National Ribat University
Institute of Forensic Evidence Sciences

Assessment of Trihexyphenidyl (kharsha) Knowledge and Abuse Among Students of one of Khartoum state Universities

Bsc. Pharmacy, University of Science and Technology (2005)

A Thesis Submitted to National Ribat University for Partial Fulfillment of the Requirements for the Master Degree in Forensic Science

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Dedication

I dedicate this work to my father who generously dedicated his life for us.
To my dear mother that the secret of my success is her du'aa.
To my wife and my beautiful children who are the joy of my life for their patience and support.
To my friend Musaab for his support and endless help.

Hawari Salih
Acknowledgment

I wish to record my thanks to all those who assisted me in the completion of this work either by support or consultation.

I owe a great deal to my academic supervisor Dr. Ahmed AwadElgamel for the patience careful direction and never-ending support.
الملخص

بنزهكسول هيدروكlorيد (تريهكسفينيديل)، يعتبر واحد مضادات الكولين القوية وقد اكتسب استخدامه على نطاق واسع في علاج مرضى الشلل الرعاش وفي السيطرة على الآثار الجانبية لدواء الشلل الرعاش. على الرغم من التقارير التي تحدثت في وقت مبكر لقاح التثبيط إلى تأثيراته النفسية وإمكانية ادمانه من الناحية النظرية على الأقل، حيث أنه لم يتم اكتشافه سريريًا حتى وقت قريب، قد لوحظ سوء استخدام بنزهكسول بوتيرة متزايدة في السنوات الأخيرة بين الشباب السافرين والمحرومين المترددين على عادات الطب النفسي، وقد أفادوا أن استخدامهم للدواء وبدافع خصائصه المهدئة والتي تزيد الاحساس بالسعادة، وقد ساهم فشالاً مختصراً في اثبات الإدمان عليه، على إمكانية الحصول على وصفات طبية لكميات كبيرة بدون صعوبة مما ساهم في زيادة الانتشار.

هذه دراسة وصفية وتحليلية مقطعية تعتمد المعرفة والانتشار والمساواة، و الآثار الجانبية بين متغطي تريهكسفينيديل. وقد تم اختيار الدراسة المقطعية لأنها المناسبة لوصف ظاهرة من الظواهر أو لوصف العلاقات بين الظواهر في نقطة ثابتة في المكان والزمن المناسب.

الهدف من هذه الدراسة تقييم المعرفة عن تريهكسفينيديل وانتشاره في الكليات الطبية في جامعة من جامعات ولاية الخرطوم، المستهدفين من هذه الدراسة هم طلاب ست كليات في هذه الجامعة، وتستتبع الدراسة الأعمار فوق 35 سنة وتحت 18 سنة. وكانت عينة الدراسة من 300 طالب، وكان معدل الاستجابة 93% وأداة الدراسة هي الاستبانة.

وفما يتعلق بالمعرفة ممن شملهم الاستطلاع عن الاكسيسول أو الخرشة كشفت الدراسة أن 48% من العينة كانت على معرفة بالإكسيسول و 21% منهم أكروا أن استخدام الاكسيسول يمكن أن يؤدي إلى الإدمان وكانت هناك نسبة من الطلاب تتعاطى الاكسيسول.

وتوصي هذه الدراسة بأن البرامج عبر وسائل الإعلام المختلفة، مهمة في تعريف الناس والطلاب حول مخاطر سوء استخدام الاكسيسول، أيضا تطوير عادات النفسية المزروعة بالأخصائيين المدربيين تدريبياً جيداً للتعامل مع المدمنين، وأيضا نشر الوعي القانوني والتحذير الواضح ضد استخدام الاكسيسول أو التسويق حتى من الصيدليات.
Abstract

Benzhexol hydrochloride (trihexyphenidyl), is a potent anticholinergic agent and has gained widespread use in the treatment of Parkinson's disease, and in the control of drug-induced extrapyramidal side-effects. Despite early reports drawing attention to its psychoactivity and potential, at least in theory, for abuse, this does not appear to have been recognised in clinical practice until recently. Abuse of benzhexol has been noted with increasing frequency in recent years amongst the disaffected and disadvantaged youths attending psychiatric clinics, who reported that their use of the drug was motivated by its hallucinogenic and euphorogenic properties. The failure by the medical profession to recognize its addictive effects resulted in a situation where prescriptions for large quantities could be obtained without difficulty.

The design of this study is descriptive, analytical, cross sectional study as it assesses the Knowledge, attitude, practice, and presence of side effects of trihexyphenidyl abusers. Cross sectional study was chosen because it appropriate for describing the status of phenomena or for describing relationships among phenomena at fixed point in time.

This study goals to assess the Trihexyphenidyl knowledge and Abuse Among medical and non medical student in one of Khartoum state Universities. The target population of this study is the students of six colleges in this University. The study excludes student's ages above 35 years and under 18 years old. The sample of this study was 300 students. The response rate was 93%. The study tool was a self-administer questionnaire.

Regarding the knowledge of the respondents surveyed about Akisol or Kharsha, the study revealed that 48% of the sample knew about Akisol and 21% of them confirmed that Akisol use can lead to addiction, finally 20% of the respondents believed that Akisol abuse has harmful consequences.

This study concludes that the media programs across various media, is important to educate people and students about the dangers of abuse of akisol, also development of well-trained psychiatric clinics to deal with addicted people, also dissemination of legal awareness and clear warning against akisol use and marketing even from pharmacy.
Table of Contents

<table>
<thead>
<tr>
<th>Items</th>
<th>page no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dedication</td>
<td>I</td>
</tr>
<tr>
<td>Acknowledgment</td>
<td>II</td>
</tr>
<tr>
<td>Arabic Abstract</td>
<td>III</td>
</tr>
<tr>
<td>English Abstract</td>
<td>IV</td>
</tr>
<tr>
<td>Table of Contents</td>
<td>V</td>
</tr>
<tr>
<td>List of Figures</td>
<td>VII</td>
</tr>
<tr>
<td>List of Tables</td>
<td>X</td>
</tr>
</tbody>
</table>
## Chapter one (introduction and literature review)

<table>
<thead>
<tr>
<th>Items</th>
<th>page no</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Introduction</td>
<td>2</td>
</tr>
<tr>
<td>1.2 Statement of the problem</td>
<td>3</td>
</tr>
<tr>
<td>1.3 Significance of the study</td>
<td>3</td>
</tr>
<tr>
<td>1.4 General objective</td>
<td>3</td>
</tr>
<tr>
<td>1.5 Specific objectives</td>
<td>3</td>
</tr>
<tr>
<td>1.6 Research questions</td>
<td>3</td>
</tr>
<tr>
<td>1.2 Literature Review</td>
<td>5</td>
</tr>
<tr>
<td>1.2.1 Drug abuse</td>
<td>5</td>
</tr>
<tr>
<td>1.2.2 Factors Influencing Drug Abuse and Dependence</td>
<td>11</td>
</tr>
<tr>
<td>1.2.3 The sequence of drug abuse</td>
<td>13</td>
</tr>
<tr>
<td>1.2.4 The public health impact of drug abuse</td>
<td>15</td>
</tr>
<tr>
<td>1.2.5 The aims of treatment of drug abuse</td>
<td>17</td>
</tr>
<tr>
<td>1.2.6 Drug Abuse and the Family</td>
<td>20</td>
</tr>
<tr>
<td>1.2.7 The Pharmacological Effects of Drug Abuse</td>
<td>21</td>
</tr>
<tr>
<td>1.2.8 Anticholinergic</td>
<td>25</td>
</tr>
<tr>
<td>1.2.9 Benzhexol</td>
<td>30</td>
</tr>
</tbody>
</table>

## Chapter two (Methodology)

2.1 Methodology                                                        | 43      |
2.2 Questionnaire content.................................................................43

2.3 Statistical Manipulation .............................................................44

Chapter three (Result)

3.1 Personal information of the study population.......................46

3.2 Medications ...........................................................................52

3.3 Kharsha knowledge ...............................................................53

3.4 Knowledge of Akisol abusers .................................................56

Chapter four (discussions, conclusion and recommendation)

4.1 Discussions...............................................................................67

4.2 Conclusion...............................................................................68

5.2 Recommendation .....................................................................68
# List of Figures

<table>
<thead>
<tr>
<th>Figure No</th>
<th>Figure Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Structural formulas of the belladonna alkaloids and semisynthetic and synthetic analogs</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>Age Distribution</td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>Gender Distribution</td>
<td>47</td>
</tr>
<tr>
<td>4</td>
<td>Residences</td>
<td>47</td>
</tr>
<tr>
<td>5</td>
<td>Marital Status</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>Living in the family house</td>
<td>48</td>
</tr>
<tr>
<td>7</td>
<td>Jobs</td>
<td>49</td>
</tr>
<tr>
<td>8</td>
<td>Monthly income</td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td>Type of study</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>Classes Distribution</td>
<td>51</td>
</tr>
<tr>
<td>11</td>
<td>Chronic medication</td>
<td>52</td>
</tr>
<tr>
<td>12</td>
<td>Analgesic use</td>
<td>53</td>
</tr>
<tr>
<td>13</td>
<td>Akisol Or Kharshaknowled</td>
<td>53</td>
</tr>
<tr>
<td>14</td>
<td>Akisol or Kharsha addiction knowledge</td>
<td>54</td>
</tr>
<tr>
<td>15</td>
<td>Akisol abuse side effects knowledge</td>
<td>54</td>
</tr>
<tr>
<td>16</td>
<td>Akisol dose and dosage form knowledge</td>
<td>57</td>
</tr>
<tr>
<td>17</td>
<td>Akisol or kharsha prevalence</td>
<td>58</td>
</tr>
<tr>
<td>18</td>
<td>Continue using akisol</td>
<td>56</td>
</tr>
</tbody>
</table>
19 Negative effects of using akisol
20 Positive effects of using akisol
21 Source of akisol (Pharmacy)
22 Source of akisol (Drugs dealer)
23 Source of akisol (Friends)
24 Akisol inducing euphoria
25 Akisol mixed with other medicines
26 Abusing another drugs
27 Alcohol consumptions
28 Criminal behavior
29 Stigma from akisol abuse
30 Family and society contributions
31 Sleep and anxiety disorder
32 Willing to stop abusing Kharsha
<table>
<thead>
<tr>
<th>Table No</th>
<th>Table name</th>
<th>Page No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Anticholinergic drugs commonly used to treat tremor in Parkinson's disease</td>
<td>29</td>
</tr>
</tbody>
</table>
Chapter one

Introduction and Literature Review
1.1 Introduction
There is no doubt that the strength of any society derives from the power of his sons, they work as a first line of defense against any breach of the social fabric, by maintaining values and morals, religion and heritage. From this standpoint, if spread phenomenon of drug and substance abuse among members of the community, especially young people, this threatens catastrophe will occur in the community.

Substance abuse and addictive behavior are universal phenomena and are regarded in the twentieth century as a major public health problem. Historical evidence suggest that since ancient times living with psychoactive substance seems to be part of the fabric of our lives. The desire to experience some altered state of unconsciousness seems to be an intrinsic part of the human condition.

The health and social costs of the abuse of these psychoactive substances unfortunately reflect most disturbing morbidity and mortality.

The squealer of the harm physical, social, psychological and economic derived from the abuse of psychoactive substance not only affect the individual user but also the family.

Kharsha also known as trihexyphenidyl, hydrochloride is a tertiary amine antimuscarinic drug with actions similar to atropine. It also has direct antispasmodic action on smooth muscle. Despite having been shown to adversely affect memory.

Benzhexol is currently used in the clinical management of tremor-related conditions such as Parkinson’s disease.

Other antimuscarinics used in parkinsonism include orphenadrine, benzatropine, and procyclidine.

Benzhexol hydrochloride (trihexyphenidyl), a potent anticholinergic agent has gained widespread use in the treatment of Parkinson's disease and in the control of drug-induced extrapyramidal side-effects. Despite early reports drawing attention to its psychoactivity and potential, at least in theory, for abuse, this does not appear to have been recognised in clinical practice until recently. Abuse of benzhexol has been noted with increasing frequency in recent years amongst the disaffected and disadvantaged youths attending psychiatric clinics, who reported that their use of the drug was motivated by its hallucinogenic and euphorogenic properties. The failure by the medical profession to recognise its potential for abuse resulted in a situation where prescriptions for large quantities could be obtained without difficulty.
1.2 Problem and justification
Drug abuse and addiction has become one of the most important public health problems in recent years. Information providing role of lay theories is undeniable in preventive and rehabilitative works related to drug addiction. Several studies investigated lay beliefs and attitudes related to different kinds of drugs. For instance, found that the participants’ political views were the most important determinant of lay beliefs about heroin addiction.

In a study conducted by national drugs control in 2010 in some universities in Khartoum, shows that increase percentage of drugs abusers among students, also a study is conducted by the Institute of forensic evidence sciences about Kersha abuse in Nile street café, shows that

Research also indicated that certain variables increase the risk of drug abuse. Younger people are more prone to drug abuse.
The increase in abuse of marketed medications in recent years has highlighted the need for abuse-liability assessment.
The abuse of kharshaamong people ages from 14 to 25years old started to be problem in Sudan.

1.3 Significance of the study
Psychoactive substance abuse problems are prevalent and widespread worldwide, and are associated with significant morbidity and mortality. The World Health Organization (WHO) has identified alcohol, tobacco, and illicit drugs as among the top 20 risk factors for ill-health and has adopted as public health approach to screening for alcohol and drug abuse, and early intervention for such problems.

1.4 General objective
This study aims to assess the abuse of trihexyphenidyl among persons who have abused trihexyphenidyl examining the level of knowledge, attitude, and practice about the drug.

1.5 Specific objectives
1-To identify the knowledge, practice, and attitude of trihexyphenidyl abuse.
2-To assess the effect of socio demographic factors (age, sex, economic status, type of education) on abuse of trihexyphenidyl.
3-To assess the effect of psychological stress on abuse of trihexyphenidyl.
4-To assess the side effects of trihexyphenidyl among trihexyphenidyl abusers.
5-To suggest recommendations for policy and decision makers regarding the opportunity to stop trihexyphenidyl abuse.

1.6 Research questions
1- Do the people who abused trihexyphenidyl have any knowledge about trihexyphenidyl?
2-What is the attitude of persons who have abused trihexyphenidyl?
3-How do the persons abused trihexyphenidyl?
4-Does age factor affect on abuse of trihexyphenidyl?
5-Does the sex factor affect the abuse of trihexyphenidyl?
6-Does the marital status factor effect the abused of trihexyphenidyl?
7-Does the kind of occupation factor affect on abused of trihexyphenidyl?
8-Does the economic status factor effect on trihexyphenidyl abuse?
9-Does the abusers has psychological stress?
10-Does the abusers complain of any side effects related to abuse of trihexyphenidyl?
1.2. Literature Review

1.2.1 Drug abuse

1.2.1.1 Introduction

Drug abuse is defined as the use of a substance for a purpose not consistent with legal or medical guidelines. It has a negative impact on health or functioning and may take the form of drug dependence, or be part of a wider spectrum of problematic or harmful behavior.

1.2.1.2 Drug Addiction

Drug addiction is a chronic, relapsing disorder in which compulsive drug-seeking and drug-taking behavior persists despite serious negative consequences. Addictive substances induce pleasant states (euphoria in the initiation phase) or relieve distress. Continued use induces adaptive changes in the central nervous system that lead to tolerance, physical dependence, sensitization, craving, and relapse.

Theories of addiction have mainly been developed from neurobiologic evidence and data from studies of learning behavior and memory mechanisms. They overlap in some aspects and are not mutually exclusive. None of them alone can explain all aspects of addiction. It is not our purpose to present a detailed assessment of these theories, especially because of the complexity of the problem. Generally, addictive drugs can act as positive reinforcers (producing euphoria) or as negative reinforcers (alleviating symptoms of withdrawal or dysphoria). Environmental
stimuli (cues) associated with drug use itself can also induce a conditioned response (withdrawal or craving) in the absence of the drug (Stolerman I., 1992). Koob and Le Moa (1997 and 2001) have proposed that the organism tries to counteract the effects of a given drug through a vicious circle in which the hedonic set point (the point at which pleasure is achieved) continually changes in response to the administration of the substance. They argue that drug addiction results from dysregulation of the reward mechanism and subsequent allostasis, the ability to achieve stability through change. (Robinson and Berridge., 2001., 2003) emphasize the dissociation between the incentive value of the drug ("wanting") and its pleasurable or hedonic effects ("liking"), so that the brain system involved in the reward mechanism becomes hypersensitized to both the direct effects of the drug and associated stimuli that are not directly attributable to the drug. This hypersensitization causes pathologic wanting, or craving, independently of the presence of withdrawal symptoms and leads to compulsive drug-seeking and drug-taking behavior. Although liking progressively decreases, drugs become pathologically wanted (craving). Complementary to this incentive–sensitization theory, (Robinson and Berridge., 2001., 2003) compulsive drug-seeking and drug-taking behavior is facilitated by difficulties in decision making and the ability to judge the consequences of one's own actions. These cognitive difficulties have been linked to deficits in the activation of areas in the prefrontal cortex. (Franklin,
An overlap in memory mechanisms and the mechanisms of drug addiction has also been proposed. (Hyman and Malenka, 2001).

1.2.1.3 Drug dependence

Dependence is diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) when three or more of the following criteria are present in a 12-month period: tolerance; withdrawal; increasing use over time; persistent or unsuccessful attempts to reduce use; preoccupation or excessive time spent on use or recovery from use; negative impact on social, occupational or recreational activity; and continued use despite evidence of its causing psychological or physical problems (American Psychiatric Association, 1994).

The diagnosis of dependence is clearest with opioids. The WHO states that:

Opioid dependence develops after a period of regular use of opioids, with the time required varying according to the quantity, frequency and route of administration, as well as factors of individual vulnerability and the context in which drug use occurs. Opioid dependence is not just a heavy use of the drug but a complex health connotation that has social, psychological and biological determinants and consequences, including changes in the brain. It is not a weakness of character or will (World Health Organization, 2006).
However, dependence, as characterized by the above definition, can also occur with stimulants and cannabis.

1.2.1.4 Tolerance
Repeated use of a drug can lead to the development of tolerance in which increased doses of the drug are required to produce the same effect. Tolerance develops to opioids, stimulants and cannabis. Cessation of use leads to reduced tolerance and this may present significant risks for individuals who return to drug doses at a level to which they had previously developed tolerance. This can result in accidental overdoses and, in the case of opioid misuse, could lead to respiratory depression and death. (World Health Organization, 2006).

1.2.1.5 Withdrawal
Withdrawal syndromes have clearly been identified after cessation or reduction of opioid and stimulant use. DSM-IV criteria for a withdrawal disorder include the development of a substance-specific syndrome due to cessation or reduction in use; the syndrome causing clinically significant distress; and symptoms not due to a general medical condition or better explained by another mental disorder (American Psychiatric Association, 1994). While withdrawal effects have been associated with cessation of heavy opioid use, their clinical significance is uncertain at present (Budney et al, 2004).
People who abuse drugs may present with a range of health and social problems other than dependence, which may include (particularly with opioid abusers):

- physical health problems (for example, thrombosis, abscesses, overdose, hepatitis B and C, HIV, and respiratory and cardiac problems).
- mental health problems (for example, depression, anxiety, paranoia and suicidal thoughts).
- social difficulties (for example, relationship problems, financial difficulties, unemployment and homelessness).
- criminal justice problems.

Many people who abuse drugs use a range of substances concurrently and regularly known as polydrug abuse. The use of opioids alongside cocaine or crack cocaine is common, with the National Drug Treatment Monitoring System (NDTMS), which collects, collates and analyses information from those involved in the drug treatment system, reporting an increase in the use of both drugs, from 18% of those presenting for drug treatment in 1998 to 24% in 2001 National Treatment Agency for Substance Misuse (National Treatment Agency for Substance Misuse, 2005). Alcohol abuse is also common in all types of people who misuse drugs; data from the National Treatment Outcomes Research Study (NTORS) on drug misuse suggested that 22% of participants also drank alcohol.
frequently, 17% drank extremely heavily and 8% drank an excessive amount on a daily basis (Gossop et al, 2000)). People who misuse opioids in particular may often take a cocktail of substances, including alcohol, cannabis and prescribed drugs such as benzodiazepines, which can have especially dangerous effects in comparison with one of the drugs taken individually.

The association between drug misuse and crime also applies in the younger population. The Home Office 2004 Offending Crime and Justice Survey (Information Centre, Lifestyle Statistics, 2006) found that young people who had used drugs in the past year were over twice as likely to have committed an offence compared with those who reported not having used drugs (52% versus 19%). In addition, young offenders who had taken a Class A drug in the past year were more likely to be frequent offenders than those who reported using other types of drugs. However, in contrast to figures for the general population, Class A drug users comprise a very small proportion (1% testing positive for heroin and 4% for cocaine) of arrestees aged below 18 years (Matrix Research and Consultancy & NACRO, 2004).
1.2.2 Factors Influencing Drug Abuse And Dependence:

1.2.2.1 Pharmacologic and Physicochemical Properties of Drugs

Pharmacologic and physicochemical properties of drugs are important factors in how drugs are consumed. Liposolubility increases the passage of a drug through the blood–brain barrier, water solubility facilitates the injection of a drug, volatility favors the inhalation of drugs in vapor form, and heat resistance favors smoking of the drug. (Farre and Cami, 1991) Characteristics such as rapid onset and intensity of effect increase the potential for abuse (Mumford et al, 1995 and Roset et al., 2001); therefore, substances that rapidly reach high levels in the brain are usually preferred (e.g., flunitrazepam is preferred over triazolam, and smoking “crack” cocaine is preferred to intranasal administration). (Farre et al, 1998 and Hatsukami and Fischman, 1996) A short half-life (e.g., that of heroin) produces more abrupt and intense syndromes of withdrawal than does a long half-life (e.g., that of methadone).

1.2.2.2 Personality and Psychiatric Disorders

Personality traits and mental disorders are major conditioning factors in drug addiction. Risk-taking or novelty-seeking traits favor the use of addictive drugs. (Helmus et al, 2001) Polydrug use is frequent among those with drug addiction, and many fulfill the criteria for dependence on or abuse of (or both) more than one substance. (Leriet et al, 2003) Psychiatric disorders, particularly schizophrenia,
bipolar disorder, depression, and attention-deficit–hyperactivity disorder, are associated with an increased risk of abuse. A dual diagnosis (substance abuse and mental disorder) has unfavorable implications for management and outcome. (Kavanagh et al. 2002)

1.2.2.3 Genetic Factors

Genetic factors that influence the metabolism and the effects of drugs contribute to the risk of addiction. (Crabbe, 2002) Men whose parents were alcoholics have an increased likelihood of alcoholism even when they were adopted at birth and raised by parents who were not alcoholic, and they also have a reduced sensitivity to alcohol that predicts the development of alcoholism. (Schuckit et al., 2001) Carriers of an allele of aldehyde dehydrogenase that encodes an isoenzyme with reduced activity are less likely to abuse alcohol owing to the presence of increased levels of acetaldehyde, which is responsible for aversive effects. (Nestler, 2000). A Leu7Pro polymorphism of the neuropeptide Y gene has been correlated with increased alcohol consumption. (Lappalainen et al., 2002) and single-nucleotide polymorphisms of the gene encoding the μ opioid receptor correlates with an increased likelihood of heroin abuse. (Kreek, 2001) A deficiency in the cytochrome P-450 2D6 gene blocks the enzymatic conversion of codeine to morphine, thereby preventing codeine abuse. (Kathiramalainathan et al., 2000)
1.2.3 The sequence of drug abuse

Drug abuse is a relapsing and remitting condition often involving numerous treatment episodes over several years (Marsden et al, 2004) While the initiation of drug use does not lead inevitably to dependence over the long term, a number of factors can potentiate this developmental course. Earlier initiation of drug use increases the likelihood of daily use, which in turn results in a greater likelihood of dependence (Kandel et al, 1986)

Among people who misuse opioids, who form the predominant in-treatment population, most individuals develop dependence in their late teens or early twenties, several years after first using heroin, and continue using over the next 10–30 years. In a long-term outcome study up to 33 years of 581 male opioid users in the US, 30% had positive or refused urine tests for opioids, 14% were in prison and 49% were dead (Hser et al, 2001). Longitudinal data from the US also showed that the average time from first to last opioid use was 9.9 years, with 40% dependent for over 12 years (Joe et al, 1990). Although it is the case that problem drug users can cease drug use without any formal treatment, particularly for individuals with primary cocaine or cannabis misuse, for many it is treatment that alters the course of opioid dependence.
Most initiation of cocaine use occurs around the age of 20, with the risk of cocaine dependence occurring early and explosively after first use, and persisting for an average of 10 years (Anthony et al, 1994)).

Cannabis use typically begins in early adolescence with heaviest use in the 15–24 age group (Harkin et al, 1997) which may in part be explained by strong peer influences (Frischer et al, 2005). Most use tends to decline steadily from the mid-20s to the early 30s (Bachman et al, 1997). Cannabis dependence persisting through adulthood is the most prevalent among those with sustained frequent use, as high as 40% among those who have used almost daily (Kandel and Davies, 1992).

Although drug abuse can affect all socioeconomic groups, deprivation and social exclusion are likely to make a significant contribution to the maintenance of drug abuse (Advisory Council on the Misuse of Drugs (ACMD), 1998). That said, an association has been found between income in adolescence and early adulthood and cannabis use (Makkai and McAllister, 1997), which may reflect the recreational nature of the majority of cannabis use.

Factors that influence the cessation of drug use in adulthood are similar to those associated with lack of drug use in adolescence. For example, transitions into social roles with greater conventionality, responsibility and contexts that are not favorable to using drugs such as employment, marriage and pregnancy; for
example, and good health are not associated with long-term use. Peer pressure is a major influence on experimental use and is also likely to affect a move towards regular use. The level of drug use is again a clear predictor of continued use. Once an individual is dependent, drug use is generally a chronic condition, interspersed with periods of relapse and remission (Marsden et al, 2004). Repeated interaction with the criminal justice system, long-term unemployment and increasing social isolation serve to further entrench drug use.

1.2.4 The public health impact of drug abuse
The harms associated with illicit drugs use include increased mortality from overdose and from other directly or indirectly associated harms such as increased risk of infection with blood-borne viruses HIV, hepatitis B and hepatitis C; high levels of depression and anxiety disorders; social problems such as disrupted parenting, employment and accommodation; and increased participation in income-generating crime.

In England and Wales, there were 1,382 drug-related deaths in 2005 (National Programme on Substance Abuse Deaths, 2005). The majority (59%) were cases of accidental poisoning, although a sizeable proportion (16%) was a result of intentional self-poisoning. Opioids alone or in combination with other drugs accounted for some 70% of the deaths, and cocaine 13%. Many of the deaths appear to be due to multiple drug toxicity, especially the presence of central
nervous system depressants for example, alcohol and benzodiazepines, rather than simply an overdose of an opioid. This is supported by research that shows those whose deaths were attributed to overdose have opioid levels no higher than those who survive, or than heroin users who die from other causes (Darke & Zador, 1996). Recent cohort studies have shown that mortality rates from methadone-related death are decreasing (Brugalet al., 2005).

Psychiatric comorbidity is common in drug abuse populations, with anxiety and depression generally common, and antisocial and other personality disorders in opioid-using populations (Regier et al., 1990, 1998). The national US Epidemiological Catchment Area study of the prevalence of mental health disorders reported a 47% lifetime prevalence rate of substance abuse drugs and alcohol among people with schizophrenia compared with 16% in the general population, and found that more than 60% of people with a diagnosis of bipolar I disorder had a lifetime diagnosis of substance misuse disorder. Drug misuse disorders complicated by other comorbid mental disorders have been recognized as having a poorer prognosis and being more difficult to treat than those without comorbid disorders; comorbid disorders are more likely to be chronic and disabling, and result in greater service utilization. Lost productivity and unemployment increase with the severity and duration of drug misuse, and personal relationships are placed under considerable strain by
dependent drug use. Problems with accommodation are also common in such groups. For example, prior to intake in the NTORS, 7% of the study group were homeless and living on the street, 5% were living in squats and 8% were living in temporary hostel accommodation (Gossop et al., 2000).

Drug abuse may also have a negative impact on children and families (ACMD, 2003).

1.2.5 The aims of treatment of drug abuse

The clinical management of drug abuse may be categorized into three broad approaches: harm reduction, maintenance-oriented treatments and abstinence-oriented treatments. All treatments aim to prevent or reduce the harms resulting from use of drugs. Care planning and key working should form a core part of subsequent treatment and care.

1.2.5.1 Harm reduction

Aims to prevent or reduce negative health or other consequences associated with drug abuse, whether to the drug-using individual or, more widely, to society. With such approaches, it is not essential for there to be a reduction in the drug use itself although, of course, this may be one of the methods of reducing harm. For instance, needle and syringe exchange services aim to reduce transmission of blood-borne viruses through the promotion of safer drug injecting behavior.
1.2.5.2 Maintenance

In the WHO context primarily refer to the pharmacological maintenance of people who are opioid dependent, through the prescription of opioid substitutes (methadone or buprenorphine). This therapy aims to reduce or end their illicit drug use and the consequential harms.

1.2.5.3 Abstinence

Aim to reduce an individual’s level of drug use, with the ultimate goal of abstinence. The NTORS found that approximately one third of those entering treatment services were abstinent 5 years later (Gossop et al., 2003). However, these treatments may be associated with an increased risk of death from overdose in the event of relapse after a period of abstinence, during which time drug tolerance is lost (Verger et al., 2003).

The clinical management of drug abuse may be categorized into three broad approaches: harm reduction, maintenance-oriented treatments and abstinence-oriented treatments. All treatments aim to prevent or reduce the harms resulting from use of drugs. Care planning and key working should form a core part of subsequent treatment and care.

1.2.5.4 Care planning

Should consider the following when any treatment or management plan is developed:
The general principles of treatment are that no single treatment is appropriate for all individuals, treatments should be readily available and begin when the service user presents, and there should be the capacity to address multiple needs. It is also accepted that treatments will change over time.

For most people in long-term treatment, that is those with opioid dependence, substitute medications, such as methadone and buprenorphine, are important elements of care. However, services also need to address coexisting problems, such as mental health and physical health problems, alongside the drug misuse.

1.2.5.5 Continous practice

The most common types of psychosocial interventions programmed specifically targeting drug-use behaviors might be based on one of a number of models, including cognitive-behavioral for example, motivational interviewing and relapse prevention, humanistic and 12-step approaches (Wanigaratne et al. 2005). Often
this is unfocused, and therapist and client may not have a clear understanding of the therapeutic goals or therapeutic method. In addition, there exist formal psychological therapies delivered within adult mental health settings, aiming to address drug users coexisting mental health problems (NTA, 2006). Brief interventions, typically empathic in nature and lasting up to two sessions, have a variety of potential advantages in the treatment of drug misuse, including ease of delivery and retention of drug users. These interventions can be conducted in a variety of settings, opportunistically to people not in formal drug treatment and as an adjunct to formal, structured drug treatment (Ashton, 2005). Although brief interventions are considered to be an important component of psychosocial treatment in open-access drug services (NTA, 2004, NTA, 2006).

1.2.6 Drug Abuse and the Family

In the literature, drug abuse is seen as both a problem of the family and a problem for the family† (Bancroft et al., 2002). The evidence that points to traumatic family experiences, such as childhood neglect, homelessness, abuse, loss and bereavement, increasing the likelihood that a person will go on to have drug problems (Kumpfer & Bluth, 2004) can be seen as a problem of the family. As 60–80% of people who abuse drugs live or are in regular contact with their family (Stanton & Heath, 2005), and approximately 2–3% of all children under the age of 16 years have parents with a drug problem (ACMD, 2003), drug abuse can
also be said to be a problem for the family. The impact may be psychological for example, depression and anxiety, physical raised blood pressure and ulcers (Velleman et al., 1993), social feelings of isolation and work, family and social difficulties (Hudson et al., 2002) and financial.

Appropriate involvement of family members and careers in the assessment and treatment process may also support the family member/career and facilitate a more successful outcome for the user. There is evidence that families including parents, children and siblings have a role to play in effective treatments.

1.2.7 The Pharmacological Effects of Drug Abuse

1.2.7.1 Opioids

Opioids have many effects on the brain, mediated through specific receptors (µ, κ, or δ). The key opioid receptor subtype is µ, which mediates ‘euphoria’, as well as respiratory depression, and is the main target for opioids (Lingford-Hughes & Nutt, 2003), while the κ receptor is involved in mood regulation. Drugs such as heroin and methadone are agonists, which stimulate the receptor. Buprenorphine is a partial agonist; that is, it occupies the receptor in the same way but only partially activates it. In addition, it is an antagonist at the κ receptor and therefore is less likely to lower mood compared with µ agonists.

Soon after injection or inhalation, heroin metabolizes into morphine and binds to opioid receptors. This is subjectively experienced as a euphoric rush, normally
accompanied by a warm flush, dry mouth, and sometimes nausea, vomiting and severe itching. As the rush wears off, drowsiness, and slowing of cardiac function and breathing (sometimes to the point of death in an overdose), persist for several hours (National Institute on Drug Abuse [NIDA], 2005). The effects of methadone are similar but more drawn out and therefore less intense lasting up to 24 hours when taken orally as prescribed; however, this may be circumvented by illicit users who inject the drug.

The most obvious consequence of long-term opioid use is the development of opioid dependence itself, and the associated harms. Repeated injection will also have medical consequences, such as scarring, infection of blood vessels, abscesses, and compromised functioning of the kidney, liver and lungs (with increased vulnerability to infections).

1.2.7.2 Stimulants

As central nervous system stimulants, cocaine and amphetamine affect a number of neurotransmitter systems in the brain but exert their effects primarily via dopamine, which mediates reward. Cocaine blocks the presynaptic reuptake of dopamine, such that it is not removed from the intracellular space and leads to extended firing of postsynaptic neurons, resulting in physiological arousal. Amphetamines also increase the availability of dopamine but are thought to do so by triggering a presynaptic leakage.
The acute subjective effects of cocaine are euphoria, increased energy, heightened alertness, sexual arousal, increased sociability and talkativeness. Physiologically there can be acute adverse effects on breathing, and the cardiovascular and central nervous systems: increased heart rate, blood pressure and body temperature, and pupil dilation. All these effects have near-immediate onset but also diminish quickly (after roughly 15–30 minutes if the drug is snorted and 5–10 minutes if smoked), as cocaine is metabolized rapidly by the body (NIDA, 2004). As acute effects wear off, users experience a rebound period crash, which may include restlessness, anxiety, agitation and insomnia. This can lead to the user bingeing on cocaine in an attempt to displace these negative effects. Chronic misuse of cocaine may lead to increased paranoia, inability to concentrate, sexual dysfunction and cognitive deficits.

For amphetamines, the acute effects are broadly similar except that they are long lasting (normally 4–8 hours), due to slower metabolism. Overdoses may lead to dangerously elevated body temperature, convulsions or even death. Chronic misuse may cause long-term damage to the brain’s ability to manufacture dopamine, possibly resulting in amphetamine psychosis.

1.2.7.3 Cannabis

Cannabis affects almost every body system, via cannabinoid receptors in the brain, which regulate a range of cognitive and motor functions (NIDA, 2005b). Within
minutes of smoking cannabis, the heart rate increases and the bronchial passages relax. Often the individual experiences intoxication, mild euphoria and increased sociability. However, anxiety or paranoia may sometimes occur, particularly among first-time or psychologically vulnerable users (Johns, 2001). Distorted perceptions are common, for example colors may appear more intense and time may seem to slow down. The euphoria reaches a plateau lasting 2 hours or more, depending on the dose, after which the individual may feel sleepy or depressed. Cannabis use also impairs memory, attention and motor coordination, with especially dangerous consequences on driving performance. Such effects may last for many hours after administration of the drug; the numerous metabolites of a single moderate dose of cannabis may require up to 4 weeks to be completely eliminated from the body (Maykut, 1985). The smoke from cannabis contains the same constituents as tobacco smoke; hence chronic cannabis smoking is associated with a range of respiratory tract disorders, including bronchitis, emphysema and cancers (Hashibeet al., 2005).
1.2.8 Anticholinergic

1.2.8.1 Introduction

Also referred to as muscarinic receptor antagonists and it includes

(1) the naturally occurring alkaloids, atropine and *scopolamine*.

(2) semisynthetic derivatives of these alkaloids, which primarily differ from the parent compounds in their disposition in the body or their duration of action.

(3) synthetic congeners, some of which show selectivity for particular subtypes of muscarinic receptors. Noteworthy agents among the synthetic derivatives are *homatropine* and *tropicamide*, which have a shorter duration of action than atropine, and *methylyatropine, ipratropium*, and *tiotropium*, which are quaternized and do not cross the blood-brain barrier or readily cross membranes. The latter two agents are given by inhalation in the treatment of chronic obstructive pulmonary disease and are pending approval for use in bronchial asthma. Ipratropium also has an FDA-approved indication for perennial- and common cold-associated rhinorrhea. The synthetic derivatives possessing partial receptor selectivity include pirenzepine, used in the treatment of acid-peptic disease in some countries, and *tolterodine, oxybutynin*, and several others, used in the treatment of urinary incontinence.
1.2.8.2 Chemistry

Atropine and scopolamine are esters formed by combination of an aromatic acid, tropic acid, and complex organic bases, either tropine (tropanol) or scopine. Scopine differs from tropine only in having an oxygen bridge between the carbon atoms designated as 6 and 7 (Figure 1). Homatropine is a semisynthetic compound produced by combining the base tropine with mandelic acid. The corresponding quaternary ammonium derivatives, modified by the addition of a second methyl group to the nitrogen, are methylatropline nitrate, methscopolamine bromide, and homatropinemethylbromide. Ipratropium and tiotropium also are quaternary tropine analogs esterified with synthetic aromatic acids.

![Figure 1: Structural formulas of the belladonna alkaloids and semisynthetic and synthetic analogs.](Goodman & Gilman's, 2006)
1.2.8.3 Mechanism of Action

Atropine and related compounds compete with ACh and other muscarinic agonists for a common binding site on the muscarinic receptor. Based on the position of retinol in the mammalian rhodopsin structure (Palczewski et al., 2000), the binding site for competitive antagonists and acetylcholine likely is in a cleft formed by several of the receptor's 7 transmembrane helices. An aspartic acid present in the N-terminal portion of the third transmembrane helix of all 5 muscarinic receptor subtypes is believed to form an ionic bond with the cationic quaternary nitrogen in acetylcholine and the tertiary or quaternary nitrogen of the antagonists (Wess, 1996; Caulfield and Birdsall, 1998). Since antagonism by atropine is competitive, it can be overcome if the concentration of ACh at receptor sites of the effector organ is increased sufficiently. Muscarinic receptor antagonists inhibit responses to postganglionic cholinergic nerve stimulation less readily than they inhibit responses to injected choline esters. The difference may be due to release of ACh by cholinergic nerve terminals so close to receptors that very high concentrations of the transmitter gain access to the receptors in the neuroeffector junction.

1.2.8.4 Adverse effects

Peripheral adverse effects of these agents include tachycardia, constipation (rarely leading to paralytic ileus), urinary retention, blurred vision and dry mouth.

Gingivitis and caries, rarely leading to loss of teeth, may occur (Lang and Blair, 1989) and reduced sweating may interfere with body temperature regulation. These effects are all reversible when diminishing or with discontinuation of the drug, and can even show some tolerance after prolonged exposure. Rarely, some of these side-effects can be beneficial at times, as is the case for dry
mouth, which can be advantageous in patients with prominent drooling. Caution must be exercised in elder male patients with comorbid prostate hypertrophy, due to a high risk for urinary retention. Blurred vision is a common side-effect, attributed to reduced accommodation due to parasympathetic blockade. Extremely rare is the occurrence of acute narrow-angle glaucoma, which can be precipitated in predisposed patients.

An impairment of higher cortical functions has been found in non-demented PD subjects with an acute subclinical dose of scopolamine and impaired neuropsychiatric function has been demonstrated even in patients without cognitive impairment. These central effects are more likely to occur with advanced age and in patients with dementia marked involvement of the cholinergic system (i.e. nucleus basalis of Meynert) in PD and in dementia with Lewy bodies pathology is probably the basis of the cognitive changes induced by anticholinergics. (Tiraboschi, et al., 2002)

1.2.8.5 Anticholinergic place in therapy

The anticholinergics currently in use are listed in Table 1. One of the first introduced synthetic drugs is a piperidine compound, trihexyphenidyl. It was initially developed as a gastrointestinal antispasmodic agent, shown in trials in the late 1940s to be as effective as belladonna alkaloids in the management of PD, with one-half of patients achieving an average of 20% improvement (
The most representative drugs of the antihistamines are diphenhydramine (Montuschi, 1949) and orphenadrine; orphenadrine is thought to be more potent because of its more potent anticholinergic activity. Another widely used anticholinergic drug is benztropine, a combination of the atropine molecule and the benzhydryl group of the diphenhydramine molecule. Developed in the 1950s, this drug is more potent than trihexyphenidyl and less sedative than antihistaminics.

**Table 1:**

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Daily dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trihexyphenidyl</td>
<td>1–20</td>
</tr>
<tr>
<td>Benztropine</td>
<td>0.5–6</td>
</tr>
<tr>
<td>Ethopropazine</td>
<td>100–800</td>
</tr>
<tr>
<td>Procyclidine</td>
<td>7.5–20</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>25–200</td>
</tr>
<tr>
<td>Bornaprine</td>
<td>8–8.25</td>
</tr>
</tbody>
</table>

**Anticholinergic drugs commonly used to treat tremor in Parkinson's disease.**

Despite a lack of definite data to confirm a special role in the management of tremor, anticholinergics are also recommended in patients in whom other therapies such as the agonists amantadine or levodopa have failed to control tremor sufficiently.

Development of tolerance to the effects of beneficial effects of anticholinergics is said to occur frequently. Such loss of therapeutic benefit is indeed a common
clinical observation after months of treatment, but should be attributed, at least in part, to disease progression. Withdrawal of anticholinergics, even in patients in whom it is thought that the drugs are no longer effective, invariably results in worsening of the parkinsonian symptoms, at times to a level worse than the patients' baseline state (Hughes, et al., 1971).

1.2.9 Benzhexol

1.2.9.1 Introduction

Benzhexol, also known as trihexyphenidyl, hydrochloride is a tertiary amine antimuscarinic drug with actions similar to atropine. It also has direct antispasmodic action on smooth muscle. Despite having been shown to adversely affect memory (Miller et al. 1987), benzhexol is currently used in the clinical management of tremor-related conditions such as Parkinson’s disease (Parkes et al., 1974). Other antimuscarinics used in parkinsonism include orphenadrine, benztropine, and procyclidine. Benzhexol hydrochloride was the first of a range of synthetic antispasmodic drugs to be made available for the symptomatic treatment of Parkinsonism. Selected as the most potent of a series of substituted piperidylropanolsexammed pharmacologically by Cunningham et al. (1949), it was shown to have half the activity of atropine sulphate in inhibiting neurogenic spasm in isolated rabbit intestine. This activity was associated with advantageously reduced
mydriatic, anti-sialogogic and vagal inhibitory properties in laboratory animals. Following its introduction in 1949, Artane has become established as a safe and effective advance in treatment (Doshay, Constable and Zier, 1954; Critchley, 1958; Miller, 1960) and has been used as a comparative standard for new antispasmodic preparations (Onuaguluchi,1963).

The reversible and minor side-effects so far described include dryness of the mouth, thirst, blurred vision, drowsiness, tinnitus, and occasionally nausea and vomiting. Critchley (1958) has drawn attention to vague cephalic sensations which patients attempt to pinpoint with terms such as dizziness, muzziness or light-headedness.

1.2.9.2 Pharmacokinetic

Benzhexol hydrochloride is well-absorbed from the gastrointestinal tract, exerting an effect within 1 hour following oral administration. Peak effects last for 2 to 3 hours, the duration of action being between 6 to 12 hours (Drug Information for the Health Care Professional (USPDI), 1992). It is excreted in the urine, probably as isomeric hydroxylated metabolites, by first-order kinetics.

1.2.9.3 Targets-Pharmacodynamics

In idiopathic Parkinson's disease, progressive degeneration of pigment-containing cells of the substantia nigra leads to deficiency of the neurotransmitter dopamine. As a consequence, there is a neurohumoral imbalance in the basal ganglia, leading
to the characteristic signs and symptoms of the disease. Like other anti-muscarinic drugs, benzhexol hydrochloride partially blocks central cholinergic receptors, thereby helping to balance cholinergic and dopaminergic activity in the basal ganglia.

1.2.9.4 Therapeutic Uses

Several studies have demonstrated that Benzhexol (10 to 45 milligrams/day) is effective in treating various dystonias, particularly if given early in the course of the disease (significant response may take months to develop) (Jabbari et al, 1989). Younger patients tend to respond better because they tolerate higher doses. Only a minority of patients with Cranial Dystonia respond to anticholinergics, but those who do respond may improve dramatically (Nutt et al, 1984).

High-dose Benzhexol (24 to 41 milligrams (mg) daily) has been effective in treating Torsion Dystonia of various etiologies (Burke et al, 1986).

Approximately 40% of patients with dystonia have demonstrated significant response to Benzhexol(10 to 45 mg/day). Patients with tonic Torticollis responded significantly better than patients with the clonic type (Jabbari et al, 1989).

Benzhexol 5 milligrams 3 times daily improved Vertical Pendular Nystagmus in a 34-year-old woman with massive Brainstem Hemorrhage secondary to eclampsia.
Therapy was continued for approximately 10 months without loss of efficacy (Herishanu and Louzoun, 1986).

The use of Benzhexol to treat various forms of nystagmus appears to be controversial. Benzhexol may only be practical for selected patients (Herishanu & Louzoun, 1986). In 4 or 5 patients, Benzhexol 20 to 40 milligrams/day was effective in treating Acquired Pendular Nystagmus, with marked relief from Oscillopsia (Jabbari et al., 1987).

Benzhexol in doses of up to 30 milligrams daily has been used in the treatment of Parkinson's disease either alone or in combination with other anti-Parkinson agents such as Amantadine or Levodopa (Martin et al., 1974). A number of studies have indicated that Benzhexol can improve symptoms of rigidity, sialorrhea, akinesia, and tremor (Lamid and Jenkins, 1975).

In combination with Levodopa, Benzhexol has improved overall ratings and scores for speech, facial abnormalities, tremor and rigidity compared with placebo alone (Martin et al., 1974).

Benzhexol 2 milligrams 4 times daily was similar in efficacy to combination Levodopa and Carbidopa in reducing parkinsonian tremor more than 50% in a double-blind study involving 9 patients (Koller, 1986). Some patients responded to one drug but not the other.
Benzhexol 6 to 40 milligrams (mg) daily has improved symptoms associated with phenothiazine-induced parkinsonism/extapyramidal reactions in some patients. Symptoms may return within 1 to 7 days of Benzhexol discontinuation. However, lower doses of Benzhexol have provided no significant benefit to clinical outcome and side effects of phenothiazine-induced extrapyramidal symptoms. (Martin, 1974)

1.2.9.5 Adverse effects

1.2.9.5.1 Bradyarrhythmia

Bradycardia occurred in a 36-year-old male psychiatric patient with normal cardiac function during trihexyphenidyl therapy, which recurred upon rechallenge. Other anticholinergic agents (orphenadrine, atropine) did not produce a bradycardic response. The mechanism of action of this effect is unclear (Blumensohn et al, 1986).

1.2.9.5.2 Dermatologic

Skin rash has been rarely reported with the use of trihexyphenidyl (Prod Info trihexyphenidyl hydrochloride oral tablets, 2006; Prod Info trihexyphenidylhcl oral elixir, 2002).
1.2.9.5.3 Gastrointestinal

Dryness of the mouth and mild nausea can occur in 30% to 50% of trihexyphenidyl treated patients. Parotitis, dilatation of the colon, and paralytic ileus have been reported rarely. Patients with a history of idiosyncratic drug reactions, or with arteriosclerosis, may experience nausea and vomiting possibly with mental confusion, agitation, or disturbed behavior (Prod Info trihexyphenidyl hydrochloride oral tablets, 2006).

1.2.9.5.4 Neurogical

Dizziness and nervousness are the most common (30% to 50%) neurologic adverse effects reported; however, all antiparkinsonian drugs, when taken in excess, can cause hallucinations, confusion, disorientation and aggressive behavior. Delusions and hallucinations have been rarely reported with trihexyphenidyl treatment. Patients with a history of idiosyncratic drug reactions, or with arteriosclerosis, may experience mental confusion, agitation, disturbed behavior or nausea and vomiting. Excessive use, eg, to sustain euphoria, may lead to psychiatric disturbances (Prod Info trihexyphenidyl hydrochloride oral tablets, 2006).

1.2.9.5.5 Ophthalmic

Blurred vision is a common (30% to 50%) finding with trihexyphenidyl use. Angle-closure glaucoma has been reported with long-term treatment and increased
intraocular pressure or dilated pupils are possible effects of any atropine-like drug (Prod Info trihexyphenidyl hydrochloride oral tablets, 2006).

1.2.9.5.6 Psychiatric

Nervousness is a commonly reported psychiatric adverse event and may occur in 30% to 50% of trihexyphenidyl-treated patients. Hallucinations have been rarely reported with the use of trihexyphenidyl. Patients with a history of idiosyncratic drug reactions, or with arteriosclerosis, may experience mental confusion, agitation or disturbed behavior (Prod Info trihexyphenidyl hydrochloride oral tablets, 2006).

1.2.9.5.7 Renal

Urinary hesitancy and urinary retention is a potential adverse effect of any atropine-like drug (Prod Info trihexyphenidyl hydrochloride oral tablets, 2006).

1.2.9.5.8 Drug dependence

Psychological and physical dependence has been reported with trihexyphenidyl (McInnis & Petursson, 1984). In 1 of 2 cases presented, withdrawal symptoms were observed, including tachycardia, restlessness, diaphoresis, irritability and headaches.

It has been reported that trihexyphenidyl may be deliberately abused for its stimulating and euphoriant effects. Trihexyphenidyl has also been reported to
induce vivid visual hallucinations, confusion and delusions. The precise psychopharmacological mechanisms for the euphoria and hallucinations is unclear. It is possible that the drug produces a form of anticholinergic delirium. Euphoric effects may be mediated via catecholamines (Mohan et al, 1981).

Investigators reported that trihexyphenidyl abusers were significantly more likely than non-abusers to be unemployed, unmarried and smokers with histories positive for familial drug abuse and mental illness. The incidences of extrapyramidal symptoms and tardive dyskinesia did not differ between groups. The sample included a total of 120 psychiatric patients (30 abusers and 90 non-abusers), primarily male schizophrenics (Qureshi et al, 1997).

All antiparkinsonian drugs, when taken in excess, can cause hallucinations, confusion, disorientation and aggressive behavior (Klawans et al, 1972). The incidence of psychiatric disturbance due to antiparkinsonian drugs appears common enough to suspect it in patients on antiparkinsonian drug therapy who present with mental confusion and other acute psychiatric symptoms. Deliberate self-overmedication in such patients may occur in response to a natural progression of the parkinsonism.

**1.2.9.5.8 Withdrawal sign or symptom**

A recognizable, although subtle, withdrawal syndrome may follow discontinuation of long-term trihexyphenidyl. Trihexyphenidyl can produce a withdrawal
syndrome characterized by anxiety, tachycardia, orthostatic hypotension and apparent deterioration of sleep quality. Extrapyramidal side effects have been noted, as well as a temporary deterioration in psychotic symptomatology. The majority of parameters returned to baseline values indicating the symptoms were related to the discontinuation of trihexyphenidyl and supporting the existence of a withdrawal syndrome (McInnis and Petursson, 1984).

Following abrupt withdrawal of trihexyphenidyl after receiving 6 mg daily for one year, a 61-year-old woman developed encephalopathy with miosis, characterized by loss of consciousness and subsequent coma, nonreactive pupils, and electroencephalograph (EEG) abnormalities; neuroleptic malignant syndrome was ruled out. Trihexyphenidyl 12 mg/day was administered via nasogastric tube, and within several days the patient normalized. Upon dechallenge, symptoms reappeared but were less severe, and were unresponsive to levodopa/carbidopa 300/30 mg given daily for 4 days. Trihexyphenidyl was restarted at 6 mg/day, after which the patient completely recovered. The authors recommend tapering the dosage of trihexyphenidyl over an 8-week period to prevent such a disturbance in consciousness (Johkura et al., 1997).

A 64-year-old woman with cranial dystonia suffered an acute severe exacerbation of her condition when her dose of trihexyphenidyl (6 mg/day) was abruptly withdrawn. Aside from an intensification of all of her previous abnormal
movements the withdrawal was associated with life-threatening respiratory difficulties (Gimenez-Roldan et al, 1989).

1.2.9.6 Abuse of Trihexyphenidyl hydrochloride

Antiparkinsonism drugs can cause CNS side effects, ranging from some rather mild symptoms to a full-blown toxic delirium. (Shader and Greenblatt, 1971.) Mild side effects include dilated pupils, dry skin, constipation, tachycardia, dryness of the mouth, and ataxia. The toxic psychosis is characterized by hallucinations, paranoid ideation, disorientation in time, and, in some cases, euphoria. Deliberate abuse of these drugs has been reported with some frequency. (Stephens, 1967.)

The following case appears to be unique in the literature. It describes a patient who deliberately feigned extrapyramidal symptoms to obtain prescriptions for antiparkinsonism drugs.

1.2.9.6.1 Report of a Case

A 27-year-old woman was brought to the psychiatric emergency room by friends who complained of her increasingly "spaced-out" and bizarre behavior. She had a long history of hospitalizations and was receiving, according to friends, maintenance therapy with thiothixene (40 mg at bedtime) and trihexyphenidyl hydrochloride (5 mg twice a day). She was a disheveled, agitated young woman who gave short, concise responses to questions. During the interview, the patient repeatedly asked the physician for "10 mg of Artane" for her "nerves."
Failing to receive the drug, she retreated to a corner of the room, returned a few moments later, gestured to her mouth, and indicated a rigidity of the fingers and arm. At this point she began to speak in a slurred manner, repeating the words "Artane, Artane." The emergency room physician withheld medication.

On admission to the ward, the patient repeated her request for trihexyphenidyl, motioning with stiff fingers to a tightly closed jaw and indicating a difficulty in speaking. The on-duty physician, unaware of the patient's behavior in the emergency room, ordered 2 mg of benztropinemesylate. Almost immediately, her physical symptoms disappeared. She spoke distinctly, voicing a preference for trihexyphenidyl. The next day, her "extrapyramidal" symptoms again appeared. Her physician, alerted to the possibility of drug abuse, ordered normal saline solution to be administered intramuscularly. The patient was assured that this was a more effective way of administering trihexyphenidyl. Immediately after receiving the injection, her fists and jaws relaxed, and she stated that she felt much better. About 20 minutes later, the patient complained to her physician that the injection was "not working after all." Shortly after establishing a rapport with her psychiatrist, the patient admitted to having abused trihexyphenidyl for years, obtaining several prescriptions concurrently from a number of physicians.

She described having "faked" symptoms of muscle stiffness, these tactics having been successful in the past. Moreover, the patient reported that these methods of
obtaining antiparkinsonism drugs were well known and commonly employed by a number of abusers known to her.

The patient had been taking 15 mg of trihexyphenidyl hydrochloride once or twice daily in the period before admission. She described the effect as a "high," inducing an animated and pleasantly hallucinogenic state. In addition, the patient admitted to often having avoided taking her thiothixene, as it seemed to interfere with the pleasurable effects of the trihexyphenidyl.

In subsequent interviews the patient completely denied this history, maintaining that the trihexyphenidyl was used only to "relax" her. For the remainder of her hospitalization, she continued to repeat her requests for the drug at frequent intervals.
Chapter Two

Methodology
2.1 Methodology
This chapter describes the methodology that was used in this research. The adopted methodology to accomplish this study uses the following techniques: the information about the research design, research population, questionnaire design, statistical data analysis, content validity, place of the study, illegibility criteria, ethical considerations, and pilot study.

2.1.1 Study Design
The design of this study is descriptive, analytical, cross-sectional study as it assesses the Knowledge, attitude, practice, and presence of side effects of trihexyphenidyl abusers. Descriptive study was chosen because it is not truly experimental.

Cross-sectional study was chosen because it is appropriate for describing the status of phenomena or for describing relationships among phenomena at fixed point in time. The first phase of the research thesis proposal included identifying and defining the problems and establishment objective of the study and development research plan. The second phase of the research included a summary of the comprehensive literature review.

The third phase of the research included a field survey. The fourth phase of the research focused on distributing questionnaire. This questionnaire was used to collect the required data in order to achieve the research objective.

The fifth phase of the research was data analysis and discussion. (SPSS) was used to perform the required analysis. The final phase includes the conclusions and recommendations.

Three hundred and twenty questionnaires were distributed to the research population and three hundred questionnaires are received.

Research methodology
2.1.2 Data Collection Methodology
In order to collect the needed data for this research, we use the secondary resources in collecting data such as books, journals, statistics, and web pages, in addition to preliminary resources that are not available in secondary resources through distributing questionnaires on study population in order to get their opinions about the research.

Research methodology depend on the analysis of data on the use of descriptive analysis, which depends on the poll and use the main program (SPSS).
2.1.3 Study Population
The study population of this study was the university students, six colleges was selected, three medical and three non medical colleges to take the study sample.

2.1.4 Sample size and sampling procedure
The sample size of the present study was calculated by the number of student in the six colleges, and questionnaires were distributed to the convenient sample and 300 questionnaires received.

2.1.5 Place of study:
This study was carried out in one University in Khartoum city in Khartoum state with sample size relatively compatible, as much as possible, with the population size of each colleges.

2.1.6 Period of study:
The study started when the researcher have approval from committee and expected to be completed by March 2016.

2.1.7 Eligibility criteria:
2.1.7.1 Inclusion criteria:
All males and females student in the six colleges in Ribatuniversity, and age from 18-35 years old.

2.1.7.2 Exclusion criteria:
Any students under or above age of 18-35.

2.1.8 Ethical consideration:
Approval from each person who will participate in the study by questionnaire.

2.2 Questionnaire content
The questionnaire included multiple choice question: which used widely in the questionnaire, The variety in these questions aims first to meet the research objectives, and to collect all the necessary data that can support the discussion, results and recommendations in the research.
The sections in the questionnaires will verify the objectives in this research related to measure the "Assessment of Trihexyphenidyl (kharsha) knowledge and abuse among students of one Khartoum state Universities by examine the level of knowledge, attitude, and practice."

2.3 Statistical Manipulation
To achieve the research goal, the statistical package for the Social Science (SPSS) was used for Manipulating and analyzing the data.
Chapter Three
Result

3.1 Personal information of the study population:
In this study 300 were included with Personal information described in the following figures.

3.1.1-Age Distribution
The data collected showed that 86.0%, 13.0% and 1.0% of the study sample (n = 300) were aged between 18 to 23, 24 to 29 and 30 to 35 years respectively (Figure No. 2)

![Age distribution chart]

Figure -(2) Age distribution.

3.1.2-Gender Distribution:
Figure No.(3) showed that 53.0% from the samples are female, and 47.0% from the samples are males.
Figure No.(3) **Gender Distribution**

**3.1.3- Residences:**
The study showed that 55.0%, 21.0%, 18.0% and 6.0% from the samples (n= 300) lived in Khartoum, Omdurman, Bahri and other cities in Sudan respectively as illustrated in Figure No.(4)

Figure No.(4) **Residences**
3.1.4- Marital Status
Figure No.(5) shows that among population studied, 94.0% were single while 6.0% of them were married.

3.1.5- Living in the family house

As showed in the figure (6), 82.0% of the study sample were lived with their families while 18.0% from the sample were stayed in a hostels.
3.1.6- Jobs

The majority of the sample interviewed was jobless (95 %) versus only 5 % of the sample have jobs. Figure No.(7)

3.1.7- Monthly Income

According to the findings of the study the monthly income of 44.0%, 23.0%, 19.0% and 14.0% of the sample studied found to be less than 5000 SDG, from 5000 to 10000 SDG, from 10000 to 20000 SDG and more than 20000 SDG respectively(Figure No8)
3.1.8- Type of study

Figure No.(9) shows that 50.0% of the samples are study in a medical colleges, and 50.0% of the samples are study in non medical colleges.
3.1.9- Classes Distribution:

Figure No.(10) shows that 30.0% of the sample are in the first year, and 13.0% of the samples are in the second year, and 18.0% of the samples are in the third year, and 12.0% are in the fourth year, and 27.0% of the samples are in the fifth year.

Figure No.(10) Classes Distribution
3.2 Medications

3.2.1- Chronic Medications

The study found that 92.0% of the sample were not chronic users of any medications, and 8.0% of them were regularly took medications for different causes as showed in Figure No.(11)

Figure No.(11) Chronic Medications

3.2.2- Analgesic use

Figure No.(12) showed that 8.0% of the samples are using analgesic, and 18.0% of the samples are not using analgesic, and 74.0% of the samples are using analgesic some times.
Figure No. (12) Analgesic use

3.3 Kharsha knowledge

3.3.1- Akisol Or Kharsha knowledge

Regarding the knowledge of the respondents surveyed about Akisol or Kharsha, the study revealed that 83% of the sample don’t knew about Akisol, and 17% of them knew Akisol. Figure No.(13)
3.3.2 Akisol or Kharsha addiction knowledge:

As shown in figure (14), 83.0% of the study population don’t know that akisol abuse lead to addiction, and 17.0% agreed that akisol abuse lead to addiction.

Figure No.(14) Akisol or Kharsha addiction knowledge

3.3.3 Akisol abuse side effects knowledge

From figure (15) we conclude that 88.0% of the study population, do not know the side effects of the akisol abuse, and only 1.0% of the study population not agree about Akisol side effects, and 11.0% know that Akisol abuse can cause series side effects.

Figure No.(15) Akisol abuse side effects knowledge
3.3.4 Akisol dose and dosage form knowledge

Figure No.(16) shows that 5.0% of the sample strongly agree that they know akisol dose and dosage form, and shows that 7.0% of the sample agree with the knowledge of akisol dose and dosage form, and 74.0% of the sample don't know about the knowledge of akisol dose and dosage form, and 10.0% of the sample don't agree with the knowledge of akisol dose and dosage form, and the figure also shows that 4.0% of the sample strongly don't agree with the knowledge of akisol dose and dosage form.

3.3.5 Akisol or kharsha prevalence

Among the respondents surveyed, the study found that 5.0% from them used Akisol and 95% of them didn’t use it at all. Figure No. (17)
Figure No.(17) Akisol or kharsha prevalence

3.4 Knowledge of Akisol abusers

3.4.1 continue using Akisol

Figure No.(18) shows that 51.0% of akisol abusers from the sample are strongly agreed that they still using akisol, and 15.0% of akisol abuser from the sample don't know if they are still using or not, and 36.0% of akisol abusers from the samples are stop using Akisol.

Figure No.(18) continue using Akisol
3.4.2 Negative effects of using akisol

Figure No.(19 ) shows that 28.0% of the sample strongly agree that the akisol abuse has a negative effects on their life, and shows that 15.0% of the sample agree that the akisol abuse has a negative effects on their life, and it shows that 7.0% of the sample do not know if the akisol abuse has a negative effects on their life, and shows that 50.0% from the sample strongly not agree that the akisol abuse has a negative effects on their life.

![Pie chart showing the distribution of responses to negative effects of using akisol.]

3.4.3 Positive effects of using akisol

Figure No.(20) tells that 15.0% of the sample strongly agree that the use of akisol have positive effects in their life, and 21.0% from the sample do not know if the use of akisol has positive effects in their life, and 43.0% from the sample not agree that the use of akisol have positive effects in their life, and 21.0% from the sample strongly not agree that the use of akisol have positive effects in their life.
Figure No.(20) **Positive effects of using akisol**

### 3.4.4 Source of akisol

#### 3.4.4.1 Pharmacy

Figure (21) shows that 57.0% of akisol abusers strongly agreed that they can get Akisol from pharmacies, 28.0% of them agreed, and 15.0% of the abusers don’t know.

Figure (21) **Source of akisol (Pharmacy)**
3.4.4.2 Drugs dealer

Figure (22) shows that 28.0% of Akisol abusers strongly agreed that they can get Akisol from dealers, and 36.0% of them agreed, and 6.0% of the abusers don’t know, and 30.0% of the in equal amount of 15.0% are not agreed and strongly not agreed.

Figure (22) Source of akisol (Drugs dealer)

3.4.4.3 Friends

Figure (23) shows that 15.0% of akisol abusers strongly agreed that they can get Akisol from friends, and 6.0% of the abusers don’t know, and 15.0% from the abuser not agreed, and 64.0% strongly not agreed that they can get Akisol from friends.

Figure (23) Source of akisol (Friends)
3.4.5 Akisol inducing euphoria

Figure No.(24) shows that 98.0% of the kharsha users strongly agreed that Akisol induce euphoria, and only 1.0% strongly not agreed that kharsha induce euphoria.

Figure No.(24) Akisol inducing euphoria

3.4.6 Akisol mixed with other medicines

Figure No.(25) shows that 6.0% of akisol abusers from the sample strongly agree with taking akisol mixed with other drugs, , and 7.0% of akisol abusers from the sample do not know if they can take akisol mixed with other drugs, and 22.0% of akisol abusers from the sample not agree with taking akisol mixed with other drugs, and 65.0% of akisol abusers from the sample strongly not agree with taking akisol mixed with other drugs.

Figure No.(25) Akisol mixed with other medicines
3.4.7 Abusing another drugs

Figure No.(26) tells that 43.0% of akisol abusers from the sample strongly agree that they are abusing other drugs, and 6.0% of akisol abusers from the sample agree that they are abusing other drugs, and 21.0% of akisol abusers from the sample do not know if they are abusing other drugs, 15.0% of akisol abusers from the sample not agree that they are abusing other drugs, 15.0% of akisol abusers from the sample strongly not agree that they are abusing other drugs.

3.4.8 Alcohol consumptions

Figure No.(27) shows that 6.0% of akisol abusers from the sample strongly agree that they are consuming alcohol, and 28.0% of akisol abusers from the sample do not know if he is consuming alcohol, and 7.0% of akisol abusers from the sample not agree that he is consuming alcohol, and 59.0% of akisol abusers from the sample strongly not agree that they are consuming alcohol.
3.4.9 Criminal behavior

Figure No.(28) shows that 2.0% from the sample are strongly agree that they are able to commit a crime for the sake of akisol, and 2.0% from the sample are agree that they are able to commit a crime for the sake of akisol, and, 2.0% from the sample don't know if they are able to commit a crime for the sake of akisol, and 3.0% from the sample are not agree that they are able to commit a crime for the sake of akisol, and 91.0% from the sample are strongly not agree that they are able to commit a crime for the sake of akisol.
3.4.10 Stigma from akisol abuse

Figure No.(29) shows that 2.0% from the sample strongly agree that they are feeling shame from akisol abuse, and 6.0% from the sample agree that they are feeling shame from akisol abuse, and 2.0% from the sample do not know if they are feeling shame from akisol abuse or not, and 1.0% from the sample not agree that he is feeling shame from akisol abuse, and 89.0% from the sample strongly not agree that they are feeling shame from akisol abuse.

Figure No.(29) Stigma from akisol abuse

3.4.11 Family and society contribution

Figure No.(30) tells that 22.0% from the sample are agree that the abuse of akisol affect the social contributions, and 21.0% from the sample dont know if the abuse of akisol affect the social contributions or not, and 21.0% from the sample are not agree that the abuse of akisol affect the social contributions, and 36.0% from the sample are strongly not agree that the abuse of akisol affect the social contributions.
Figure No.(30)**Family and society contribution**

### 3.4.12 Sleep and anxiety disorder

Figure No.(31) shows that 21.0% from the sample strongly agree that they feel sleep and or anxiety disorder, and 21.0% from the sample agree that they feel sleep and or anxiety disorder, and 7.0% from the sample do not know if they feel sleep and or anxiety disorder, and 36.0% from the sample not agree that they feel sleep and or anxiety disorder, and 15.0% from the sample strongly not agree that they have sleep and or anxiety disorder.

Figure No.(31)**Sleep and anxiety disorder**
3.4.13 Willing to stop abusing Kharsha

Figure No.(32) shows that 43.0% akisol abusers from the sample are strongly agree they are willing to stop, 15.0% akisol abusers from the sample do not know if they are willing to stop, and 6.0% akisol abusers from the sample are not agree they are willing to stop, and 36.0% akisol abusers from the sample are strongly not agree they are willing to stop.

Figure No.(32) **Willing to stop abusing Kharsha**
Chapter four

Discussion, Conclusion and Recommendations
4.1 Discussion:
- The age of 30 to 35 is only 1% of population, because the population of the study was a college student.

- Male and female balance are almost equal, but 32% of Kharsha are female which may reverse to that the female are more than male (53% to 47%)

- 82.0% of the Akisol addicted are staying in hostel, this finding consider as strong evidence to rise a flag about what is going on in the student hostel.

- 94.0% of the Akisol addicted students are single, that means early marriage may be the may be one of this problem solution.

- 19.0% of the Akisol abusers mix it with other drugs, this lead us to the finding that there other drugs available in the market, to me the excessive presence of refugees from certain country in which this type of drugs are predominant.

- According to the findings there is no connection between the consumption of alcohol and the use of kharsha, this not align with my previous knowledge, this may reverse to the consumption of alcohol is not a habit of college students.

- 44.0% of Akisole users has monthly income (them self’s or family), of less than 5000, this lead us to find that the addiction of kharsha has no connection with the high income, this may be due to akisol low price.

- 5.0% of the sample taken from akisol abusers, taking in consideration that the samples were college students, this finding is seems high and horrible and the percentage within other sectors of the society is expected to be strongly higher.

- 85.0% of akisolabusers agreed that they can get Akisol from pharmacies, this finding seems to not be consistent with restrictions made by the general directorate of pharmacy to adopt Benhexol as a controlled medicine.

- the problem of stigma is that it may be strong obstacle in front of the will of seeking medical help in order to quit Akisol use, in this study 89.0% of the abusers not feeling shame of using kharsha, this may be due to the ease of the use of drug.
4.2 Conclusion
4.2.1 Knowledge

Regarding the knowledge of the respondents surveyed about Akisol or Kharsha, the study revealed that 88.0% of the study population, do not know the side effects of the Kharsha abuse, and only 1.0% of the study population not agree about Kharsha side effects, and 11.0% know that Kharsha abuse can cause serious side effects.

26.0% of the sample knew Kharsha dose and dosage form, and 74.0% of the sample don't know about the Kharsha dose and dosage form.

4.2.2 Akisol or Kharsha prevalence

Among the respondents surveyed, the study found that 5% from them used Kharsha and 95% of them didn’t use it at all, 52.0% of the akisol users are still using the akisol, all of them knew about all the consequences of using akisol.

4.3 Recommendation

1- Encourage programs across various media, to educate people and students about the dangers of abuse of Kharsha.
2- Organizing awareness campaigns against kharsha abuse at schools and universities.
3- Development of well-trained psychiatric clinics to deal with addicted people.
4- Dissemination of legal awareness and clear warning against Kharshause and marketing even from pharmacy.
5- Legal bodies should enforce strict laws against drug dealers.
6- Dissemination of religious consciousness, and religious culture, and the consolidation of the social and educational values to the students.
References


Brugal MT, Domingo-Salvany A, PuigR,: Evaluating the impact of methadone maintenance programmes on mortality due to overdose and AIDS in a cohort of heroin users in Spain( 2005).

Addiction.;100:981–989.


Franklin TR, Acton PD, Maldjian JA. Decreased gray matter concentration in the insular, orbitofrontal, cingulate, and temporal cortices of cocaine patients. Biol Psychiatry2002;51:134-142


Goodman &gilman's the pharmacological basis of therapeutics - 11th ed. section ii - drugs acting at synaptic and neuroeffector junction sites chapter 7. muscarinic receptor agonists and antagonists - joanheller brown and palmer taylor figures figure 7-2(2006)


Hatsukami DK, Fischman MW. Crack cocaine and cocaine hydrochloride: are the differences myth or reality? JAMA 1996;276:1580-1588.


Regier DA, Farmer ME, Rae DS,: Comorbidity of mental disorders with alcohol and other drug abuse. Results from the epidemiologic catchment area (ECA) study( 1990).


Annexes
جامعة الرباط الوطني
معهد علوم الادلة الجنائية

استبيان حول سوء استخدام الاكيزول (الخرشة) واثارها

استبيان رقم: 
التاريخ: 1-2016

1- العمر: 
2- النوع: ذكر، ذكر، اخرى
3- الاعلان: جزيرة، أخرى
4- الحالة الاجتماعية: عازب، متزوج، مطلق، ارمل
5- هل تسكن في: منزل العائلة، داخل
6- هل لديك عمل: نعم، لا
7- الدخل الشهري لك أو للعائلة: أقل من خمسة الف جنية، من خمسة حتى عشرة الف جنية، أكثر من عشرة الف جنية

8- 
9- المستوى: الأول، الثاني، الثالث، الرابع، الخامس
10- هل تتعاطي أي إدوية بصورة مستمرة؟ نعم، لا
11- هل تستعمل أي أدوية مسكنة؟ نعم، لا

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