mashhad. Given the possibility of lack of cooperation and time consuming process, 21 students are selected using voluntary sampling and are randomly assigned to experimental and control groups (7 subjects per group).

Research tools: Image index on hookah craving software: in this researcher developed scale the factors and signs that can cause the craving are studied and identified. Then, with the collaboration of photography group in the laboratory the images and situations causing craving are photographed. These signs included images of hookah preparation, hookah presentation environments and hookah smokers. Then, the images are computerized to design a test to analyze the cause of craving. The computer tests are designed such that when they are displayed the subject is asked how much carving is aroused in you and he is asked to display his carving on a line one end of which leads to none and the other one leads to very much. The computer program is designed such that the participant's determined point (by mouse) is converted into a digit between 0 and 100 and recorded as the report of craving.

Dependence on a hookah questionnaire: To measure basic craving the hookah dependence has been used. The validity and reliability of the questionnaire has been studied by Mohammad *et al*. (2000). He states that in order to check the validity the face validity is used based on the expert opinion and construct validity is used based on exploratory factor analysis. Implementation of exploratory factor analysis showed that the KMO index is equal to 0.79 which is an acceptable figure. Bartlett index is equal to 303.7 which is significant at $p \leq 0.01$. To determine reliability, the split-half and Cronbach's alpha are used that alpha coefficient is equal to 0.79 which is acceptable figure. The results showed that the split-half correlation coefficient of the odd and even questions is equal with 0.83 which indicates a strong correlation between the two parts thus the validity and reliability of the tool are confirmed.

tDCS devices: It is a small electrical stimulation devise that is installed on the skin by via electrodes with anode (activator) and cathode (inhibitor) polarities that transfer fixed electric current from the skull to the brain. Electrodes are conductive and made of carbon and used to prevent

chemical reaction between electrode and skin they are placed in synthetic sponge soaked in saline. The electric source is a 9 V battery that the maximum current is 4 mA and the maximum voltage is 80 V as DC.

After obtaining the required permissions, referring to recreational centers and parks and distributing the announcements of the research in high traffic areas among the people fitting the inclusion criteria 16 cases are selected randomly and assigned to the experimental and control groups. The logic of therapy and the treatment objective is described for the participants and they fill written consent form. Also they are ensured that all their information will remain confidential. In the next step, which is the pre-test, the questionnaires are distributed to measure the dependent variable. After this step, the experimental group subjects sign a contract to participate in therapy sessions. After completion of therapy sessions both groups of participants are studied in terms of the dependent variable as post-test. Finally, the pre-test and post-test data are analyzed.

Intervention: Given that so far that so far no studies have examined the effectiveness of tDCS to reduce the craving of hookah smokers; in this study the package presented by Fregni *et al.* (2008) is used to analyze the effectiveness of tDCS on cigarette craving is applied.

Given that the Dorsolateral Prefrontal Cortex (DLPFC) is involved in in processing cigarettes and drugs craving, this area will be considered as the basis of the operation. tDCS effects depend on the direction of the electric current such that it increases anode stimulation and brain activity and reduces cathodic stimulation. In this study, the hypothesis that whether anodic tDCS stimulation is effective by left DLPFC of the right one is tested. In this study, the participants received three different types of brain stimulation by tDCS: fabricated tDCS, anodic left tDCS and anodic right tDCS with 48 h between the sessions to prevent the transmission effect. In addition, the stimulation will be random. The treatment sessions will be performed for 20 min by the current 2 mA by the researcher.

The hookah dependence questionnaire (to measure basic craving) and visual indicator test (to measure the induced craving) are administered once before the first session and then after the 7th session.

Each group received 7 sessions with 24 h intervals between 20 min stimulation sessions with 2 mA current. At the beginning of each session, the measurement is performed on the head of the participants and this measurement is based on the global system 10-20 and the F3 and F4 points are marked and then the electrodes are put in the pad that are soaked in saline and the pads are fixed on the F3 and F4 points then the stimulation started for 20 min.

In the first group that is the left anode group, the anode electrode is placed on F3 and the cathode electrode is placed on F4 and in the second group the anode electrode is placed on F4 and the cathode electrode is placed on F3 but in the third group that the stimulation was artificial, the anode electrode was placed on F3 or F4 randomly.

In previous studies, the control group received about 2 min or less and then the devise was turned off. But, the researchers decided to work with the turned off devise with the control group for two reasons such that the electrodes were fixed on the head similar to the first and second group and the start button was pushed but the stimulation was turned off but since the monitor turned on, the subjects supposed that they are receiving the treatment and the reasons are as follows:

- In previous studies it had been mentioned that the primary stimulation has no effect on the sham group but this claim is not recorded in any sturdies using brain imaging devises
- The test taker guessed that many of the signs announced by the participants of the test group are hypnotic. Since, the side effects have been described for the third group they had complaints such as headache or nausea which largely confirmed the assumptions of the tester of these states which needs to be analyzed more

RESULTS AND DISCUSSION

Based on the results of Kolmogorov-Smirnov (K-S), it can be stated that the distribution of scores on two variables of basic and induced cravings is normal. The results of Levene's test indicate that the convergence of the variances in three tests and control groups and control of the basic and induced craving variables is satisfied.

First hypothesis: tDCS method reduces basic craving in hookah smokers.

Based on observing the assumptions of normal distribution of basic craving scores in the experimental and control groups as well as the convergence of variances the covariance test is used in these groups to test the hypothesis. The results of ANCOVA are presented in Table 1.

Table 1: The results of covariance to compare the basic craving in the experimental and control groups

Source of changes	Sum of squares	df	Mean Square	F-values	Significance level	PES	The observed power
Pre-test	118.317	1	118.317	3.032	0.1	0.151	0.357
Group	493/925	2	246.962	6.329	0.009	0.427	0.837
Error	663.397	17	39.023	-	-	-	-
Total	6054	21	-	-	-	-	-

Adjusted $R^2 = 0.34$

Table 2: Results of post hoc test

Group 1	Group 2	Mean difference	SD error	Significance level
Group 1	Group 2	-3.966	3.552	0.280
Group 1	Control	*-15.072	4.431	0.003
Group 2	Control	*-11/106	3.748	0.009

Based on the results of ANCOVA with the pre-test score control, there is a significant difference between the experimental and control groups' basic craving scores at 99% confidence level ($F_{(2, 17)} = 6.329$, $p<0.01$). As a result, the null hypothesis based on the lack of significant difference between the groups is rejected.

In order to compare the two groups the post hoc LSD test is performed the results of which are presented below. Based on the results of the ad hoc test there is no significant difference between the basic carving of the left and right anode experimental groups ($p>0.05$). There is a significant difference between the basic carving of the left anode experimental group and the control group at the level of 99% difference ($p<0.01$). Also there is a significant difference between the basic carving of the right anode experimental group and the control group at the level of 99% difference ($p<0.01$). And, due to reduced mean cravings of the experimental groups compared to the control group, it can be said that the tDCS method reduces the basic craving of the hookah smokers (Table 2).

tDCS method reduces induces craving in hookah smokers. Based on observing the assumptions of normal distribution of induced craving scores in the experimental and control groups as well as the convergence of variances the covariance test is used in these groups to test the hypothesis. The results of ANCOVA are presented in Table 1.

Based on the results of ANCOVA with the pre-test score control, there is a significant difference between the experimental and control groups' induced craving scores at 99% confidence level ($F_{(2, 17)} = 146.217$, $p<0.01$). As a result, the null hypothesis based on the lack of significant difference between the groups is rejected (Table 3).

In order to compare the two groups the post hoc LSD test is performed the results of which are presented in Table 4.

Based on the results of the ad hoc test there is no significant difference between the induced carving of the left and right anode experimental groups ($p>0.05$). There is a significant difference between the induced carving of the left anode experimental group and the control group at the level of 99% difference ($p<0.01$). Also there is a significant difference between the induced carving of the right anode experimental group and the control group at the level of 99% difference ($p<0.01$). And due to reduced mean cravings of the experimental groups compared to the control group, it can be said that the tDCS method reduces the induced craving of the hookah smokers.

The results of testing the first hypothesis indicate that there is no significant difference between the basic carving of the left and right anode experimental groups. There is a significant difference between the basic carving of the left anode experimental group and the control group at the level of 99% difference. Also there is a significant difference between the basic carving of the right anode experimental group and the control group at the level of 99% difference. And due to reduced mean cravings of the experimental groups compared to the control group, it can be said that the tDCS method reduces the basic craving of the hookah smokers.

The findings of this part of the research are consistent with Shahbabaie and coauthors, Amiaz *et al.* (2009), Boggio *et al.* (2008), Fregni *et al.* (2008), Uher *et al.* (2005) and Eichhammer *et al.* (2003). The mentioned studies showed that this method can reduce methamphetamine, smoking and alcohol consumption craving in people.

Shahbabaie and coauthors showed that after tDCS stimulation in right DlPFC, methamphetamine craving decreased and reduced after 10 min.

Amiaz *et al.* (2009) in a study titled "The Impact of high frequency tDCS on reducing dependence on and craving for cigarettes" investigated the effect of magnetic stimulation on reducing craving in smoking. Participants were randomly assigned to real and sham stimulation groups. Each group was randomly divided into two groups of provided with smoking images or neutral images just before the TMS daily intervention. After ten sessions of magnetic stimulation applied results show that multiple frequencies stimulation has reduced nicotine craving.

Boggio *et al.* (2008) showed that anodic and cathodic stimulations have significant impacts on craving control and loss of induction in alcohol abuse. Fregni *et al.* (2008) showed that smoking craving is significantly reduced after left and right DLPFC stimulation significantly and

Table 3: The results of covariance to compare the induced craving in the experimental and control groups

Source of changes	Sum of squares	Df	Mean square	F	Significance level	PES	The observed power
Pre-test	1041.535	1	1040.535	0.209	0.653	0.012	0.072
Group	1456477.545	2	728238.773	146.217	0.000	0.945	1
Error	84669.002	17	4980.530				
total	4027239.978	21					

Adjusted $R^2 = 0.93$

Table 4: Results of post hoc test

Group 1	Group 2	Mean difference	SD error	Significance level
Group 1	Group 2	35.725	39.393	0.377
Group 1	Control	*-540.054	38.126	0.000
Group 2	Control	*575/78	83.965	0.000

concluded that cortex stimulation with tDCS is suitable to reduce reduced cigarette smoking. Uher *et al.* (2005) concluded that stimulation of the cortex by tDCS is effective to reduced induced craving. Eichhammer *et al.* (2003) concluded that tDCS is effective to reduced induced craving.

To explain the above findings it should be noted that craving is an uncontrollable desire for consumption, this desire if not satisfied, can cause psychological and physical sufferings such as fatigue, anorexia, anxiety, insomnia, aggression and depression and the basic craving means the level of consumption desire at the current time.

So, to avoid the above consequences such as fatigue, anxiety, psychological distress etc. the tDCS method was used in the present study which reduced the hookah base craving among the smokers; in other words in this method the electric current passes through the hair, skin, skull, meninges and cerebrospinal fluid to reach the brain and given that different parts of the brain have different impacts on various disorders and the literature considers posterior prefrontal stimulation effective in drug cravings (Rostami *et al*., 2012), in this study stimulation was performed by the same method and its effects on reducing hookah smoking became obvious, therefore in this method by tDCS the polarity in the brain is modified and this strengthens the brain cortex of the addict and controls the subcortical brain nuclei increases the addict's resistance againt carving for drug abuse. On the other hand, addictive drugs increase dopamine (reward and encouragement on the brain) in the prefrontal cortex of meso-cortico-limbic system (Rostami *et al*., 2012). Possibly the stimulation of this part of brain may reduce craving in addicts by affecting hormone levels as well.

It can be concluded that changes in cortical stimulation during tDCS create the membrane potential in target neurons and leads to changes in brain functional networks. On the other hand, this method can also be involved in the modulation and regulation of systems such as dopamine and this type of stimulation could empower the addicts.

The results of testing the second hypothesis suggest that there is no significant difference between the induced carving of the left and right anode experimental groups. There is a significant difference between the induced carving of the left anode experimental group and the control group at the level of 99% difference. Also there is a significant difference between the induced carving of the right anode experimental group and the control group at the level of 99% difference. And due to reduced mean cravings of the experimental groups compared to the control group, it can be said that the tDCS method reduces the induced craving of the hookah smokers.

The findings of this part are consistent with Boggio *et al.* (2008). They showed that cathodic and anodic stimulations are effective in controlling craving and reducing induction of craving in alcohol abusers.

In explaining the above result it should be noted that World Health Organization (Mokri *et al*., 2008) defines craving as the foundation for starting drug dependency, loss of control and relapse and argue that it is created in the face of symptoms associated with experiences or the patients' imaginations under the drug abuse conditions. Craving plays an important role in the phenomenon of relapse after treatment and maintaining consumption dependence. In fact, the presentation of the signs to induce craving is possible in various aspects and these aspects include image, smell, taste, touch, hearing and imagination (Garavan *et al*., 2000).

Thus to explain the hypotheses it can be said that this treatment method increases the resistance of the drug addicts against tempting. This reduced the induced carving of the experimental group significantly compared to the control group. Also, when a person is separated from the abuse the negative symptoms caused by the consumption gradually disappear which could be pleasant to the person and it is a factor to resist against carving.

CONCLUSION

In general, it could be mentioned that in brain function networks regulation of nerve systems caused by direct stimulation on the one hand and the elimination of negative symptoms of drug abuse on the other hand may make the addict to overcome the symptoms of consumption.

SUGGESTIONS

The suggestions for future studies are as follows:

- It is suggested to use this method versus the cognitive, behavioral and emotional. In other words, the external treatments that are out of control such as tDCS should be compared with treatments in which the individual analyzes and changes his cognitive, behavioral and emotional methods. Also, the two methods can be tested and on the addicts and its effectiveness should be analyzed by tDCS alone
- Although tDCS modulates the membrane potential and synaptic processes the proprietary Polar Modulation mechanism is unclear. Future studies should use non-invasive methods such as direct recording in nonhuman primates to better understand electrical stimulation on the nerve function. This will indicate the electrical stimulation to modulate the Synaptic plasticity and influencing the behavior
- Future studies can be focused on topics such as tDCS changes on these systems, the consequences of such modulations and the relationship between the Neurological/modulators transmitters
- It is better for brain mechanisms to show changes by advanced tools of neuroscience such as fMRI, QEEG and ERP instead of questionnaires
- Given that part of the literature argues that female methamphetamine addicts have higher craving during the treatment than men that use the same drug (Culbertson *et al*., 2010), it is suggested to include gender in craving and desire to use drugs to highlight differences
- It is suggested to use 3 groups, one group for electrical stimulation of the brain, one group for problem-solving skills and a mixed group to provide a better and clearer understanding of the effectiveness

LIMITATIONS

- The possibility to use follow-up to measure long-term effects of tDCS
- Given that so far that so far no studies have examined the effectiveness of tDCS to reduce the craving of hookah smokers; in this study the package presented by Fregni *et al*. (2008) is used to analyze the effectiveness of tDCS on cigarette craving is applied
- This research is conducted on hookah smokers and the results cannot be generalized to other drug users
- Few numbers of participants is also considered as one of the limitations of this study. Failure to cooperate to increase the volume of the groups and higher generalizability is considered as another limitation

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