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## Research article

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# Melitracen and flupentixol (deanxit) use disorder in Lebanon

Tharwat El Zahran<sup>a,\*</sup>, Sally Al Hassan<sup>a</sup>, Malak Khalifeh<sup>c</sup>, Diana Aboukhater<sup>a</sup>, Lina Hammoud<sup>a</sup>, Moustafa Al Hariri<sup>a</sup>, Ziad Kazzi<sup>a,b</sup>

<sup>a</sup> Department of Emergency Medicine, American University of Beirut Medical Center, Beirut, Lebanon

<sup>b</sup> Department of Emergency Medicine, Emory University, Atlanta, GA, USA

<sup>c</sup> Stony Brook Cancer Center, Stony Brook University, NY, USA

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#### ABSTRACT

*Introduction:* Deanxit is a combination of melitracen and flupentixol, not approved as an antidepressant for sale and use in several countries but still widely available and commonly used among the Lebanese population. The study aimed to assess Deanxit use disorder, assess the source of the medication, and the consumers' awareness of the therapeutic and side effects of Deanxit, among the Lebanese population.

*Methods:* This is a cross-sectional study that included all patients taking Deanxit and visited the Emergency Department between October 2019 and October 2020. All patients who agreed to participate in the research through written consent forms were contacted by telephone and a questionnaire was filled out.

*Results*: A total of 125 patients taking Deanxit were included in the study. According to the DSM-V criteria, 36% (n = 45) had a Deanxit use disorder. Most of the participants were females (n = 99, 79.2%), married (n = 90, 72%), and between the ages of 40–65 years (n = 71, 56.8%). Most patients (n = 41, 91%) had Deanxit prescribed by a physician for anxiety (n = 28, 62%), and obtained it using a prescription (n = 41, 91%). Almost half of all patients (n = 60, 48%) did not have sufficient knowledge of the reason it was prescribed, 54.4% (n = 68) were not sure they are taking the medication appropriately, and 19.2% (n = 23) were satisfied by the overall explanation of the physicians concerning Deanxit use.

*Conclusion:* Deanxit use disorder is underrecognized among Lebanese patients. Most of our patients were prescribed Deanxit by their physicians but reported inadequate knowledge of its side effects and risk of abuse.

## 1. Introduction

Deanxit is a combined medication of a tricyclic antidepressant (10 mg of melitracen) and an antipsychotic (0.5 mg of flupentixol) that is marketed as an anxiolytic and antidepressant based on the potential synergistic effects of these two drugs on mood improvement [17]. Flupentixol acts as a dopamine 1 and 2 receptor antagonist and melitracen acts similarly to other tricyclic antidepressants by blocking the reuptake of serotonin and norepinephrine in presynaptic terminals [3]. Deanxit therapeutic effects have been sought to treat several illnesses, including anxiety, post-stroke depression, chronic subjective dizziness, and schizophrenia. However, Deanxit side effects include dry mouth, constipation, fatigue, appetite and weight change, blurry vision, headache, tardive dyskinesia, and

\* Corresponding author. *E-mail address:* te15@aub.edu.lb (T. El Zahran).

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## akathisia [11].

Deanxit originated in Denmark in 1971 by Lundbeck as an oral tablet but was not approved for use and sale in its country of origin. The company has never applied for registration for marketing approval of the drug in Denmark. Additionally, Deanxit is not approved for use and marketing in several developed markets, including the United States, United Kingdom, Canada, Ireland, Japan, and Australia. The Union health ministry in India has banned the manufacture and sale of the controversial fixed-dose combination (FDC) of Flupentixol and Melitracen that is sold under the name of Deanxit as it is likely to involve risk to humans and whereas safer alternative drugs are available [15]. The Food and Drug Administration (FDA) in the Philippines disapproved of Deanxit as an anti-depressant and warned against its purchase and use. Although not approved for use and sale in multiple countries, Deanxit is still registered in 21 countries by Lundbeck, including Lebanon, Cyprus, and Belgium, and is still being manufactured in Chittagong-Bangladesh [2,9].

Deanxit is widely available in Lebanese pharmacies, and patients can get it without a prescription which puts the patient at risk for adverse health effects and potential use disorder [10]. A study by Hitti et al. showed that 2.7% of toxicological exposures reported at a tertiary care hospital in Lebanon were related to Deanxit overdose [8]. To date, there is no published study that assessed Deanxit use disorder in general and specifically among the Lebanese population despite being commonly prescribed by physicians and used by patients. Hence, this study aimed to assess Deanxit use disorder, assess the source of the medication, and the consumers' awareness of the therapeutic and side effects of Deanxit, among the Lebanese population.

## 2. Methods

## 2.1. Design and setting

This is a cross-sectional survey that assessed all patients taking Deanxit who presented to the American University of Beirut Medical Centre (AUBMC) Emergency Department (ED) between October 2019 and October 2020. The hospital is the largest tertiary care centre in Lebanon, it has 358 beds and receives approximately 55,000 ED visits and approximately 25,000 inpatient admissions annually. Pediatric patients comprise 20.0% of ED visits and 17.0% of hospital admissions.

The design of this study ensured that it strongly abided by all ethical considerations according to the Institutional Review Board (IRB) of AUBMC. The study protocol was ID SBS-2019-0304.

### 2.2. Selection of participants

Patients who presented to the ED and reported using Deanxit as part of their home medications were identified through the electronic health system (Epic Systems, Verona, WI, USA). The research assistants received an electronic message through the EPIC inbasket system 24/7 to alert them of potential subjects. All patients approved through written consent to be called and participate in the study during their ED visit. Patients were contacted by telephone and verbally consented again using a phone-based questionnaire (Appendix A).

Between October 2019, and October 2020, all patients older than 18 years of age who presented to the ED and reported taking Deanxit were included. Patients were excluded if they did not speak English or Arabic, refused to participate, were not reached after three attempts of calling, were critically ill patients, or died during the period from initiating an ED visit and time of contact.

## 2.3. Study measures

The questionnaire was adopted based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) to assess the presence of Deanxit substance use disorder [6]. Substance use disorder was defined by at least two criteria of the DSM-5. A mild use disorder was defined as the presence of 2–3 DSM-5 criteria, a moderate disorder was defined as the presence of 4–5 DSM-5 criteria, and a severe disorder was defined as the presence of 6 or more DSM-5 criteria [9]. Demographic data were collected, including age, gender, marital status, educational level, and employment status. Information on the patient's health was also collected, including perceived health status, chronic medical problems, current medications, psychiatric comorbidities, and primary care physician/psychiatrist follow-up. Patients were also asked about their history of substance use. Additionally, all detailed information on Deanxit uses in the last six months, including frequency, duration, medication use, the reason for its use, co-use with other benzodiazepines and anxiolytics, and ways to obtain the medication were collected. Information on perceptions of use and misuse was also collected.

### 2.4. Statistical analysis

The Statistical Package for Social Sciences (IBM SPSS 25.0) (Armonk, NY: IBM Corp) was employed to execute the statistical analysis. A descriptive analysis was conducted by calculating frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Bivariate analysis was performed using Chi-square or fisher's exact test to examine associations between different variables and substance use disorder when appropriate. A p-value of <0.05 was considered statistically significant.

#### 3. Results

A total of 129 patients on Deanxit presented to the ED. They consented to participate and were contacted by phone. At the time of contact, two patients were deceased for a cause that was unrelated to their Deanxit use. In addition, two patients refused to participate without clarifying the reason. We ended up with 125 patients who consented and answered the questionnaire.

## 3.1. Demographics and general health

Overall, we had a total of 125 patients, 64.0% (n = 80) had no use disorder according to DSM V and 36.0% (n = 45) had Deanxit use disorder. We compared both group characteristics, most of the participants were females (79.2%, n = 99), 40–65 years (56.8%, n = 71), are married (n = 90, 72.0%). Approximately half of the participants were smokers (57.6%, n = 72), while the majority did not drink alcohol (76.0%, n = 95). Regarding educational and occupational status, around 64.0% (n = 80.0) were unemployed, 56.0% (n = 70) had a university degree, and 44.0% (n = 55) had finished at least secondary school.

Furthermore, a total of 71.2% (n = 89) had associated chronic diseases, including hypertension, diabetes, and dyslipidemia. Only one-third (31.2%, n = 39) of participants are diagnosed with a psychiatric illness. Almost half of the patients with a psychiatric disease had Deanxit use disorder (46.7%). In total, 71.2% (n = 89) followed up with a primary care physician and around 73.0% of patients with Deanxit use disorder, are followed up with a primary care physician. The primary care physicians were either a psychiatrist (7.2%), a cardiologist (19.0%), a family physician (12.0%), a neurologist (4.8%), an endocrinologist (5.6%), or a rheumatologist (3.2%). In addition, only 2.4% (n = 3) had concomitant substance abuse (Table 1).

#### 3.2. Deanxit use and co-ingestion patterns

Most of the participants reported daily administration of Deanxit. Deanxit was mostly used for the treatment of anxiety (53.6%, n = 67), or for relaxing and getting high (29.6%, n = 37) (Table 2). Most patients learned about Deanxit from their physicians (84.8%, n = 106), and the rest (12.8%, n = 16) learned about it from friends, family members, or on their own. Most patients obtained Deanxit from pharmacies with a prescription (80.8%, n = 101), and it was the most common source of Deanxit in patients with substance abuse disorder (Table 2). Most patients used Deanxit for more than 1 year (76.6%, n = 95).

Deanxit was commonly used in adjunct with other medication, mostly selective serotonin reuptake inhibitors (SSRI) medications (17.4%, n = 22), followed by benzodiazepines (14.4%, n = 18), and lastly magnesium supplements (8.0%, n = 10) (Table 2). We also

|                                             | Option                  | Total $n = 125$ | No use Disorder $n = 80$ | $Deanxit \ Use \ Disorder \ n=45$ | p-value |
|---------------------------------------------|-------------------------|-----------------|--------------------------|-----------------------------------|---------|
| Age (years)                                 | <40                     | 22 (17.6%)      | 14 (17.5%)               | 8 (17.8%)                         | 0.802   |
|                                             | 40–65                   | 71 (56.8%)      | 44 (55.0%)               | 27 (60.0%)                        |         |
|                                             | >65                     | 32 (25.6%)      | 22 (27.5%)               | 10 (22.2%)                        |         |
| Gender                                      | Female                  | 99 (79.2%)      | 61 (76.3%)               | 38 (84.4%)                        | 0.279   |
|                                             | Male                    | 26 (20.8%)      | 19 (23.8%)               | 7 (15.6%)                         |         |
| Marital Status                              | Married                 | 90 (72.0%)      | 54 (67.5%)               | 36 (80.0%)                        | 0.135   |
|                                             | Not married             | 35 (28.0%)      | 26 (32.5%)               | 9 (20.0%)                         |         |
| Educational Level                           | University Degree       | 70 (56.0%)      | 44 (55.0%)               | 26 (57.8%)                        | 0.764   |
|                                             | Under University degree | 55 (44.0%)      | 36 (45.0%)               | 19 (42.2%)                        |         |
| Currently Employed                          | Yes                     | 45 (36%)        | 33 (41.3%)               | 12 (26.7%)                        | 0.103   |
|                                             | No                      | 80 (64.0%)      | 47 (58.8%)               | 33 (73.3%)                        |         |
| Smoking                                     | Current Smoker          | 72 (57.6%)      | 47 (58.8%)               | 25 (55.6%)                        | 0.729   |
| 0                                           | Not currently smoking   | 53 (42.4%)      | 33 (41.3%)               | 20 (44.4%)                        |         |
| Alcohol                                     | Yes                     | 30 (24.0%)      | 20 (25.0%)               | 10 (22.2%)                        | 0.727   |
|                                             | None                    | 95 (76.0%)      | 60 (75.0%)               | 35 (77.8%)                        |         |
| Perceived overall health over the last year | Excellent               | 8 (6.4%)        | 8 (10.0%)                | 0 (0%)                            | 0.126   |
|                                             | Very good               | 29 (23.2%)      | 19 (23.8%)               | 10 (22.2%)                        |         |
|                                             | Good                    | 47 (37.6%)      | 30 (37.5%)               | 17 (37.8%)                        |         |
|                                             | Fair                    | 23 (18.4%)      | 11 (13.8%)               | 12 (26.7%)                        |         |
|                                             | Poor                    | 18 (14.4%)      | 12 (15.0%)               | 6 (13.3%)                         |         |
| Presence of psychiatric diseases            | Yes                     | 39 (31.2%)      | 18 (22.5%)               | 21 (46.7%)                        | 0.005   |
|                                             | No                      | 86 (68.8%)      | 62 (77.5%)               | 24 (53.3%)                        |         |
| follow up with a primary care physician     | Yes                     | 89 (71.2%)      | 56 (70.0%)               | 33 (73.3%)                        | 0.693   |
|                                             | No                      | 36 (28.8%)      | 24 (30.0%)               | 12 (26.7%)                        |         |
| Presence of chronic diseases                | Yes                     | 89 (71.2%)      | 59 (73.8%)               | 30 (66.7%)                        | 0.401   |
|                                             | No                      | 36 (28.8%)      | 21 (26.3%)               | 15 (33.3%)                        |         |
| Still taking Deanxit                        | Yes                     | 88 (70.4%)      | 56 (70.0%)               | 32 (71.1%)                        | 0.896   |
|                                             | No                      | 37 (29.6%)      | 24 (30%)                 | 13 (28.9%)                        |         |
| Other Substances                            | Marijuana               | 1 (0.8%)        | 1 (1.3%)                 | 0 (0%)                            | 1.000   |
|                                             | Other drugs of abuse    | 2 (1.6%)        | 1 (1.3%)                 | 1 (2.2%)                          | 1.000   |

## Table 1 Baseline characteristics of study participants.

Data are presented as numbers with percentages.

The P-value for the difference between two adjacent columns is calculated by chi-square or Fisher's exact test where appropriate.

#### Table 2

Pattern of use of Deanxit among study participants.

|                         | Option                                       | Total N = 125 | No use Disorder $n = 80$ | Deanxit Use Disorder $n = 45$ | p-<br>value |
|-------------------------|----------------------------------------------|---------------|--------------------------|-------------------------------|-------------|
| Daily use of Deanxit    | Yes                                          | 93 (76.2%)    | 54 (70.1%)               | 39 (86.7%)                    | 0.038       |
|                         | No                                           | 29 (23.8%)    | 23 (29.9%)               | 6 (13.3%)                     |             |
| Reason for Deanxit use: | To relax or get high                         | 37 (29.6%)    | 28 (35.0%)               | 9 (20.0%)                     | 0.078       |
|                         | Insomnia                                     | 9 (7.2%)      | 4 (5.0%)                 | 5 (11.1%)                     | 0.281       |
|                         | Anxiety or to relieve tension                | 67 (53.6%)    | 39 (48.8%)               | 28 (62.2%)                    | 0.147       |
|                         | Panic attack                                 | 17 (13.6%)    | 11 (13.8%)               | 6 (13.3%)                     | 0.948       |
|                         | Depression or low mood                       | 19 (15.2%)    | 14 (17.5%)               | 5 (11.1%)                     | 0.340       |
|                         | Other <sup>a</sup>                           | 32 (25.6%)    | 21 (26.3%)               | 11 (24.4%)                    | 0.824       |
| Prescribers of Deanxit  | From physician                               | 106 (84.8%)   | 65 (81.3%)               | 41 (91.1%)                    | 0.140       |
|                         | From friends or family                       | 16 (12.8%)    | 12 (15.0%)               | 4 (8.9%)                      | 0.326       |
| Sources of Deanxit      | From the pharmacist, with a prescription.    | 101 (80.8%)   | 60 (75.0%)               | 41 (91.1%)                    | 0.028       |
|                         | From the pharmacist, without a prescription. | 14 (11.2%)    | 10 (12.5%)               | 4 (8.9%)                      | 0.539       |
|                         | From my friends/family                       | 11 (8.8%)     | 8 (10%)                  | 3 (6.7%)                      | 0.745       |
| Co-medications          | Benzodiazepines                              |               |                          |                               |             |
|                         | Xanax (alprazolam)                           | 10 (8%)       | 7 (8.8%)                 | 3 (6.7%)                      | 1.000       |
|                         | Lexotanil (bromazepam)                       | 7 (5.6%)      | 4 (5%)                   | 3 (6.7%)                      | 0.702       |
|                         | Valium (diazepam)                            | 3 (2.4%)      | 2 (2.5%)                 | 1 (2.2%)                      | 1.000       |
|                         | Stilnox (zolpidem)                           | 1 (0.8%)      | 1 (1.3%)                 | 0 (0%)                        | 1.000       |
|                         | SSRI                                         |               |                          |                               |             |
|                         | Cipralex (escitalopram)                      | 14 (11.2%)    | 8 (10.0%)                | 6 (13.3%)                     | 0.571       |
|                         | Zoloft (sertraline)                          | 2 (1.6%)      | 2 (2.5%)                 | 0 (0%)                        | 0.535       |
|                         | Prozac (fluoxetine)                          | 1 (0.8%)      | 1 (1.3%)                 | 0 (0%)                        | 1.000       |
|                         | Seroxat (paroxetine)                         | 4 (3.2%)      | 2 (2.5%)                 | 2 (4.4%)                      | 0.619       |
|                         | Favarine (fluvoxamine)                       | 1 (0.8%)      | 0 (0%)                   | 1 (2.2%)                      | 0.360       |
|                         | Brintellix (vortioxetine)                    | 1 (0.8%)      | 1 (1.3%)                 | 0 (0%)                        | 1.000       |
|                         | Magnesium Supplement                         | 10 (8.0%)     | 4 (5.0%)                 | 6 (13.3%)                     | 0.166       |
|                         | Muscerol <sup>b</sup>                        | 2 (1.6%)      | 1 (1.3%)                 | 1 (2.2%)                      | 1.000       |

Data are presented as numbers with percentages.

The P-value for the difference between two adjacent columns is calculated by chi-square or Fisher's exact test where appropriate.

<sup>a</sup> Stomach pain, angina/shortness of breath, bruxism, dizziness, esophageal spasm, gastroesophageal reflux disease, hypertension, hysterectomy, hormone replacement, irritable bowel syndrome, menopause, obsessive-compulsive disorder, shoulder pain, and tremor.

<sup>b</sup> Muscerol is a combination of paracetamol and orphenadrine citrate.

further investigated the source and reason for use of the mentioned co-medication. Almost all got a prescription from a physician (95.2%, n = 92), and the rest learned about it from a pharmacist or on their own. They were mainly prescribed to relieve anxiety and tension (22.4%), to relax and get high (16.0%), depression (9.6%), panic attacks (8%), or insomnia (3.2%) (Table 2). About 88.2% (n

## Table 3

DSM-5 criteria for substance use disorders.

|                                                                                           | Options                                                                                                                                                                                        | Frequency<br>(%) |
|-------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| Substance Amount                                                                          | I sometimes take the substance in larger amounts or over longer periods than I initially intended to                                                                                           | 36 (28.8%)       |
| Tolerance                                                                                 | I have felt a need to increase the amount of the medication I use to get the same effect, or I feel that the same amount of medication I always take is not producing the same effect anymore. | 23 (18.4%)       |
| Withdrawal                                                                                | I feel depressed, irritable, tired, or shaky whenever I'm not using this medication, or I feel better once I retake the medication.                                                            | 46 (36.8%)       |
| Craving and difficulty in stopping drug                                                   | I constantly desire/crave the medication or have tried unsuccessfully to cut down or control my use of these medications                                                                       | 25 (20.0%)       |
| Time spent to obtain and recover from the drug                                            | I spend a lot of time and make a lot of effort to acquire this medication, use it or recover from its effect                                                                                   | 20 (16.0%)       |
| Effect on major role obligations and social life                                          | I have had to reduce some of my social or occupational activities because of the effects of this medication.                                                                                   | 8 (6.4%)         |
| Physical and psychological effects                                                        | I have continued using this medication despite having a physical or psychological problem<br>which is likely due to using it.                                                                  | 10 (8.0%)        |
| Neglected major roles to use; hazardous; social/<br>interpersonal problems related to use | I neglected major roles; had social and interpersonal problems with its use, and continued using despite risky/hazardous situations                                                            | 0 (0%)           |
| Deanxit Use Disorders                                                                     | <2                                                                                                                                                                                             | 80 (64.0%)       |
|                                                                                           | $\geq 2$                                                                                                                                                                                       | 45 (36.0%)       |
| Deanxit Use Disorder severity                                                             | Mild (2–3)                                                                                                                                                                                     | 29 (64.4%)       |
|                                                                                           | Moderate (4–5)                                                                                                                                                                                 | 12 (26.6%)       |
|                                                                                           | Severe ( $\geq 6$ )                                                                                                                                                                            | 4 (8.8%)         |

Data are presented as numbers with percentages.

= 85) of these medications were dispensed mainly in pharmacies with a prescription, while 9.8% (n = 9) were dispensed in the pharmacy without a prescription, and only one patient received the medication from a friend or family member.

## 3.3. Deanxit use disorder and dependence

Among our participants, 36.0% (n = 45) had Deanxit substance use disorder and approximately 28.8% (n = 36) of respondents reported using the medication in large amounts and over a long period. In addition, 36.8% (n = 46) experienced withdrawal symptoms upon trying to stop the medication or missing a dose, and 20.0% (n = 25) had difficulty or failed in stopping the medication due to constant cravings. Moreover, 16.0% (n = 20) spent a lot of time obtaining Deanxit and recovering from its effects, and about 14.4% (n = 18) reported it affecting their work, and social life, and causing them physical and psychological disturbances. Most of the Deanxit substance use disorder patients had mild severity disease (64.0%, n = 80), followed by moderate severity (26.6%) (Table 3).

## 3.4. Knowledge and attitude toward deanxit use

Our study showed that most of the participants who frequently used Deanxit had suboptimal knowledge of the therapeutic indication. About half of the patients (48.0%, n = 60) did not know sufficiently the reason it was prescribed. Additionally, 54.4% (n = 68) were not sure they were taking the medication appropriately. Only 19.2% (n = 23) were satisfied by the overall explanation of the physicians concerning Deanxit use.

Most participants did not know the name of medications or food or beverages they should not use with Deanxit (85.5%, n = 105). Most participants did not understand all the side effects of Deanxit (82.4%, n = 103), especially the risk of developing an addiction. (Table 4).

## 4. Discussion

Deanxit is a combined medication of a tricyclic antidepressant (TCA) and an atypical antipsychotic that is marketed as an anxiolytic and antidepressant. Despite being unapproved by drug regulatory agencies in several countries, Deanxit is still widely available and sold in multiple countries, including Lebanon. Deanxit use disorder in Lebanon poses a significant public health problem that requires further characterization and mitigation strategies. In this cross-sectional study, we assessed Deanxit use disorder, the source of the medication, and the consumers' awareness of the therapeutic and side effects of Deanxit, among the Lebanese population. Our findings show that around 36% (n = 45) of our patients had a Deanxit use disorder according to DSM V criteria. Most of our patients were married females, aged 40–65 years, smokers, and have reported daily Deanxit use. Most of our patients were prescribed Deanxit by a physician for anxiety and obtained it using a prescription. Additionally, the majority of Deanxit users lacked adequate knowledge regarding the therapeutic indications, side effects, and addiction potential.

There are no prior published studies that assessed Deanxit use disorder. Our study is unique since it is the first in the Middle East and North Africa (MENA) region to describe the utilization patterns and Deanxit use disorder among a subset of ED patients in

#### Table 4

|                                                                                     | Option   | Total       |
|-------------------------------------------------------------------------------------|----------|-------------|
| Does the patient confidently know the reason for the use of Deanxit?                | Disagree | 60 (48.0%)  |
|                                                                                     | Neutral  | 8 (6.4%)    |
|                                                                                     | Agree    | 57 (45.6%)  |
| Does the patient confidently know how to use Deanxit?                               | Disagree | 68 (54.4%)  |
|                                                                                     | Neutral  | 10 (8.0%)   |
|                                                                                     | Agree    | 47 (37.6%)  |
| Can the patient confidently describe the therapeutic use of Deanxit?                | Disagree | 73 (58.9%)  |
|                                                                                     | Neutral  | 9 (7.3%)    |
|                                                                                     | Agree    | 42 (33.9%)  |
| Can the patient confidently name the medications that cannot be taken with Deanxit? | Disagree | 106 (85.5%) |
| 1 2                                                                                 | Neutral  | 7 (5.6%)    |
|                                                                                     | Agree    | 11 (8.9%)   |
| Can the patient confidently name the food that cannot be taken with Deanxit?        | Disagree | 105 (84%)   |
|                                                                                     | Neutral  | 9 (7.2%)    |
|                                                                                     | Agree    | 11 (8.8%)   |
| Was the patient educated on Deanxit upon receiving the prescription?                | Disagree | 89 (74.2%)  |
|                                                                                     | Neutral  | 8 (6.7%)    |
|                                                                                     | Agree    | 23 (19.2%)  |
| Does the patient know the side effects of Deanxit?                                  | Disagree | 103 (82.4%) |
|                                                                                     | Neutral  | 8 (6.4%)    |
|                                                                                     | Agree    | 14 (11.2%)  |
| Does the patient know the probability of drug addiction from Deanxit?               | Disagree | 93 (75.0%)  |
|                                                                                     | Neutral  | 11 (8.9%)   |
|                                                                                     | Agree    | 20 (16.1%)  |

Data are presented as numbers with percentages.

Lebanon. Despite concerns about Deanxit, no published local or regional studies assess Deanxit use in-depth. In our study, 18.4% reported tolerance and 36.8% reported withdrawal symptoms from the drug. It is unclear whether the atypical antipsychotic or the TCA component of Deanxit is responsible for the patient's tolerance, withdrawal, and dependence. Withdrawal has been reported with tricyclic antidepressants due partly to their effects on the cholinergic and serotonergic systems. Rapid discontinuation of TCAs has been reported to cause antidepressant discontinuation syndrome and cause signs of parkinsonism and balance problems [11]. Additionally, TCA abuse has been reported, and most of the reported cases have involved abuse of the tertiary TCAs. The more prominent anticholinergic and antihistamine effects of tertiary TCAs may be contributing to their abuse liability [12].

On the other hand, antipsychotic withdrawal syndrome has been debated and reported. A meta-analysis by Brandt L et al. showed that 53.0% of individuals showed withdrawal symptoms after abrupt antipsychotic discontinuation and substitution with a placebo drug [13]. Misuse of atypical antipsychotics has also been reported in conjunction with alcohol and other drugs of abuse. Data from inpatient rehabilitation and detoxification units showed that 17.0% had a history of misusing atypical antipsychotics combined with alcohol and/or other drugs of abuse. Quetiapine is the most abused drug [14].

Our findings show that most of our patients on Deanxit were females. A study by Hitti et al. on patients presenting to the largest ED in Lebanon for xenobiotic overdose showed that women constituted most of the population presenting with an intentional overdose [8]. This may be explained by the greater likelihood of women suffering from anxiety disorders such as generalized anxiety disorder (GAD), panic disorder, and particular phobias. Additionally, the Collaborative Psychiatric Epidemiology Studies revealed that women have higher lifetime diagnosis rates for almost all anxiety disorders in a sample of more than 20,000 people [5]. Another study found that women are more likely than men to report using psychotropic medication [16].

Interestingly, our results show that the majority of Deanxit users were smokers. This is consistent with another study conducted in Lebanon by Zahlan et al., where smokers were five times more likely to use sedatives, tranquilizers, and sleeping medication when adjusted for sex, age, and education level. Additionally, smoking was associated with a three-fold increase in the use of sedatives/ tranquilizers, a four-fold increase in pain relievers, and a five-fold increase in sleeping medicines [19]. Other studies have also linked alcohol use to higher rates of prescription drug abuse and dependence. In our study, only a few patients (24.0%) reported using alcohol, and there was no difference among those who have a Deanxit use disorder versus those who do not. The rate of alcohol dependence is reported to be low (5.0%) compared to 12.5% in the USA [1,7,18].

In our study, half of the patients on Deanxit had little to no knowledge about the drug or its side effects. This is in line with a recent study done in Lebanon by Mallah et al. who showed that the less knowledge about the hazards and side effects of tranquilizers, the higher the risk of misuse. Additionally, most patients (91.0%) with Deanxit use disorder learned about Deanxit from their physicians, obtained it from the pharmacy using a prescription, and were following up with their primary care physician. This suggests that physicians are overprescribing Deanxit and lack adequate knowledge about its potential use disorder and dependence. The study by Mallah et al. found that subjects who have been followed up by a physician are less likely to misuse tranquilizers. This is in contrast to our study's findings, where there was no significant difference in following up with a primary care physician between those with Deanxit use disorder and those without [13].

Based on the DSM-5 criteria, only 20.0% of the participants had signs of dependence, and about a third suffered withdrawal symptoms when they tried to decrease their use. This low number of patients with withdrawal symptoms can be explained by the fact that only 25 participants out of 125 have tried to discontinue using Deanxit [6]. When assessing the reasons for Deanxit use, almost all (95.5%) patients who were classified with Deanxit use disorder were using it, either for panic attacks, anxiety, or to relax. This is consistent with a previous study by Haddad et al. in Lebanon that showed significantly high rates of anxiety disorders in people with substance use disorder [4].

Interestingly, our data show that 75.0% of patients believe that there is a low chance of addiction to Deanxit. Patients in Lebanon perceive Deanxit as a safer alternative to other antidepressants and benzodiazepines; however, this perception is not based on any proven robust published data. This could be because many prescribers also have the same perception towards Deanxit. In addition, our study results show that patients can develop dependence and a Deanxit use disorder.

Deanxit use disorder was significantly associated with being diagnosed with a psychiatric illness. This is not surprising, as a dual diagnosis of substance use disorder and a mental disorder is not uncommon. Moreover, dual diagnosis in young people puts them at a greater risk for multiple hospital visits, suicide attempts, interpersonal connection issues, homelessness, worse treatment results, participation with the criminal justice system, and premature mortality. Therefore, early intervention for substance use disorder is a must, especially since the earlier onset of substance use disorder has been linked with poorer outcomes [14].

Our study had some limitations, it is a single-center cross-sectional study conducted via a telephone survey that subjected our results to recall and social desirability bias. Nevertheless, recall bias was limited because approximately (76.2%) of those who were called were still using Deanxit at the time of the phone call. Additionally, the COVID-9 pandemic has limited our data collection to be telephonic rather than face-to-face. However previous nationwide studies have used telephonic interviews.

## 5. Conclusion

In conclusion, Deanxit use disorder is underrecognized among Lebanese patients who have easy access to Deanxit through prescription and at pharmacies without a prescription. Most of our patients who have a use disorder learned about Deanxit from physicians and followed up regularly with their physicians but still reported inadequate knowledge of its adverse effects and abuse potential. These findings highlight the lack of proper patient education. Future research efforts should be directed at collecting epidemiologic data regarding Deanxit misuse to better characterize the scope of this problem. Additional studies are required to gain further insight into the specific pharmacologic properties contributing to Deanxit misuse. To limit Deanxit use disorder, we advocate that the ministry restricts or bans the use of Deanxit as there are no robust studies on the efficacy of Deanxit and its comparison to other alternatives for anxiety and depression. In addition, proper education is needed for both physicians and the population on these medications to decrease utilization and side effects.

### Author contribution statement

Tharwat El Zahran, MD: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Sally Al Hassan, MD: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Malak Khalifeh, MD: Lina Hammoud, MD: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Diana Aboukhater: Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper. Moustafa Al Harirri, MD: Conceived and designed the experiments.

Ziad Kazzi, MD: Conceived and designed the experiments; Wrote the paper.

## Data availability statement

Data will be made available on request.

## Additional information

Supplementary content related to this article has been published online at [URL].

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15847.

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