American Journal of Psychiatry and Neuroscience
2016; 4(6): 87-90
http://www.sciencepublishinggroup.com/j/ajpn
doi: 10.11648/j.ajpn.20160406.11
ISSN: 2330-4243 (Print); ISSN: 2330-426X (Online)

A Single-Center, Randomized, Double-Blind, Placebo-Controlled Study on the Efficacy of Clonidine in Detoxification of Opioid Dependency

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To cite this article:

Mani B. Monajemi, Seyyed Mohammad Moosavi. A Single-Center, Randomized, Double-Blind, Placebo-Controlled Study on the Efficacy of Clonidine in Detoxification of Opioid Dependency. *American Journal of Psychiatry and Neuroscience.* Vol. 4, No. 6, 2016, pp. 87-90. doi: 10.11648/j.ajpn.20160406.11

Received: September 19, 2016; **Accepted**: February 9, 2017; **Published**: March 9, 2017

Abstract: Background: Clonidine is α² adrenergic receptor agonist with detrimental effect on locus coeruleus. It is considered as one of the detoxification drugs in order to reduce opiate withdrawal syndrome. We conducted this study in order to assess clonidine effect on withdrawal symptoms and signs. Materials and methods This double blind, clinical trial, single centered study was conducted among 104 male inpatient heroin dependent patients in Psychiatric Center. They were selected via convenient sampling method. Subsequently, they were divided randomly into two matched groups: trial–control (clonidine –placebo) groups. Withdrawal symptoms and signs based on DSM–5 were compared in groups. Results: In 14 day detoxification period (in 7^{th} and 14^{th} day examination), the effect of clonidine on craving and agitation ($p < 0.01$) was significant. With respect to other symptoms and signs, clonidine was not effective prominently. Discussion: Due to different results compared to previous studies in this area. Clonidine use with respect to opioid withdrawal syndrome needs further evaluation or may need to revise.

Keywords: Clonidine, Drug Dependency, Withdrawal Syndrome

1. Introduction

Heroin is an illegal, highly addictive drug derived from morphine, a naturally occurring substance extracted from the seed pod of certain varieties of poppy plants. It is typically sold as a white or brownish powder that is “cut” with sugars, starch, powdered milk, or quinine. Opium derivatives are one of the most prevalent abused substances in Iran. Some of dependent individuals tend to use this drug in order to reach euphoria and afterward they tend to repeat the act in order to re-experience the feeling. After the while, expenses of using a drug, adverse vocational of family problems caused by abuse, force individuals to ask for professional treatment. There are various drugs and therapeutic approaches with respect to dealing with opium derivatives. One the promising drugs worth mentioning is Clonidine. Clonidine is α² adrenergic receptor agonist, which was firstly administered in order to treat hypertension. Afterwards, it’s usage was extended in dealing with various problems such as alleviating withdrawal symptoms, sedative property, anti-anxiety and reducing stress level before surgery [1]. Other usage includes, alleviating symptoms induced by nicotine withdrawal [2], treating withdrawal syndrome of children of substance dependent mothers [3], soothing agitated children in ICU [4]. Clonidine appears to be efficient in detoxification, specifically regarding treating opium dependency treatment; this can be due higher tendency of opium dependent patients in comparing to heroin dependent patients [6, 7]. However, some studies have discussed tramadol as more efficient drug comparing to clonidine [7]. It appears plausible that clonidine specifically inhibits neuroimmune activities and consequently it enhances glial

cells activities and finally it will elevate secretion of cytokine [8]. Reducing symptoms of withdrawal syndrome is due to partial inhibition of Adrenergic system; this effect is as same as prazosin and propranolol [9]. With respect to conspicuous contradictory results in various studies and in practice, regarding efficacy of clonidine in dealing with symptoms of withdrawal syndrome, we conducted this study in order to assess efficacy of clonidine in treatment of opioids withdrawal syndrome.

2. Materials and Methods

In order to assess efficacy of clonidine in treatment of opioids dependent individuals, we conducted this single-center, randomized, double-blind, placebo-controlled study on the efficacy of Clonidine in Detoxification of Opioid Dependency. We chose statistical sample via convenient sampling method. Opioids dependency was confirmed via criteria of DSM-V and patients' declaration. Regarding confirmation of dependency, urinary test was conducted. Participants of the study included all opioids dependent men, between 20-50 year old, with history of 3-5 years dependency with daily abuse dosage of 2-5 grams. After explaining the study to participants, conducting motivational interview, acquiring written consent forms, necessity of staying two weeks hospitalization was explained to participants. Inclusion Criteria: Adults aged 15-18 year old; 2. Inpatients in Bandar-abbas psychiatric Hospital; 3. Meeting substance dependent criteria of DSM-5; Exclusion Criteria: 1. Having serious physical or psychiatric disease; 2. Using alcohol or other substances; 3. Patients who were under medical or psychotropic medications; 4. Patients, who were discharged from hospital sooner than 14 days period.

One hundred fourteen individuals were chosen via inclusion criteria and subsequently 36 patients were ruled out based on exclusion criteria. Finally, 102 individuals who maintained criteria of this study were chosen and they were randomly assigned into two groups of case group and control group. Regarding all patients, ECG, CBC, Sedimentation Rate Test, Fasting Blood Glucose, Liver Function Test(LFT) and Urine Test were done. Participants' substance abuse was stopped from the first day of the study. Administered divided dosage of clonidine was administered orally between 0.6-0.8 mg/d; drug is produced by Tolid. Daroo Co. Regarding both groups Flurazepam capsule (40-60mg/d) and Tramadol (300-400mg/d) were administered; all drugs except clonidine in case group and placebo in control group were reduced gradually and stopped by the end of first week. In cases that experienced severe agitation or aggression, haloperidol (5-10mg) IM was administered. In case of diarrhea, nausea and vomiting symptoms based treatment was conducted. Participants of both groups were under same group-therapy treatment. Participants of both groups maintained physical examination, psychiatric interview every other day; probable side effects of clonidine and withdrawal symptoms (agitation, substance abuse tendency, aggression, insomnia, diarrhea, nausea and vomiting), were assessed based on DSM-5 criteria. Both medical doctor and patients were oblivious of administered substance (clonidine/placebo) and medical doctor assessed withdrawal symptoms independently. Data regarding withdrawal symptoms were recorded by day 7 and 14. Sample number was specified according to two sided alpha level of 0.05 and power of 0.80. After gathering data via T-test, data were analyzed via SPSS-19.

3. Results

In current study, firstly 140 individuals were chosen based on inclusion criteria. Afterwards, 36 individuals were ruled out according to exclusion criteria. One hundred four individuals were entered in this study; forty-two individuals were excluded from the study before ending 14 days period due to various reasons (Based on medical doctor comments or participants' request). Number of individuals in case-group and control-group were 32 and 30 respectively. Mean ages of individuals were 28.6 and 29.7 in case and control group respectively (Table 1) and in both groups we didn't notice meaningful difference with respect to level of significance. According to Table-No1, average dosage substance abuse in case and control groups were 2.9gr and 2.7gr respectively that maintained no significant difference. Average duration of substance abuse were 3.9(year) and 4.1(year) in case group and control group respectively that maintained no significant difference (Table 1). On 7^{th} day assessment, substance abuse tendency and agitation were reduced in case group comparing to control group. However, with respect to aggression, insomnia, nausea and vomiting, diarrhea, muscle aching and lack of appetite, no significant difference was noticed between two groups. Thus, clonidine didn't have significance impact on alleviating these symptoms (Table 2). On 14^{th} day assessment, significance impact of clonidine on alleviating agitation and substance abuse tendency were noticed, however clonidine didn't have any impact on alleviating other symptoms (Table 3).

Table 1. *Demographic Characteristics of Participants in Both Groups.*

Group	Total Number	Number of Participants Who Finished the Study	Mean Age of Participants	Mean dosage of Substance Abuse	Mean Duration of Substance Abuse (Year)
Clonidine(CaseGroup)	52	32	28.6	2.9	3.9
Placebo(ControlGroup)	52	30	29.7	2.7	4.1

Table 2. *Assessment of Withdrawal Symptoms On 7th day assessment.*

Groups and Indexes	Clonidine		Placebo		Level of Significance (P)
Withdrawal Symptoms	**SD**	**Mean**	**SD**	**Mean**	
Substance Abuse Tendency	11.8	3.1	6.4	2.2	<0.01
Agitation	6.8	2.3	2.3	1.1	<0.01
Aggression	28.6	6.79	26.9	4.8	NS
Insomnia	29.6	9.5	28.3	11.7	NS
Nausea and Vomiting	21.6	5.3	20.4	6.3	NS
Diarrhea	40.6	7.2	38.9	11.7	NS
Muscle Aching	11.4	3.7	12.8	2.9	NS
Lack of Appetite	30.8	6.7	31.9	9.6	NS

NS: Not Significant (P>0.05)

Table 3. *Assessment of Withdrawal Symptoms On 14th day assessment.*

Groups and Indexes	Clonidine		Placebo		Level of Significance (P)
Withdrawal Symptoms	**SD**	**Mean**	**SD**	**Mean**	
Substance Abuse Tendency	2.2	6.4	3.1	11.8	<0.01
Agitation	3.5	8.4	9.6	20.9	<0.01
Aggression	6.3	20.4	5.3	21.6	NS
Insomnia	10.8	22.1	9.4	23.8	NS
Nausea and Vomiting	2.9	12.8	3.7	11.8	NS
Diarrhea	8.2	41.7	12.7	39.9	NS
Muscle Aching	6.7	30.8	9.6	31.9	NS
Lack of Appetite	13.2	30.3	10.6	31.8	NS

NS: Not Significant (P>0.05)

4. Discussion

According to the results of current study, clonidine maintained positive effect on agitation and substance abuse tendency in both steps of assessment (7th, 14th day). However clonidine didn't have noticeable impact on other withdrawal symptoms (Aggression, Insomnia, Nausea and Vomiting, Diarrhea, Muscle Aching and Lack of Appetite). Ziaadinni and Colleagues assert that, clonidine is efficient in reducing tendency toward abuse and even fast substance withdrawal [10]. Noticing that in contrart to current study, in aforementioned study, no specific screening was done in order to separate participants according to their type of substance they abuse. In other study, alleviating withdrawal symptoms was not noticeable [11] which is consistent with the result of current study in terms of clonidine not having significant efficacy in alleviating withdrawal symptoms (Aggression, Insomnia, Nausea and Vomiting, Diarrhea, Muscle Aching and Lack of Appetite). According to Salehi and Colleagues [12], clonidine is partly efficient in reducing withdrawal symptoms and tolerating symptoms induced by clonidine can be hard for some patients [12]. With respect to different research methods, less tolerance of withdrawal symptoms in former study can be compared to non-efficacy of clonidine regarding most of the withdrawal symptoms. Sobey and Colleagues (2003), asserted that tramadol is more efficient than clonidine with respect to reducing withdrawal symptoms. With respect to partial efficiency of clonidine in current study, results of aforementioned study are partly consistent with the result of current study. Broom and Colleagues (2011) and Alexander and Colleagues (2009) postulate that clonidine is efficient in reducing withdrawal symptoms. However in aforementioned studies, newborns of dependent mothers were assessed and clonidine was not the main drug regarding treatment [13, 14]. Naderi and Colleagues (2010), administered Naloxone, Midazolam, propofol simultaneously with clonidine and the result was promising [15]. In aforementioned study, clonidine was not the first line medication for treatment and it was administered supplementary. Noticing this point is essential; there is no magical medication for treating substance abuse and behavioral modifications should be accompanied with drugs [16]. According to the result of current study, clonidine solely, is not ample treatment for substance abuse; hence future researches should aim to find other efficient drugs and approaches.

Authors' Contribution

MBM conceived and designed the study, performed statistical analysis of the study. SMM interpreted clinical data, drafted the manuscript. All authors read and approved the manuscript.

References

[1] Grogoretti C, Moglia B, Pelosi P. Clonidine in Preoperative Medicine and Intensive Care Unit more than an Anti – hypertensive Drug. Curr Drug Targets 2009; 10 (8): 799–814.

[2] Kelly P Cosgrov, Jeffery Bati, Feredric Bois. Nicotinic acetylcholine receptor availability during acute and prolonged abstinence from tobacco smoking. Arch Gen Psychiatry 2009. 66 (6): 666–676.

[3] Esmaeili A, Kennhorst AK, Schuster T. Treatment of neonatal abstinence syndrome with clonidine and chloral hydrate. Acta Pediatr 2010. 99 (2): 209–214.

[4] Jenkines LA, Playfor SD, Bevan C. Current Tinted Kingdom sedation practice in pediatric intensive care. Pediatr Anesth 2009. 17 (7): 675–683.

[5] Stroobe S, Brower KJ, Galen LW. Predicting completion of outpatient opioid detoxification with clonidine. Am J Addict 2003. 12 (3): 260–269.

[6] Umricht A, Hoover DR, Tucker JM. Opioid detoxification with buprenorphine and clonidine or methadone in hospitalized heroin dependent patients with HIV infection. Drug Alcohol Depend 2003. 69 (3): 268–272.

[7] Sobey PW, Parran TV, Grey SF. The use of tramadol for acute heroin withdrawal. J Addict Dis 2003. 22 (4): 13–25.

[8] Feng X, Zhang F, Dong R. Interathecal administration of clonidine attenuates spinal neuroimmune activation in a rat model of neuropathic pain with existing hyperalgesia. Journal Article. Eur J Pharmacol 2009. Apr 24.

[9] Bruijnzeel AW, Bishoni M, Tuijl IA. Effect of prazocin, clonidine and propranolol on the elevations in brain reward threshold and somatic sign associated with nicotine withdrawal in rats. Journal Psychopharmacology 2010; 10.

[10] Ziaadinni H, Quhestani A, Moin Vaziri M. Comparing Symptoms of Wthdrawal Rapid Detoxification and Detoxification with Clonidine in Drug Dependent Patients. Addiction & Health 2009; 1 (2).

[11] Ziaadinni H, Nasirian M, Nakhaei N. A Comparation of the Efficacy of Buprenorphine and Clonidine in Detoxification of Heroin- Dependent and the Following Management treatment. Addiction & Health 2010; 2 (1).

[12] Salehi B, Jafarinia N, Ghebleh F, Mansouri A. A comparative Study on opium Withdrawal of Buprenorphine and clonidine. The Journal of Qazvin University of Medical Science 2007; 11 (3 (44)): 57-64.

[13] Broome L, Tsz- Yin. The Use of Clonidine as a Treatment Option. NEO Reviews 2011; 2 (10): 575-584.

[14] Alexander G. Agthe, George R. Kim, Kay B. Mathis, Craig W. Hendrix, Raul C. Valdez, Laurren Jansson et al. Clonidine as an Adjunct therapy to Opioid for Neonatal Abstinence Syndrome: A Randomized Controlled Trial. Pedeitrics 2009; 123 (5).

[15] Naderi A, Naderi M, Rahmani F, Salimi R, Gleiss A, Kasper S. Ultra- Rapid Detoxification Followed by Nine Month of Naltroxane Maintenance Therapy in Iran. Thieme 2010; 43 (4): 130-137.

[16] Lobmaier P, Gossop M, Waal H, Bramness J. The pharmacological Treatment of Opioid Addiction- a Clinical Prospective. Europian Journal of Clinical Pharmacology 2010; 66 (6): 537-545.