

Amphetamine Related Symptoms: Descriptive Analysis and Reasoning

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Abstract

At the last few years a lot of data in the gulf region reported that amphetamine psychosis became more common and more prolonged. This study was done to: 1) assess clinical features related to amphetamine withdrawal, 2) assess if there are changes in these features in comparison to other previous studies or not, 3) study the relation between amphetamine and chronicity of psychotic symptoms, 4) Find a reason for such suspected changes if present. A total of 150 male amphetamine dependent inpatient were selected according to ICD-10 research diagnostic criteria. Patients were subjected to the following procedures: 1) Oral informed consent. 2) Full psychiatric interview. 3) Urine test for common addictive substances on admission. 4) Symptoms checklist which have been designed by the authors to assess Clinical features associated with amphetamine. 5) Symptom Checklist-90—Revised (Derogates 1994). Generally the present study shows that the psychotic symptoms were very common with Amphetamine dependent patients and the severity of all symptoms decreased significantly during the different phases of treatment. Delusions and hallucinations were very common during 2nd week (54% and 51% respectively) and persisted for more than 8 weeks in 24% and 10% of patients respectively. 1999 and Koyama et al 1991 but still the duration of psychosis is much longer. There is increased risk of psychosis with use of amphetamine and a lot of reasons may play role as starting abuse at early age, sensitization process that may lead to chronic psychosis, and adulterating substances like ephedrine that may be dangerous and can lead to permanent damage of brain serotonin nerve endings.

Introduction

Drug dependence is a chronic problem in all countries of the world. The prevalence of Drug abuse and addiction continue to be among the largest and most challenging health, economical, ethical and social problems facing society.

Many studies raised great concern about the prevalence of amphetamine dependence and its associated problems especially psychosis (Farrel et al 2002, Dalamu et al, 1999, Muray, 1998 and Koyama et al, 1991).

The classic amphetamines have their primary effects by causing the release of catecholamine particularly dopamine from presynaptic terminals. The effects are particularly potent for the dopaminergic

neurons that project from the ventral tegmental area to the cerebral cortex and the limbic areas. That pathway has been termed the rewarding pathway and its activation is probably the major addicting mechanism for the amphetamines. Amphetamine induced psychosis has been extensively studied because of its close resemblance to paranoid schizophrenia. Several studies have also found that, although the positive symptoms of schizophrenia and amphetamine induced psychosis are similar, the affective flattening of schizophrenia and also alogia are generally absent in amphetamine induced psychotic disorder. Clinically, however, acute amphetamine induced

psychotic disorder can be indistinguishable from schizophrenia and only the resolution of the symptoms in a few days or a positive finding in a urine drug screening test eventually reveals the correct diagnosis.

Some evidence indicates that the long term use of amphetamines is associated with an increased vulnerability to the development of psychosis under a number of circumstances including alcohol intoxication and stress. Previous studies reported that psychotic symptoms only develop after prolonged use and typically at high doses and usually only hours in length and maximum for few days (*Kaplan and Sadock, 2000*). However at the last few years a lot of data in the gulf region reported that amphetamine psychosis became more common and more prolonged.

Patients admitted to Al-Amal complex are subjected to a preset program as patients are received in a detox unit for few days till they recover from physical withdrawal symptoms and/or psychotic symptoms then patients are transferred to rehabilitation units to receive other modalities of therapies. In the last few years it was noticed that the mean duration of stay in detox units was increasing. Also, cases of amphetamine dependence increased gradually along these years (*annual Report 2005, Alamal complex*). These observations has led the authors to investigate symptoms related to amphetamine especially psychotic features.

Aim

This study was done to: 1) Assess clinical features related to amphetamine withdrawal. 2) Assess if there are changes in these features in comparison to other previous studies or not. 3) Study the relation between amphetamine and

chronicity of psychotic symptoms. 4) Find a reason for such suspected changes if present.

Methods

This study was done in Al-Amal Complex for mental health which is located in Al-Dammam, Kingdom of Saudia Arabia (KSA). It is a 500 bed hospital, 200 for addiction, 150 bed for half way house for abstinent patients and 150 bed for psychiatric patients. The complex serves all the Eastern and Northern provinces of KSA in addition to nearby other gulf countries like Bahrain, Kuwait, Doha, etc. yearly the Addiction treatment in patient units in this complex dealt with more than 2000 case. At the last three years patients dependent on amphetamine only constitute more than 50% of patients dependent on one substance (*Al-Amal complex annual report 2005*)

A total of 150 male amphetamine dependent inpatient at Al Amal Mental Health complex were selected according to ICD-10 research diagnostic criteria (during a period of 8 months. Cases who reported any significant history of other substances use within past two years or who had a previous history of a major psychiatric disorder not related to amphetamine were excluded. After start of the study 19 cases were excluded after getting data from their informants about history of previous depression, schizophrenia, mania and use of other substances.

All patients subjected to the following procedures: 1) Oral informed consent to take part in the study. 2) Complete psychiatric interview. 3) Urine test for common addictive substances on admission to confirm the diagnosis of amphetamine use without any other substances. 4) Symptoms checklist which have been

designed by the authors to assess Clinical features associated with amphetamine. It was applied daily from the first day of admission till the second week then weekly till discharge. 5) Symptom Checklist-90—Revised (SCL-90-R) (Derogates 1994) which is a quick screening instrument, to measure the status of psychopathology, and as a quantification of current psychopathology along nine symptom constructs: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic-Anxiety Paranoid Ideation, and Psychoticism. It is a self-administrated questionnaire. Instructions direct respondents to report how much discomfort each item caused them during the previous weeks. Items are numbered rejoinders to the opening stem “How much were you distressed by . . . ?” Respondents mark one numbered circle for each item on a Likert-type scale of 0 = not at all, 1 = a little bit, 2 = moderately, 3 = quite a bit, and 4 = extremely. SCL-90 6) Each patient was asked specifically during the interview about, starting age of abuse of amphetamine, duration of abuse, dose, number of previous hospitalizations and past history of psychosis related to use of amphetamine. 7) In addition to the procedures done for patients, 7 different types of amphetamine tablets available in the market were collected through narcotic prevention department and the content of such types were analyzed through the central toxicology laboratory in Dammam central Hospital by expert professor of chemistry and toxicology.

Only data of 131 patients were subjected to the statistical analysis. The symptoms checklists results were collected and statistically analyzed utilizing mean, standard deviation, and frequencies, discriminate function analysis, to compare the daily differences. All collected data were Statistical analyzed using SPSS version 12 (2003). All given percentages are approximated numbers done by the computer.

Results

The Mean age of the patients included in the sample was 26.24 ± 5.4 . Regarding the demographic data of this sample, 76 % were currently single, 14 % were married, and 8% divorced, 2% widows. Regarding Educational level 51% were graduated from Middle school, 22% Primary school, 11% Secondary school, 6% illiterate and 4 % can read and write, while there were 6% University graduates. In regard of the Place of residence, 78% were from eastern province, 7% from western province, 5% from south and 4% from north province and 6% from other nearby Gulf countries. The results of urine toxicology showed that 42% had negative results, where 58% had positive results on admission. The samples were collected on the second day of admission. Regarding the family history of substance use, the majority of that sample 82% had negative results and 18% had positive results. Although no personality tests were administered on our patients, the results of clinical evaluation revealed that 22 % were diagnosed as having personality disorder.

Tables 1: the common symptoms of the Amphetamine patients in the first and 2nd weeks

Symptoms	Frequency(first week)		Frequency(second week)	
Objective symptoms (Physical)	Normal	high	Normal	high
Blood pressure	%96	%4	%98	%2
Sweating	%64	%36	%20	%80
Tachycardia	%84	%16	%90	%10
Vomiting	%90	%10	%100	%0
Diarrhea	%94	%6	%100	%0
Sneezing	%88	%12	%100	%0
Sleep disorder	%42	%58	%42	%31
Dilated pupils	%90	%10	%100	%0
Tremors	%82	%18	%100	%0
Back pain	%90	%10	%100	%0
Running nose	%86	%14	%100	%0
Fever	%96	%4	%100	%0
Subjective symptoms (Psychological)				
Headache	%76	%24	%98	%2
Delusions	%72	%28	%46	%54
Hallucinations	39%	61%	49%	51%
Chest tightness	%89	%12	%98	%2
Anxiety	%56	%44	%57	%43
Abdominal pain	%98	%2	%100	%0
Restless	%66	%34	71%	29%
Depressed mood	%54	%46	%62	%38
Irritability	%58	%42	%88	%12
Abnormal behavior	%68	%32	%12	%88

Tables 2: the common symptoms of the Amphetamine patients in the 3rd and 4th weeks

Symptoms	Frequency(3 rd week)		Frequency(4 th week)	
Objective symptoms (Physical)	Normal	high	Normal	high
Blood pressure	%97	%3	%99	%1
Sweating	%81	%19	%88	%12
Tachycardia	%92	%8	%94	%6
Vomiting	%100	%0	%100	%0
Diarrhea	%99	%1	%100	%0
Sneezing	%99	%1	%100	%0
Sleep disorder	%73	%27	%77	%23
Dilated pupils	%100	%0	%100	%0
Tremors	%100	%0	%100	%0
Back pain	%99	%1	%100	%0
Running nose	%98	%2	%100	%0
Fever	%100	%0	%100	%0
Subjective symptoms (Psychological)				
Headache	%97	%3	%96	%4
Delusions	%55	%45	%61	%39
Hallucinations	68%	32%	79%	21%
Chest tightness	%95	%5	%97	%3
Anxiety	%51	%49	%71	%29
Restless	79%	%21	%76	%24
Depressed mood	%65	%35	%77	%23
Irritability	%90	%10	%96	%4
Abnormal behavior	%68	%32	%69	%21

Generally the present study shows that physical symptoms were mild and uncommon with Amphetamine withdrawal and the severity of symptoms decreased significantly within short time. The physical withdrawal symptoms generally peak in 2 to 4 days and are resolved in most of cases within first week. The most common physical withdrawal symptoms were excessive sleep and sweating while the most serious physical withdrawal symptom was tachycardia (16% in first week).

The most common psychological withdrawal symptoms were delusions, hallucinations, depressed mood and anxiety symptoms. The most serious psychological withdrawal symptom was depression that can be severe after sustained use of high doses and can be associated with suicidal ideation or behavior. Psychological withdrawal symptoms started during the first week and in some cases persisted for more than 8 weeks. Percentage of cases had delusions increased during the second week

and decreased gradually during the following weeks.

84% of cases reported a previous history of psychotic symptoms associated with use of amphetamine. 34% of the sample reported that they had used amphetamine on over 100 separate occasions. Those frequent users were at greater risk of psychosis than those who had used less extensively. For those who had used amphetamine on over 100 occasions, the risk of delusions was more than double that of other users (OR=2.37, $P < 0.01$).

Starting use of amphetamine before the age of 18 years also doubled the risk of developing delusions odd ratio = 2.73, $P < 0.05$. Early amphetamine use before age of 18 years has been also, associated also with multiple hospitalizations.

Also, there was positive correlation between presence of delusions and history of previous psychosis, number of previous hospitalizations, duration of stay in the hospital and daily dose of amphetamine.

Tables 3: the mean Score on SCL-90 R of the Amphetamine patients.

Scale Items	Mean	SD
Somatization	.43	.32
Obsessive-compulsive	.97	.81
Interpersonal Sensitivity	1.69	.33
Depression	1.23	.67
Anxiety	1.12	.39
Hostility	1.20	.42
Phobic- anxiety	.80	.22
Paranoid ideation	1.48	.47
Psychoticism	1.01	.32

The results showed that there were high scores of Interpersonal Sensitivity, hostility due to suspiciousness, delusion of persecutions, Paranoid ideation, and Psychoticism. In the other side, the depression was also higher than average level.

Duration of hospitalization was 4-5 weeks in 21% of cases, 5-6 weeks in 34%, 6-8 weeks in 30%, and 15% more than 8 weeks. At discharge 24% of patients still have delusions and 10% still have hallucinations.

Analysis of the amphetamine tablets revealed that each tablet contain different amounts from different substances even if it is from the same type (same the shape and color). Some of the tablets analyzed have no amphetamine at all. Ephedrine and pseudoephedrine were common finding in most of tablets analyzed. Other substances like caffeine, theophylline, diphenhydramine, methyle salicylates, quinine and ascorbic acid were also found.

Discussion

Previous studies denoted that typically symptoms of amphetamine psychosis remit within a week, but in a small proportion of patients, psychosis may last for more than a month (*Kaplan and Sadock, 2000; Koyama et al, 1991; and Kandel and Davis 1996*). Some amphetamine users may develop persistent psychosis and those who recover remain at high risk of reexperiencing psychosis even if they don't use amphetamines again (*Hyman and Nesteler, 1996; and Farrel et al 2000*)

Although Amphetamine dependent patients are usually of a younger age (*Battaglia and Napier, 1998*), the results showed that there are no cases below 18 years (Mean age of 26.24 $SD \pm 5.4$), Because of the admission

policy of Al-Amal mental complex, which does not permit admission below this age. Regarding the educational level of our sample, only 6% was university graduated, which could be explained on basis of level of education and more maturity. The Middle school graduated represented the highest percentage of the sample because at this level of education they sought to work in governmental places, and some of them are referred from their work for assessment and management. Regarding marital status the results showed that 86% the sample were singles probably due to social stigma of addiction, and unemployment.

As regards to the physical withdrawal symptoms, all results were concordant with results of previous studies (*Dalamu et al 1999 and Koyama et al 1991*) which denoted that most of physical symptoms disappeared during the first week and that the most resistant objective symptoms are sleep disorders and sweating (*Iwanami, et al 1994*). Sleep disorders are explained by the powerful effect of the amphetamine as a stimulant on reticular activating system while the prolonged sweating is explained by the tendency of autonomic disturbance to persist more and to adapt more slowly than other body systems (*Kaplan and Sadock, 2000*).

Patients were examined daily by symptom checklist and to avoid biased judgment from patients and clinician themselves application of SCL-90 R was done weekly. High scores of Interpersonal Sensitivity, hostility, delusion of persecutions, Paranoid ideation, depression and psychoticism confirmed the clinical assessment done and gave an objective score. Delusions and hallucinations were more common in the second week than in the first week as patients are more distressed by physical

symptoms and increased sleep during first week and when they start to communicate these psychotic features started to appear more prominently.

Persistent mood symptoms like depressed mood for more than 4 weeks in 23% of cases is concordant with other studies (*Koyama et al 1991 and Murray 1998*) as amphetamine is powerful stimulant for dopamine and its ingestion for long periods will be followed by dysregulation of dopamine receptors and readjustment of these receptors after withdrawal will take time because it is a structural brain change (*Farrel et al 1998*).

Persistent delusions, hallucinations, and abnormal behaviors for 4 weeks in 39%, 31% and 29% of cases respectively confirmed the clinical observation noticed empirically. Previous studies about duration of psychotic symptoms denoted that only 15% of patients persisted to be psychotic at the 4th week (*Brabbins and Poole, 1996, Brady et al, 1991, and Satu et al, 1990*). The argument that the subjects found in this study are not suffering from psychosis but simply manifesting the toxic effects of amphetamine has been examined and excluded because toxic effects by definition in ICD-10 research diagnostic criteria don't exceed 48 hours. ICD-10 Classifications permitted for psychosis to appear within two weeks from taking the substance and to last at least more than 48 hours and at most 6 months (*WHO, 1992*) but there is idea about the commonest duration of psychosis as classifications addressed other issues like medicolegal aspects

This persistence of psychotic symptoms can be attributed to the change in structure of amphetamine tablets as analysis of tablets revealed wide use of ephedrine as an additive and it is well known in the

literature that this substance can lead to permanent damage of brain serotonin nerve endings that have a major role in psychosis and depression (*Ellenhorn, et al, 1990*). The second major cause for persistence of psychotic symptoms was the kindling process (*Kaplan and Sadok, 2000*) as denoted by The positive correlation between early use of amphetamine before age 18 years, duration of use of amphetamine, dose, number of hospitalizations. Where as dopamine neurotransmission is increased in response to a single dose of amphetamine and this would suggest that repeated increases in dopamine release may produce secondary changes that are more directly responsible for the persistence of psychosis (*Cherland and Fitzpatrick, 1999 and Farrel et al 1998*).

Another possible interpretation of persistence of psychotic features with amphetamine is that individual with predisposition to psychosis are more likely to use drugs and drugs work as precipitating factor not an inducing factor. But this interpretation can be minimized by the fact that drug induced psychosis is not common with other substance like opiates or benzodiazepines as with amphetamine (*Peroutka, 1988 and Murray 1998*)

Reports from narcotic prevention department revealed that most of amphetamine was imported from outside the country in the past but at the last few years there is local synthetic amphetamine and this interpretate the different structure of different types of amphetamines and interpret adulteration with many things like salicylic acid, antihistaminics, quinine and the most dangerous was ephedrine.

Conclusion

It is misleading and dangerous, to our youth in particular, to label Amphetamine as “soft drug” and to be socially accepted. In fact the serious adverse effects of Amphetamine let it as one of the worst substances in our countries.

Policy implications

Severe dependence on amphetamine was associated with higher risk of psychosis so services should be directed more toward this type of addiction especially that current services are more directed toward substances like heroin.

Opening of special units for drug induced psychosis will be beneficial because those cases block detox units and will disturb rehabilitation units. This research help to stress that the plan of narcotics prevention should be adapted and modified to restrict local synthesis of these substances.

Clinical implications

This work reflects the importance of clinical observation to monitor changes in the presentation of patients. Also it reflects the importance of integrating clinical observation with chemical assessment of the available illicit drugs

Following recovery persons who have experienced an amphetamine-induced psychosis seem to be sensitized and will experience acute paranoid psychosis on reexposure to small doses of amphetamines.

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