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Trihexyphenidyl (Artane®): A Brazilian Study of Its Abuse[1]

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In Brazil, the medicinal misuse of trihexyphenidyl (Artane®) has been observed among several segments of society. The present study was conducted in the city of São Paulo during 2002 to characterize this abuse. A sample of 21 users and 16 ex-users was interviewed using qualitative methodology; the subjects were single, unemployed, male polydrug users, who used trihexyphenidyl in order to attain states of mental alterations, mainly hallucinations and deliriums. Trihexyphenidyl is consumed in association with alcohol, other licit drugs (benzodiazepines), or illicit drugs, impairing cognitive functions such as memory, attention, and learning, intervening with some activities of users' daily life.

Keywords anticholinergics; Artane®; hallucinogens; qualitative study; trihexyphenidyl

Introduction

Review articles describing anticholinergic drugs as "agents of abuse" in several countries are available (Marken et al., 1996). Brazil is no exception concerning this subject. The first report of anticholinergic intoxication goes back to the nineteenth century (Lima, 1866), describing the intoxication of two black slaves after they ingested an infusion of *Datura sp*. During the second half of the twentieth century, Braga et al. (1972) described 40 patients, who were 15 to 24 years of age, suffering from intense psychotic episodes due to Artane®. Beyond its nonmedicinal consumption, trafficking with Artane® has also occurred in several Brazilian states from at least the early 1970s; prescription forgeries also have been detected (Braga et al., 1972; Carlini, 1994).

[1]The journal's style utilizes the category *substance abuse* as a diagnostic category. Substances are used or misused; living organisms are and can be *abused*. Editor's note.

This study was performed at the Department of Psychobiology of the Federal University of São Paulo (UNIFESP).

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According to a recent survey performed in the 107 largest Brazilian cities (Carlini et al., 2002), 1.1% of the population (nearly 500 thousand persons), aged 12–65 years, reported lifetime use of anticholinergic drugs, mostly Artane®.

All the previously mentioned studies, in general, are case reports describing a few cases, emphasizing the mental alterations brought by Artane® or are quantitative surveys carried out to establish the number of persons who were engaged in nonmedical anticholinergic use. Very few studies, if any, have been conducted so far, employing qualitative research methodology, aimed at delineating the social aspects and mores of such use. The present study was conducted to better our understanding of the nonmedical misuse of trihexyphenidyl and, consequently, to help promote more adequate prevention programs to curb such use.

Methodology

A qualitative methodological approach was chosen, as users of Artane® constitute a hidden population engaged in an unfamiliar behavior. The aim of this study design was to obtain data to help understand the view that users have about their own drug use, letting them judge or categorize it through their own values and mores (Creswell, 1998).

Sample

A purposeful sample selected by criteria (Patton, 1990) consisted of users and ex-users, aged 20 years or older. The sample participants had to have used trihexyphenidyl at least 10 times in their lifetime, thus avoiding experimental users/ex-users (Siegel, 1985). Individuals were continuously selected, until their information reached redundancy or the theoretical saturation point, at which time, new information no longer contributed to the further understanding of the phenomenon (Patton, 1990; WHO, 1994); 37 persons were interviewed to reach this point. There were no refusals.

The sample was recruited through the "snowball technique" (Biernacki and Waldorf, 1981). Users/ex-users from eight different chains were investigated, comprising eight groups living in different areas of the city. This strategy made it possible to have the sample composed of users/ex-users of different profiles.

Instruments

Based on a World Health Organization questionnaire (WHO, 1994) and on an "Informal Conversational Interview" (Patton, 1990; Creswell, 1998), a series of basic questions was formulated for all the interviewees in a way that permited the comparison of answers. These basic questions approached items on the trajectory and phases of drug use, reasons for use, and changes in the lifestyle.

A semistructured, in-depth interview was elaborated and conducted with all elements of the sample, in which the interviewer tried to identify the interviewee's view on different topics. An informed consent was obtained and the interviews, which lasted about 80 minutes, were taped. They were carried out in 2002, in São Paulo City, in neutral and safe places inside the Psychobiology Department of the Federal University of São Paulo, after which the interviewees were rewarded (US$ 10.00) based on the time spent.

The diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, (DSM-IV) (APA, 1994) were employed to investigate the incidence of dependence among the interviewees.

Data analysis of the transcribed material was performed according to the following steps: fluctuating lectures, exploratory procedures, preparation and categorization of material, and treatment of data to obtain the final interpretations and hypotheses related to the subject (Bryman and Burgers, 1999).

The final data were divided into two main topics: 1) analysis of characteristics of trihexyphenidyl as a "drug of abuse" by the interviewee, and 2) a self-evaluation of the reasons for the interviewee's indulging in its nonmedicinal use.

Results and Discussion

1) Characterization of Trihexyphenidyl as a Drug of Abuse

a) Effects of Trihexyphenidyl Ingestion. The blockade of the muscarinic peripheral receptors by trihexyphenidyl yields physical symptoms such as hypertension, fever, dry mouth, nausea, and blurred vision (Kulik and Wilbur, 1982). The blockade of central nervous system (CNS) receptors results in significant psychic effects such as euphoria, disinhibition, depersonalization, perception alterations including visual and auditory hallucinations and delirium, inability to concentrate, fleeing of ideas, psychomotor agitation, and temporal-spatial discrimination losses (Braga et al., 1972; Kulik and Wilbur, 1982; Guthrie et al., 2000). Affectivity is also altered and feeling guilty is common, together with a sensation of anguish persisting for 24–48 h (Baeza, 1993).

On the other hand, interviewees described, according to their feelings and sensitivity, effects of trihexyphenidyl that could be classified as positives, negatives, or mixed (Table 1). *Positive effects* seemed to depend on the place and circumstances in which Artane® was used, and were intensified by parties and jubilant environments and by friends. They were described as:

- being bold, industrious, and awake;
- disinhibition in speaking or dancing: "I was taken by an exaltation and began singing and dancing.";
- euphoria, agitation, and humor improvement;
- improvement of auditory, visual, and tactile sensations, including sexual relationships.

Negative effects were either physical (dry mouth, blurred vision, nausea, stomach pain, tremors, and tachycardia) and/or mental (nervousness, aggressiveness, memory loss, decreased attention, loss of appetite, insomnia and depression postuse):

Table 1
Previous knowledge about trihexyphenidyl effects

Known effects reported	N (Number of subjects)	%
Negative Effects (hallucinations, delirium, etc)	11	30
Positive Effects (euphoria, counteracting depression due to alcohol, etc.)	8	22
None	18	48

The distortion of physical space and mental disturbances, which can be a physical menace to the user's health, may be also considered as a negative effect: "I dived into the sidewalk, as I was sure it was a river."

Furthermore, several users did not use Artane® when ill-tempered, as the substance seemed to potentiate this state, making them more aggressive.

Hallucinations and delirium are examples of *mixed effects*, which may be considered as positive or negative. When they assume the form of peaceful animals, beautiful objects, or even friendly persons, they are considered as positives by the interviewees; however, when the visions assume terrifying images, placing the user in a situation of intense distress, they are considered as negatives. The users could not predict which form of hallucination they would undergo:

"Artane® makes it possible to deal with things that are difficult for me, and since I started using it, I contacted a person who appears in front of me whom I called my brother. And I only managed to deal with my sexuality when I started talking to him."

"I was terrified when I perceived that there were snakes on the wall."

When the effects begin to wear off, uncomfortable sensations may appear such as fatigue, hunger, thirst, nervousness, and depression, which could be overcome by a new ingestion of the medication.

b) Consequences of Artane® Use. Because trihexyphenidyl is an anticholinergic substance, causing cognitive problems such as attention deficit and memory impairment, it may impair study and work activities, as reported by a large majority of the interviewees:

"Letters kept moving on the blackboard and everything became blurred." The interviewees also reported a decline in physical and mental health: dry mouth, gastritis, vomiting, tachycardia, urinary retention, and even dental caries (probably due to the absence of salivation) were the most common physical symptoms reported.

The consumption of Artane® seems to improve interpersonal relationship, but its effects on sexual activities are not unanimously considered as positive. The large majority of users (N = 22) believed that Artane® use could increase the possibility of infection by sexually transmitted diseases, since under drug effect, safe-sex practice and condom use are forgotten or not considered important.

Although only two interviewees reported the occurrence of accidents under trihexyphenidyl effects, these should be taken into consideration as trihexyphenidyl consumption causes a reality disruption:

"I have ever crashed my car under trihexyphenidyl effects. The street became too broader. . ."

c) Dependency. The majority of interviewees (N = 29) accepted the possibility of a dependence state induced by Artane®. Their opinion is supported by the fact that 20 sample members met at least three criteria of DSM-IV (APA, 1994) (Table 2).

Data in Table 2, which show the criteria of the American Psychiatric Association most frequently reported by interviewees, shows that trihexyphenidyl may induce dependency. In fact, a few authors admit the possibility that long-term trihexyphenidyl use is able to induce a state of dependence, although the length of time of abuse and dosage needed to reach this state are still undefined (Oliveira and Evans, 1988; Marken et al., 1996). Characteristic symptoms of an abstinence state were observed in patients who had been receiving trihexyphenidyl for more than three months (McInnis and Peturson, 1985).

Table 2
DSM-IV (APA, 1994) criteria most frequently reported

Criteria	N (Number of subjects)	%
1) Tolerance (diminished effects; markedly increased amounts of the substance)	19	51
2) Withdrawal	18	49
3) The substance is taken in larger amounts or over a longer period than was intended	8	22
4) Persistent desire or unsuccessful efforts to cut off or control substance use	15	40
5) Spent of a great deal of time to obtain the substance or recover from its effects	7	19
6) Important social, occupational or recreational activities are given up or reduced because of substance use	11	30
7) The substance use is continued despite knowledge of a persistent physical or psychological problem caused by the substance use	15	40

Oliveira and Evans (1988) reported that 61% of schizophrenic patients receiving long-term trihexyphenidyl therapy met DSM-III criteria for dependency.

d) Forms and Patterns of Consumption. All interviewees reported consuming trihexyphenidyl orally; three of them described unsuccessful attempts to use it through intravenous injection. The ingestion of Artane® pills may be combined with alcoholic beverages, coffee, or cola drinks, all of which are believed to improve trihexyphenidyl effects. According to the interviewees, one-half to four Artane® pills is the amount necessary to yield the desired effects, which appear 30 to 60 min after ingestion and persist 1–4 h depending on the amount ingested and the environment of use. A few users reported that the effects could return about 24 h later, a phenomenon known as "flashback," as previously described by Baeza (1993):

Most interviewees believed that Artane® does not provoke symptoms of overdose, a belief contrary to the information contained in the package insert of the medication.

2) Characterization of Trihexyphenidyl Users

a) Sociodemographic Data. Subjects included 21 users and 16 ex-users of trihexyphenidyl, all of them living in São Paulo City. Their sociodemographic characteristics are shown in Table 3. As seen in the table, the sample was composed mostly of single men (N = 29), with poor schooling. Most of them were jobless (N = 26) and the others, when working, were engaged in informal activities.

Their physical and psychiatric conditions were not evaluated through appropriate instruments and interviews. However, they could be inferred through the answers to the questions given during the interview, demonstrating that the interviewees did not present gross physical and psychological problems and were able to understand the questions and objectives of the interview.

Table 3
Sociodemographic characteristics of users/ex-users of trihexyphenidyl in the city of São Paulo

Parameters	Number of subjects (N)	Sample percentage (%)	Parameters	Number of subjects (N)	Sample percentage (%)
Gender			Employment status		
Male	29	78.4	Employed	11	29.7
Female	8	21.6	Unemployed	26	70.3
Age (in years)			Education level		
20–30	14	37.8	1st cycle[c]	19	51.4
30–40	18	48.6			
40 or more	5	13.6			
			2nd cycle[d]	15	40.5
Civil status			College[e]	03	8.1
Married[a]	13	35.1			
Single[b]	24	64.9			
			Social status[f]		
Living with			Higher-income	08	21.6
Parents/brother(s)	18	48.6	Middle-income	14	37.8
Spouse/children	13	35.1			
Relatives	2	5.4	Lower-income	15	40.6
Alone	4	10.9			

[a]People who are legally married or living with a mate (girlfriend/boyfriend).
[b]Here were included single, widowed, and divorced people.
[c,d,e]In these items people were included who completed or not completed the informed grade.
[f]Interviewees were asked about the socioeconomic class in which they were included, and how much money the entire family earned per month. Afterward, these data were compared with the table: "Brazilian economic classification criteria" from IBOPE (Research and Public Opinion Brazilian Institute).

Although the sample cannot be considered as representative of the whole population, it may well represent a heterogeneous group of users for various reasons. On the other hand, it is worth mentioning that men were the main consumers of trihexyphenidyl, as has been reported for users of other psychotropic drugs (Al-Kandari et al., 2001; Carlini et al., 2002). The sample's low educational and socioeconomic conditions also agreed with other reports on drug users in general, a fact that according to several authors may be attributed to the drug use (Nappo et al., 1996).

b) Trajectory of Trihexyphenidyl Use. As is commonly known for other drugs (Sanchez and Nappo, 2002), a large part of the sample (N = 23) consumed trihexyphenidyl for the first time on the street or at school, with friends.

Trihexyphenidyl was neither the initial drug in the substance user's career nor their main drug. Alcohol and tobacco were most commonly the first drugs used and marijuana and cocaine were the more important drugs used in their lifetime, according to the users' reports.

The age of first use of trihexyphenidyl ranged from 12 to 30 years old, indicating the nonexistence of a specific age for starting Artane®'s consumption. The vast majority of

interviewees (N = 32) obtained trihexyphenidyl (for the first time) from friends, who also advised the amount of drug to be ingested, which varied from one-half to three pills.

This first use seemed to be the result of peer pressure. Although 11 (30.0%) interviewees were aware of the negative effects (hallucinations, delirium, etc.) of trihexyphenidyl ingestion and 18 (48.0%) had no information at all, the remaining 8 interviewees (22.0%) declared knowing only about the "positive" effects (euphoria, counteracting depression due to alcohol, etc.) (Table 1).

c) Reasons for Consumption. According to 16 interviewees, a conflictive and dysfunctional family environment, mostly due to alcohol or other drug consumption, was the reason for their indulging in drug use. The father was frequently considered as the one responsible for the discord and, thus, indirectly encouraged the drug use, a fact that has also been reported by users of other drugs (Sanchez and Nappo, 2002).

On the other hand, another 16 users/ex-users claimed that trihexyphenidyl consumption is stimulated by a drug-user mate (girl/boyfriend), with no pressuring behaviors between them to stop use.

A cycle of friendship with persons much involved in the use of various drugs is another factor stimulating the continuity of trihexyphenidyl use, corroborating previous reports (Swadi, 1988).

d) Changes in Life. The majority of interviewees (N = 30) denied improvements in any domain in life due to trihexyphenidyl use. A few reported beneficial effects related to a seeming betterment in sociability, helping them to make new friends and to improve sexual behavior.

The majority of users, however, reported a deterioration of performance at school (N = 24) and at job and attributed to trihexyphenidyl use their difficulty in maintaining good school attendance and a negative impact on job productivity, which resulted in dropping out of school and job loss:

"It turned out to be just one more drug I indulged in; but then, more problems arose, including fierce arguments at home."

"I was always late for work and everything I earned was spent on drugs; because of this misconduct I lost a lot of jobs."

Conclusions

This study was conducted on a purposeful sample of a hidden population (Patton, 1990). Therefore, in spite of reaching the theoretical saturation point or information redundancy (WHO, 1994), the results obtained can not be generalized for the whole population. In other words, being a qualitative research, it did not look for how many subjects are engaged in trihexyphenidyl misuse; on the contrary, this qualitative research looked for the why, how, when, and under what circumstances certain individuals indulge themselves in the non-medical use of tryhexyphenidyl, from their own perspective. Even so, the data of the present study should draw the attention of authorities to the misuse of trihexyphenidyl (Artane®), and thus contribute to the development of preventive and control measures which are necessary to curb this medicine's misuse.

Trihexyphenidyl is a "drug of abuse," whose use is intensified due to its euphoria-producing effect and other positive actions. According to the users, jubilance and increased sociability are the main factors leading to abuse. However, as with the majority

of psychotropic drugs, it can induce a dependency state and promote marked alterations, mostly negative ones, in the daily life of users, leading them to be marginalized by society. Unemployment, abandoning school activities, worsening of physical and mental health and an increased risk for accidents are the main consequences of trihexyphenidyl use.

The recreational use of Artane® is extended to polydrug users and also reaches curious adolescents and street children in addition to the psychotic and affect-disturbed patients that have been extensively reported on in the past. The major distinction of trihexyphenidyl as compared to other psychotropic drugs such as cocaine and marijuana, lies in the fact that it is a licit drug (or medication), a condition that facilitates its being sought out and its consumption. The de facto reality is that Brazilian police and health authorities are not engaged in curbing Artane®'s illicit commerce and misuse in São Paulo City as well as throughout Brazil.

Finally, the present study followed all ethical principles adopted by Brazilian authorities. Thus, the subjects were previously briefed on the study details, signed an informed consent and had the right to refuse participation if they so desired. And they could benefit from the study, by the fact that health authorities, being aware of the situation of this hidden population, could provide medical and psychological help and ways to control the undesired effect of trihexyphenidyl misuse.

Triexafenidila (Artane®): Un estudio brasilero de su abuso

RESUMEN

En Brasil, el abuso de Triexafenidila ha sido observado entre varios segmentos de la sociedad. El presente estudio fué realizado en la ciudad de São Paulo (San Pablo) durante el año de 2002, para caracterizar ese abuso. Una amuestra, de 21 usuarios e 16 ex usuarios, fué entrevistada utilizándose la Metodologia Qualitativa; (ellos) eran hombres, solteros, poliusuarios, desempleados que abusaban de Triexafenidila para buscar alteraciones mentales, principalmente alucinaciones y delirios. Triexifenidila es consumida en asociación con alcohol, otras drogas lícitas (Benzodiazepínico) o ilícitas perjudicando las funciones cognitivas como memória, atención y aprendizaje, interfiriendo con algunas actividades del cotidiano del usuario.

Triexafenidila (Artane®): Um estudo brasileiro de seu abuso

RESUMO

No Brasil, o abuso de Triexafenidila tem sido observado entre vários segmentos da sociedade. O presente estudo foi conduzido na cidade de São Paulo durante o ano de 2002, para caracterizar esse abuso. Uma amostra de 21 usuários e 16 ex-usuários foi entrevistada utilizando-se Metodologia Qualitativa; eles eram homens, solteiros, poliusuários desempregados que abusavam de Triexafenidila para conseguirem alterações mentais, principalmente alucinações e delírios. Triexafenidila é consumido em associação com o álcool, outras drogas lícitas (Benzodiazepínico) ou ilícitas prejudicando as funções cognitivas como a memória, atenção e aprendizado, interferindo no cotidiano do usuário.

Triexafenidila (Artane®): Une étude brésilienne de son usage abusif

RÈSUMÈ

L'usage abusif de la Triehexafenidila a été observé parmis plusieurs segments de la société brésilienne. Cet étude a été conduite dans la ville de São Paulo (Brésil) dans l'année 2002.

Pour démontrer cet usage abusif, 21 utilisateurs et 16 ex-utilisateurs ont été interrogés par la Méthode Qualitative; l'echantillon a été constitué par des individus du sexe masculin, célibataires, poli-utilisateurs, au chômage, que avaient envisagé d'obtenir um changement mental, principalement par des hallucinations et par des accès de délire. La Triexafenidila a été utilisée em association avec l'alcool, ou de drogues licites (Benzodiazepinique) ou illicites, préjudicables aux fonctions cognitives, comme la mémoire, l'attention et l'apprentissage, intervenant sur quelques activités de leurs quotidien.

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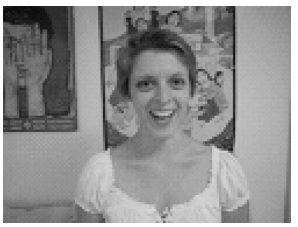

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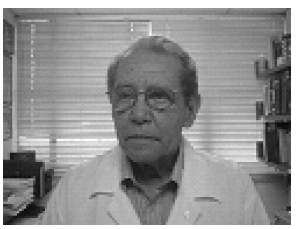

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