Ministry of Higher Education & Scientific Research

Republic of Iraq

University Of Basrah

College Of Pharmacy

Graduation project
(2022\2023)

Anxiety, depression and antidepressant drug usage among Iraq medical universities students.

Presented by:

Kawthar Mazin Hassan

Fatima Bashir jawad

Ohoud Alaa Abdul-Latif

Supervised by

department of pharmacology and toxicology:

Dr. Shaima nadim

Dr. Zainab Harun

بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

الحمد لله، والصلاة والسلام على رسول الله وآلِ بَيتهِ الطيبين الطاهرين ، أما بعد : يقول الله تبارك وتعالى:

(وَآخِرُ دَعْوَاهُمْ أَنِ الْحَمْدُ لِلَّهِ رَبِّ الْعَالَمِينَ)

[يونس:١٠]

Dedication

إهداء..

الى شهدائنا الملائكه..

الى كل من علمني حرفاً..

الى من سنا ضيائهم ينير الطريق .. العائلة الساندة..

الى من حصد الاشواك ليمهد لنا طريق المعرفة ، آبائنا العظماء.

الى من طرّزن أيامنا بالسعادة ، و جعلنَ للابتسامة معنى، أمهاتنا الشامخات.

الى العائلة الصغيرة التي انجبتها مواقف الأيام ، رفاق الخطوات الأولى والأخيرة.

نحن ممتنون

Acknowledgment

We would like to express our special thanks of gratitude to Dr. Shaima nadim as well as Dr. Zainab Harun who gave us the golden opportunity to do this wonderful project on the topic “Anxiety, depression and antidepressant drug usage among Iraq medical universities students”,which also helped us in doing a lot of research and We come to know about so many new things.

We would like to thank Dr. Muhsin Sagheer Ghalib ,the leader of department of pharmacology and toxicology for his encouragement .Also to our college and all the doctors that were a part of our journey to make our dream come true and make us proud to complete these road successfully with them.

Finally, would also like a thank our friends who helped us a lot in finishing this project within the limited. It helped us increase our knowledge and skills.

THANKS AGAIN TO ALL WHO

SUPPORTED

Project Accomplishers :

Kawthar Mazin Hassan

Fatima Bashir jawad

Ohoud Alaa Abdul-Latif

Abstract

Depression is a mental health disorder effect more than 300M people world wide, characterised by sadness, loss of interest or pleasure, feelings of guilt or low self- worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration. Depression can be long- lasting or recurrent, substantially impairing an individual's ability to function at work or school or cope with daily life. At its most severe, depression can lead to suicide. It involves two subcategories are major depressive disorder or episodes and dysthymia .The dysthymia symptoms are similar to depressive disorder , but be mild and stay longer. There are other contrast for people with depression is the history the manic episode which is elevation in mood , Like in patients with bipolar episodes.

Anxiety disorders are mental disorders that characterised by anxiety and fear feelings, including post-traumatic stress disorder (PTSD), panic disorder, phobias, obsessive-compulsive disorder (OCD),social anxiety disorder and generalised anxiety disorder (GAD).symptoms can range from mild to severe as with depression it's duration when experienced with people with anxiety disorders become more chronic than episodic. Even more sever cases of depression could be treated if treatment began Earlier.The depression treatment usually involved medications , psychotherapy or a combination of them. electroconvulsive therapy (ECT) and other brain stimulation therapy may be an option if medication not elevate the symptoms .

There are a multiple types of psychotherapy can help people by make them learn how think and behave and how to change the bad habits of depression.

Antidepressants use as treatment of depression. They control the brain certain chemicals to regulate the mood and stress. The goal of the treatment: is to increase the neurotransmitter (serotonin & norepinephrine) by inhibiting its reuptake or its break down by using : Selective Serotonin Reuptake Inhibitors , Serotonin-Norepinephrine Reuptake Inhibitors, Monoamine Oxidase Inhibitors, Atypical Antidepressants and Tricyclic Antidepressants By trying many antidepressants to find the one that treat the patient better with fewer side effects. It takes around 4-8 weeks to work , usually other symptoms like sleep, appetite, and concentration will be better before mood lift .

Introduction

Depression is one of the mood disorders that make a continuous sad feelings and lack of interest. called clinical depression or major depressive disorder, it change how you think, react ,see things and feel it and can result in a different emotional and physical complications. You may face some difficulty through your daily life[1]. clinical depression isn't only a bad mood, it's not a weakness and you simply can't just "get out" of it. It dose required a long-term treatment[2]. You should have a commitment to continue your therapy by psycho therapy, medication or both and have faith that you will be be better.[3]

General symptoms of depression: Depression could happened once in life time or may experience multiple episodes . The episodes involved many symptoms that happened most of the day or all day long [4]. These symptoms include:

1-emotional symptoms (due to low serotonin): Depressive people have variety of symptoms . The severity , frequency and duration of them. will vary depending on the person him self and The symptoms are :

~ Persistent sadness , anxiety or feeling empty .

~ Feeling hopeless and/or pessimism.

~ Feelings of guilt.

~ Have a suicidal thoughts or attempts.

2-biological symptoms (due to low norepinephrine) :

~ Insomnia, early-morning wakefulness, or excessive sleeping.

~ Overeating, or appetite loss,Persistent aches or pains, headaches, cramps or digestive.

A lot of depressed people deal with severe symptoms .That cause a noticeable effect on daily activities , like work, college ,relationships and social life. Leads to feel very sad and unhappy with our knowing why .[5]

TYPES OF DEPRESSION

Mood regulation disorders : Severe recurrent outbursts of temper without much provocation + constantly irritable throughout the day. **Major depressive disorder :** Depressed Mood\ Lack of interest in activity for 2 weeks + the following symptoms: Change in sleep, lack of appetite, Feeling worthless, Guilt ridden. which involves symptoms such as depressed mood, loss of interest and enjoyment, and decreased energy; depending on the number and severity of symptoms, a depressive episode can be categorised as mild, moderate, or severe. **Dysthymia :** chronic mild depressive episode for 2 years at least, for the most week days .[6] **Bipolar disorder :** mood cycling changes from very highs (e.g., mania is high energy and mood elevations , resulted in hyper activity, speech pressure and less sleep) to very lows (e.g., depression) separated by periods of normal mood.**Substance induced depressive disorder :** Due to direct physiological effects of a substance or medical condition. **Premenstrual depression :** Outbursts of Temper,Irritability,Fighting with loved ones starting a week before menses and improving after your cycle. **Postpartum depression :** much more serious than the "baby blues" when hormonal and physical changes and the new responsibility of caring for a newborn can be overwhelming.[7] **Because another medical condition :** Most episodes of depression has direct physiological effect of substance including medication. **Atypical depression :** Characterised by oversleeping and over-eatingFor instance, mood brightens in response to positive events. **Seasonal effective disorder :** depression in months of winter.[8]

Causes depression

Caused by multiple factors like genetic some types run in the family however could happen without family link , environmental, biochemical and psychological . The depressive illnesses are a one of brain disorder . Genetics research shows increase the risk of depression caused by various genes acting together with environmental or other factors. Also having trauma , losing a beloved one , having difficulties with your relationships like family and in addition to any stressful conditions going through that act as triggering factors for depressive episodes that may happen with or without the trigger .

Magnetic resonance imaging (MRI) one of Brain-imaging technologies, show there are differences between brain of normal and depressive people in figure1. Some parts appear to be abnormal like that responsible of the mood, thinking, sleep, appetite and behaviour. Also , Some neurotransmitter get imbalanced . But these imaging not show particular reason of is circumstance. [9]

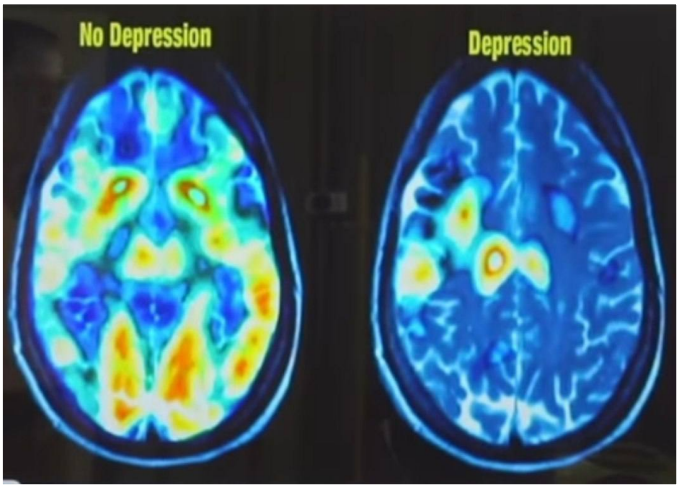

Figure 1: MRI show differences between brain of normal and depressive people.

Pathophysiology of depression according to two theories:

firstly could be genetic (due to four gene) . Secondly biological amine and receptors theory: mostly common suggests that depression resulted from decreasing in neurotransmitters as serotonin & norepinpherine levels Or from increase in serotonin receptors as 5HT-2A &“ 5HT-2C .[2]

Depression detection and treatment

Depression, consider a highly treatable even some of sever cases. Like many other illnesses when treatment begin earlier the more efficient the results are this may lessen the recurrence of it is. Firstly getting a suitable treatment is by visiting appropriate physicians. There are some medication and conditions like thyroid disorders or some types of virus can make symptoms like depression. A physician can eliminate these possibilities by making some lab tests , physical examination and doing some interviews. So if confirmed that may have a psychological issue refer it to mental health professionals , then they continue to get the diagnosis. By discussing the family history with depression and history of the symptoms when dose it start , it's duration and severity and also asking if it happened before and what they get to treat it , if they take any drug , alcohol or other medication. Importantly should ask if had suicidal thoughts or attempts. Whenever the diagnosis completed starting his healing gurney using psychotherapy or /and medication.[4]

Psychotherapy or talk therapy

There are a several types that approved to help people with their depression. The regimes are different depending on the person state so there're a short term ones for 10 to 20 weeks or others may be longer.

There're two main types CBT and IPT have shown their effectiveness by help the patient to adapt new ways to think and act away . Firstly CBT stands for cognitive behavioural therapy helps people to change the negativity of thinking and behaving that contribute with their depression and the second is IPT for interpersonal therapy that helps people to get over , understand and working a troubles in their personal relationships that may cause or make their depression worse. For mild to moderate depression this therapy may be the best treatment to their case .However in certain cases or major depression this therapy may not be enough so the studies suggest the psychological therapy with certain types of medications is the best approach to adolescence has the previous cases of depression and may reduce it's recurrence [10].similar to that other studies that have examined treatment of depression to older adults found that patient who responded to initial treatment of medication and IPT were less likely to have depression recurrence if they take their compilation therapy continuously for 2 years.[11]

Pharmacological treatment

(1) Tricyclic antidepressants: The efficacy is equal to SSRIs but with more anticholinergic adverse effects and the lowest dose to reach overdose [12,13].

MOA: They block the reuptake of serotonin and norepinephrine in presynaptic terminals, which leads to an increased concentration of these neurotransmitters in the synaptic cleft. The increased concentrations of norepinephrine and serotonin in the synapse likely contribute to its anti-depressive effect [14,15], In addition to that it had antimuscarinic &antihistaminegic effects . According to the structure affinity towards the receptors different Secondary amines including [desipramine, nortriptyline, and protriptyline] that have a greater affinity to blockage norepinephrine reuptake, while tertiary amines consist of a [amitryptiline, clomipramine, doxepin, imipramine, and trimipramine] that have a greater affinity as serotonin reuptake inhibitors [16]and serotonine syndrome.

Route of administration: Orally [tablet and capsule&solution].

AE/SE: Anticholinergic side effect +orthostatic hypotension (due to alpha 1 receptors blocked) and increased appetite, weight gain, confusion, sedation (anti histaminergic effects) and suicid behaviours [17,18].

Pregnancy and breastfeeding : Pregnancy [congenital defect especially eye, neck, ear, face defect, cardiac defect(especially with clomipramine) [19,21]and for breastfeeding: Nortriptyline is the safest one due to its non sedation effect All other TCAs are not safe except Doxepin, nortriptyline[20].

Contraindication: family history of cardiac death or QT interval prolongation ,hypersensitivity, reaction to TCAs, with MAOIs due to risk of developing serotonin crisis , So patients should be discontinued MAO is 2 weeks before starting TCAs, patient suffering from a seizure which leads to an increased risk of attack (decrease seizure threshold)and patient with prostate (urinary retention)+hepatic disease [19,20,21].

(2) SSRI: include fluoxetine (Prozac), citalopram (Celexa), sertraline (Zoloft), and several others. Serotonin and norepinephrine reuptake inhibitors (SNRIs) are similar to SSRIs and include venlafaxine (Effexor) and duloxetine (Cymbalta). SSRIs and SNRIs are more popular than the older classes of antidepressants, Considered the first-line antidepressant due to their safety &efficacy &tolerability and they are approved to use in children and adolescents patients [22]

MOA: acts by inhibiting presynaptic reuptake of serotonin to increase its concentration in the synaptic cleft . Reverse other antidepressants have a lower effect on other neurotransmitters (dopamine, norepinephrine)[22,23] have lowered side effects (anticholinergic, antidopaminergic, and antihistaminic side effects) in comparison with another antidepressant [24]. Available orally (tablet, capsule, liquid) once daily administration in the morning or nighttime regardless of the meals (except vilazodone taken with food) [24]. The effect of SSRIs may take up to 6 weeks before the patients feel the effects of treatment.[24,25] If patients tolerate the current dose well, the clinician can consider an increase in dosage after several weeks. All patients under the age of 25 should be continually assessed for suicidal ideation and other unusual behaviours, as highlighted in the FDA black box warning for all SSRI medications.

SE/AE: The most common side effects associated with SSRIs and SNRIs include: Headache usually temporary and will subside. Nausea—temporary and usually short lived. Insomnia and nervousness (trouble falling asleep or waking often during the night may occur during the first few weeks but often subside over time or if the dose is reduced, Agitation (feeling jittery) and sexual problems in both men and women can experience sexual problems including reduced sex drive, erectile dysfunction, delayed ejaculation, or inability to have an organs Serotonin syndrome [24,25,26].

Contraindications: Use with MAOIs, linezolid, and other medication that increase serotonin level. In pregnancy category D/X (especially paroxetine causing cardiac malformation, especially in the first trimester[27,28]. SSRI overdose is relatively infrequent due to their increased safety profile and

tolerability compared to other classes of antidepressants. SSRI overdoses are rarely fatal and usually do not have serious consequences. Out of all the SSRIs, citalopram and escitalopram are more likely to cause overdose due to differences in their structures. Citalopram and escitalopram have an increased risk of cardiotoxicity due to QT prolongation, which can progress to serious arrhythmias such as Torsades. Serotonin syndrome is a life-threatening consequence of increased serotonergic activity. It can result from overdosing on SSRIs . Serotonin syndrome is characterised by mental status changes, autonomic dysfunction, and dystonias. Findings may include agitation, tachycardia, hypertension, hyperthermia, hyperreflexia, tremor, nausea, vomiting, and clonus.[29] Serotonin syndrome may present similarly to neuroleptic malignant syndrome and malignant hyperthermia. This is especially important to keep in mind since commonly prescribed psychiatric medications can cause both serotonin syndrome and neuroleptic malignant syndrome. Serotonin syndrome also has a rapid onset and resolution.

Management : there's no definitive treatment only supportive initially SSIRS discontinuation,benzodiazepines for agitation and Cyproheptadine has shown some success in several small studies and case reports for patients who do not respond to initial treatment.[29]

(3)Monoamine oxidase inhibitors (MAOIs) :

are a separate class from other antidepressants, treating different forms of depression and other nervous system disorders such as panic disorder, social phobia, and depression with atypical features. Even though MAOIs were the first antidepressants introduced, they are not the first choice in treating mental health disorders due to several dietary restrictions, side effects, and safety concerns. MAOIs are only a treatment option when all other medications are not useful .[30]

MOA: Monoamine oxidase inhibitors are responsible for blocking the monoamine oxidase enzyme. The monoamine oxidase enzyme breaks down different types of neurotransmitters from the brain: norepinephrine, serotonin, dopamine, and tyramine. MAOIs inhibit the breakdown of these neurotransmitters thus, increasing their Level. There are two types of monoamine oxidase, A and B. The MAO A is mostly distributed in the placenta, gut, and liver, but MAO B is present in the brain, liver, and platelets. Serotonin and noradrenaline are substrates of MAO A, but phenylethylamine, methylhistamine , antryptamine are substrates of MAO B. Dopamine and tyramine are metabolized by both MAO A and B. Selegiline and rasagiline are irreversible and selective inhibitors of MAO type B, but safinamide is a reversible and selective MAO B inhibitor. MAOIs are reversible or irreversible. Moclobemide is an example of a reversible MAOI I (RIMA), tranylcypromine, phenelzine, isocarboxazid, and selegiline irreversibly inhibit MAO. Selegiline in low doses is a selective, irreversible MAO B inhibitor, but it is no longer selective at higher doses.[30]

Administration: MAOI administration is almost always orally but sometimes comes in the form of a skin patch.The skin patches were FDA approved and can be more beneficial to patients than oral dose forms. An example of this is selegiline, which can be given in a skin patch and causes fewer side effects than oral administration.Patients with lower doses of MAOIs may not have to be as strict with their diet as those with higher doses.[30]

AE/SE : Hypotension, Atropine like effects:dry mouth ,blurred vision, urinary retention, CNS stimulation: Insomnia Tremors excitement convulsions ,shifting to the mania and weight gain associated with increased appetite 5-Hypertensive crisis (cheese effect)[30] MAOIS Contraindications: Contraindicated when one of the following is present: Cerebrovascular disease Hypertension Congestive heart failure Liver disease Food with tyramine and dopamine[30]

Toxicity : there is no specific antidote for MAOI toxicity, and dialysis is unhelpful in removing the drug. An overdose of MAOIs, or use in combination with other serotonergic agents, may lead to serotonin toxicity. Likewise, the use of MAOIs with sympathomimetic agents may lead to the development of a hypertensive crisis.

When managing serotonin syndrome, early transfer to a medical ICU and consultation with a toxicologist is strongly advised. Diagnosis of serotonin toxicity is possible using the “Hunter criteria” or the “Sternbach criteria” based on physical manifestations.[22] The mainstay of management is the discontinuation of the serotonergic agent and supportive care, where most patients improve within 24 hours.[31] In cases of hypertensive crisis, immediate admission to the ICU for prompt blood pressure control with a parenteral, titratable antihypertensive agent while the patient remains on a vitals monitor is necessary. Urine output measurements and a neurologic examination should also take place. BP correction should be slowly achieved over several minutes to an hour, and not immediately. The goal is to lower the BP to no less than 20% to 25% during the first hour.[32]

ICU for prompt blood pressure control with a parenteral, titratable antihypertensive agent while the patient remains on a vitals monitor is necessary. Urine output measurements and a neurologic examination should also take place. BP correction should be slowly achieved over several minutes to an hour, and not immediately. The goal is to lower the BP to no less than 20% to 25% during the first hour.[32].

(4) SNRIs The serotoninergic system is known to modulate mood, emotion, sleep and appetite and thus is implicated in the control of numerous behavioural and physiological functions. Decreased serotoninergic neurotransmission has been proposed to play a key role in the aetiology of depression. The concentration of synaptic serotonin is controlled directly by its reuptake into the pre-synaptic terminal and, thus, drugs blocking serotonin transport have been successfully used for the treatment of depression.

The class of serotonin and norepinephrine reuptake inhibitors (SNRIs) now comprises three medications: venlafaxine, milnacipran, and duloxetine. These drugs block the reuptake of both serotonin (5-HT) and norepinephrine with

differing selectivity. Whereas milnacipran blocks 5-HT and norepinephrine reuptake with equal affinity, duloxetine has a 10-fold selectivity for 5-HT and venlafaxine a 30-fold selectivity for 5-HT. All three SNRIs are efficacious in treating a variety of anxiety disorders. There is no evidence for major differences between SNRIs and SSRIs in their efficacy in treating anxiety disorders. In contrast to SSRIs, which are generally ineffective in treating chronic pain, all three SNRIs seem to be helpful in relieving chronic pain associated with and independent of depression. Tolerability of an SNRI at therapeutic doses varies within the class. Although no direct comparative data are available, venlafaxine seems to be the least well-tolerated, combining serotonergic adverse effects (nausea, sexual dysfunction, withdrawal problems) with a dose-dependent cardiovascular phenomenon, principally hypertension. Duloxetine and milnacipran appear better tolerated and essentially devoid of cardiovascular toxicity.[33]

There is evidence that the serotonin norepinephrine reuptake inhibitors (SNRIs) venlafaxine, milnacipran, and duloxetine, have probable superior antidepressant activity to most selective serotonin reuptake inhibitors (SSRIs), especially in more severe depression. Some patients, however, respond better than others to SNRIs. Several factors influencing response to milnacipran have been recently studied. The presence of certain polymorphisms related to noradrenergic neurotransmission has been shown to be related to different degrees or rapidity of response to milnacipran. In addition, patients with low pretreatment levels of plasma 3- methoxy-4-hydroxyphenylglycol have a better response to milnacipran. These recent genomic and neurochemical data confirm that milnacipran, in contrast to SSRIs and venlafaxine, has an impact on the noradrenergic system. Differences in metabolism determined by genetic variables in cytochrome P450 (CYP) 2D6 activity are a major determinant of venlafaxine levels to such an extent that genetically determined decreases in CYP 2D6 activity have been associated increased adverse effects. Milnacipran, which is not metabolized by the enzymes of the CYP system is not influenced by polymorphism of these enzymes. These preliminary data suggest that a patient's biochemical and pharmacogenetic characteristics may be useful in the future to help clinicians chose the most effective antidepressant medication [34] SNRIs decrease the neuroinflammation through multiple mechanisms including the reduction of blood or tissue cytokines or regulating complex inflammatory pathways: nuclear factor kappa-light-chain-enhancer of

activated B cells (NF-κB), inflammasomes, Toll-like receptor 4 (TLR4), peroxisome proliferator-activated receptor gamma (PPARγ). SNRIs show these effects in association with an antidepressant action. SNRIs have an anti-neuroinflammatory role which might contribute the antidepressant effect.[35]

Randomized trials have shown that selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have better safety profiles than classical tricyclic antidepressants (TCAs). We focused on comparing the common side effects of TCAs with those of newer generation antidepressants including SSRIs, SNRIs, mirtazapine, and bupropion. Some other side effects such as sexual dysfunction, bleeding, and hyponatremia were more prominent with either SSRIs or SNRIs.[36]

(5) Atypical antidepressants: are defined as not belonging strictly to a set classification of antidepressants. They are not SSRIs, cyclic antidepressants, or MAOIs. Most are derivatives of SSRIs and have additional pharmacologic effects that were selected in an attempt to decrease the undesirable side effects of traditional antidepressants.[37]

Atypical antidepressants have various mechanisms of action. Bupropion, for example, works by inhibiting the reuptake of dopamine and norepinephrine at the presynaptic cleft.[38]. Agomelatine works as an agonist at melatonin receptors MT1 and MT2. It also antagonizes serotonergic 5-HT2C receptors, promoting dopamine and norepinephrine release.[39]. Mirtazapine works by blocking alpha-2 adrenergic receptors on the cell bodies and nerve terminals, promoting the release of norepinephrine into the synapse. Furthermore, mirtazapine antagonizes the 5-HT receptor, which has been shown to increase norepinephrine and dopamine in the brain's cortical regions.[40] Adverse effect: Agomelatine-Hepatotoxicity , Mirtazapine-Sedation, Weight gain [41] and Bupropion-Seizures[42].

CI: Bupropion, an atypical antidepressant, has seizure disorder listed as a major contraindication. This contraindication applies to patients with an active seizure diagnosis or prior seizure activity history. Like other antidepressants, bupropion should not be used in patients taking monoamine oxidase inhibitors or drugs that can lower the seizure threshold.[43]

Materials and Methods Study

population

This was a cross-sectional study which the prevalence of anxiety, depression and use of antidepressants drugs among students, were investigated at Basrah University around Basrah city, Iraq on the month of December 2022 to April 2023. The study subjects included the pharmacology students of Basrah University participated in the study. In this regard, those who were refuse to fill the questionnaire, were absent during the study period, would not complete the questionnaire, or already were diagnosed with a mental illness or on treatment.

Study methodology

The study was performed through 3 stages of the procedure. In the beginning, literature review was done from online literature regarding the prevalence of anxiety, depression and use of antidepressants among going university students. The aim of literature review was to observe the rate of depression, anxiety prevalence and antidepressants drug use in other studies in both male and female students. Followed by the literature review, data collection step was executed by collecting data with the help of a survey questionnaire. Demographic data were collected on age, gender, course, year of study, year back status, number of siblings, birth order, relationship status with family and friends, and family income status. Also antidepressants and illegal drug usage was assessed by two types of questions about frequency of use and type of use. The alcohol, coffee consumption and exercise, sleeping patterns and smoking habits were also evaluated, how to use the medication ,When needed, the way to use the medicine diagnosed by a physicianAdvice friend’s regularly Parents' advice, did your condition improve after using these medicines, did your condition worsen after using these medicines, IF suffering from another chronic disease and it is treated Anxiety and depression were evaluated using a valid and reliable 14-item self-administered scale “Hospital Anxiety and

Depression Scale" (HADS). The questionnaire comprises seven questions for anxiety and seven questions for depression, and takes 2-5 min to complete.To assure the data quality more emphasis was given in designing data collection instrument. For its simplicity's Questions prepared and published electronically (as Google form). As a self-administered questionnaire, it can be designed to be answered easily. Proper instruction was given before the survey as to the importance of the study for the study subjects, the data collectors as well as the supervisors. The collected data has been reviewed and checked for completeness before data entry, thus the incomplete data has been discarded. The study was conducted after obtaining permission . They were requested to complete the questionnaire with full assurance about the confidentiality and anonymity of their information. The subjects were assured that the data will be used only for scientific purpose of the study. Pharmacy students were invited to fill out Google forms from different Universities From all over Iraq.

Statistical analysis Data entry and statistical analysis performed by google forms that get filled by medical student .To address the objectives of this thesis, both descriptive (percentages, mean and standard deviation) and inferential statistics were used.To analyse categorical variables, we calculated frequencies and percentages.

Results

Table 1. Shows the demographic and health characteristics of the university student population, including psychological distress load, gender and age.Among 400 invited candidates, 375 (response rate = more than 90%) medical, dentistry and pharmacy colleges students, who agreed to participate and completed the questionnaires and were included in the analysis.

Of the 375 students participated in the study, 94(25%) were males and 282 (75%) were females. Among of 375, 16\5(43.9%) were 20 or under 20 years old and 211 (56.1%) above 20 years old. 337 (89.6%) of the participants were healthy, while 39(10.4%) had a chronic diseases.

The details of the baseline demographic and socioeconomic characteristics are presented in table 1. Included variables on: Marital Status, 343(91.2%) of the students were single and the others were married or divorced ,88 (23.5%) of students were in a graduation year and the rest 287(76.5%)were not. 361(96%) had no year of Failure, 11(2.9%) had one year of failure and 4(1.1%) have more than one year of Failure. The majority of the participants 314(83.5%) were studying in in the same governorate and 26 (16.5%) were studying in College out of their governorate. The highest percentage of the participants (87%) were satisfied with their study and (13%) were not satisfied. worried of future life status was found in 263 (69.9%) of participants and 113(8.75%) They weren't worried.

Variable	**Participant (n=430)**	
	N	**(%)**
Age		
=< 20	165	43.9%
> 20	211	56.1%
Sex		
Male	94	25%
Female	282	75%

Study Years		
1st Year	55	14.6%
2nd Year	96	25.5%
3rd Year	73	19.4%
4th Year	47	12.5%
5th Year	17	4.5%
Graduation Year	88	23.4%
Years of Failure		
No Year of Failure	361	96%
One Year of Failure	11	2.9%
Twe Years of Failure	4	1.1%
Colleage in same Governorate		
Colleage in same Governorate	314	83.5%
Colleage out Governorate	26	16.5%
Family Ordering		
Oldest	120	31.9%
Middle	167	49.7%
Youngest	63	16.8%
The Only Son	6	1.6%
Marital Status		
Maried	30	8%
Single	343	91.2%
Divorced	3	0.8%
Family Relation		
Good	290	77.1%
Fair	72	19.1%
Bad	14	3.7%
Friends relation		
Good	218	58%
Fair	142	37.8%
Bad	16	4.3%
Missing one of Parent		
No	328	87.2%
Yes	49	12.8%
Study Satisfy		
Study Satisfy	327	87%
Study Unsatisfy	49	13%
worried of future life		
They weren't worried	113	30.1%
Worry of Future	263	69.9%

Table1 .Demographic and health characteristics of the student population

Table2. The details of daily activities and social habits are summarised in table 2. The majority of student stated daily sleeping hours about 5-8 hours, about 221 (58.8%) participants did not intake coffee. Regarding smoking habits status, 35(94.4%) were non-smoker. Of the 376 participants 148 (39.4%) were not complaining from depression or Stress while 120 (31.9%) of them had depression or stress before college and 108 (28.7%) had depression or stress after college. Also, 92.6% of study participants never took any psychotropic medicines, while7.4% used these medicines.

Variable	**Participant (n=430)**	
	N	**(%)**
Sleep Hours		
1-4 hrs	22	5.9%
5-8 hrs	234	62.2%
>8 hrs	120	31.9%
Smooking		
Non Smooker	355	94.4%
Smooker	21	5.6%
Coffae Drinking		
Not Drinking Coffae	221	58.8%
Drinking 1-2 Cups of Coffae	140	37.2%
Drinking >2 Cups of Coffae	15	4%
Depression or Stress		
Not Complain from Depression or Stress	148	39.4%
Have Depression or Stress Before Colleage	120	31.9%
Have Depression or Stress After Colleage	108	28.7%
Take psychotropic drug		
No take drug	348	92.6%
Take drug	28	7.4%

Table 2: The details of daily activities and social habits in study population.

Table 3. Shows the demographic and health characteristics of the psychotropic drug user, including psychological distress symptom, gender stratified. 89.3% of students were female, and (85.7%) of them were more than 20 years old. 89.3% of the user were single, 7.1% were divorced and 3.6% were married .The majority of the student were non smoker. 89.3% of the psychotropic drug user were healthy and had no chronic diseases. Furthermore 12 (42.9%) 0f them stated daily sleeping hours more than 8hrs.Half of the drug user were drinking 1-2 Cups of Coffee.
10(35.7%) were in Graduation Year and 18 (64.3%) were in non graduation year. 35.7% of the drug user had depression or stress before college and 60.7% had depression or stress after college. Prevalence of psychotropic drug using in students of first year, second year, third year, fourth year, fifth year and final year 7.1%, 3.6%, 21.4%, 28.6%, 3.6% and 35.7% respectively. 89.3% were had no Years of Failure, 3.6% had one year of failure and 7.1% had more than one year of failure.

67.9%0f the drug user students were Satisfied with their college but most of the user (71.4%) were worried of their future life. The proportion of participants those using the psychotropic drug was associated with birth order most of them 1(17, 60.7%) were the middle son in their family. 82.1% of drug user were living with parents and 17.9% were missing one parent. (10.7%) of the drug user had abad relationships with their families and friends.

Variable	**Take psychotropic drug (n=28)**	
	N	**(%)**
Age		
=< 20	4	14.3%
> 20	24	85.7%
Sex		
Male	3	10.7%
Female	25	89.3%
Family Ordering		
Oldest	5	17.9%
Middle	17	60.7%
Youngest	5	17.9%
The Only Son	1	3.6%

Marital Status		
Maried	1	3.6%
Single	25	89.3%
Divorced	2	7.1%
Family Relation		
Good	16	57.1%
Fair	9	32.1%
Bad	3	10.7%
Friends relation		
Good	11	39.3%
Fair	14	50%
Bad	3	10.7%
Missing one of Parent		
No	23	82.1%
Yes	5	17.9%
Graduation Year		
Graduation Year	10	35.7%
Before Graduation Year	18	64.3%
Chronic Diseases		
Healthy	25	89.3%
Have Chronic Diseases	3	10.7%

Variable	**Take psychotropic drug (n=28)**	
	N	**(%)**
Study Years		
1st Year	2	7.1%
2nd Year	1	3.6%
3rd Year	6	21.4%
4th Year	8	28.6%
5th Year	1	3.6%
Graduation Year	10	35.7%
Years of Failure		
No Years of Failure	25	89.3%
One Year of Failure	1	3.6%
Two Years of Failure	2	7.1%
Colleage in same Governorate		
Colleage in same Governorate	18	64.3%
Colleage out Governorate	10	35.7%

Study Satisfy		
Study Satisfy	19	67.9%
Study Unsatisfy	9	32.1%
worried of future life		
Not worried	8	28.6%
Worry of Future	20	71.4%

Table4. Showed the medication knowledge among the psychotropic drug user. The items included those on the source of taking the drugs in which the higher percentage(23,82.1%)taking the drugs by doctor and pharmacist guidance while (3,10.7%) on self medications and (2,7.1%)taking their drugs based on family and friend advice.

Also on rhythm of drug use (17,60,7%)were taking the drug on need and (11,39.3%) were taking drug regularly,(168,44.8%). Regarding health status Improvement after psychotropic drug use most of the participants (67.9%) had improvement, (17.9%) had no health improvement and (14.3%) of them feel worse.

Variable	**Take psychotropic drug (n=28)**	
	N	**(%)**
Sleep Hours		
1-4 hrs	5	17.9%
5-8 hrs	11	39.3%
>8 hrs	12	42.9%
Smooking		
Non Smooker	26	92.9%
Smooker	2	7.1%
Coffae Drinking		
Not Drinking Coffae	10	35.7%
Drinking 1-2 Cups of Coffae	14	50%
Drinking >2 Cups of Coffae	4	14.3%

Depression or Stress		
Not Complain from Depression or Stress	1	3.6%
Have Depression or Stress Before Colleage	10	35.7%
Have Depression or Stress After Colleage	17	60.7%

Variable	**Participant (n=28)**	
	N	**(%)**
How Take Drug		
On Need	17	60.7%
Regularly	11	39.3%
Way Take Drug		
Doctor Prescription	23	82.1%
self midications	3	10.7%
Family and Friend advise Advice	2	7.1%
Health status Improvement after taking drug		
Health status Improved	19	67.9%
No Health Improvement	5	17.9%
Health status Worsed	4	14.3%
Chronic Disease Drug		
No Medication taken	21	53.8%
Chronic Disease Drug	18	46.2%

Table 4. Medication knowledge among the psychotropic drug user.

Figure2

Regarding the type of psychotropic medicines used (Figure1), the most common medications included sedatives and hypnotics (46.4%), selective serotonin reuptake inhibitor (SSRIs) (42.9%) followed by tricyclic antidepressants (21.4%),and atypical antipsychotic (7.1%).

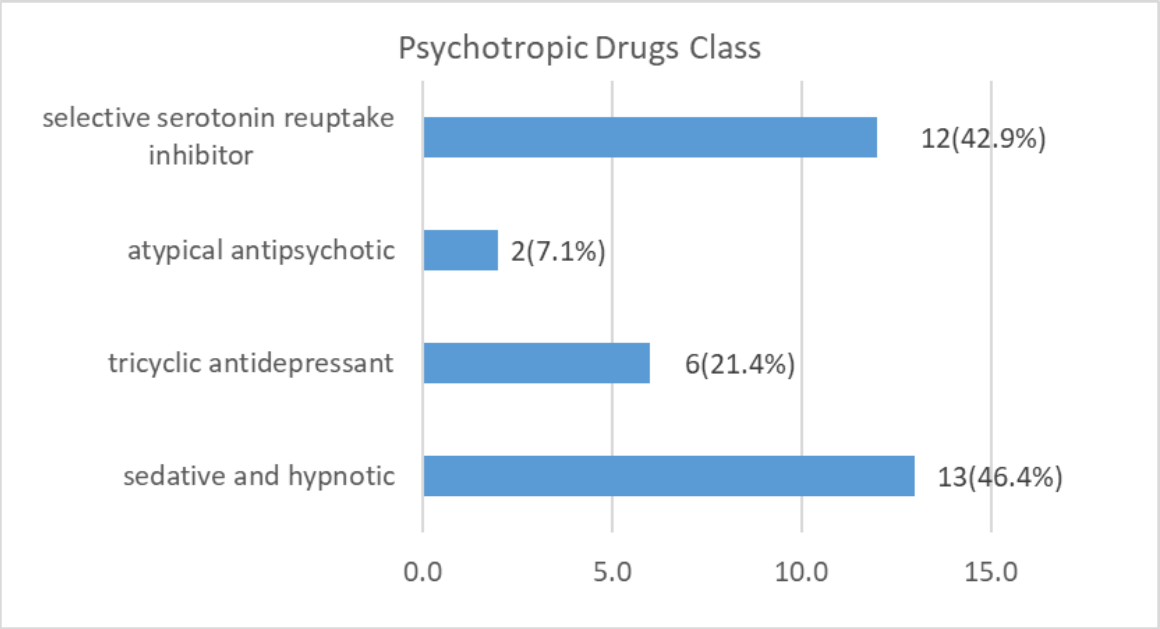

Figure 2: psychotropic drug type intake

Discussion

This large, wide study of more than 400 Iraq students from all medical faculties and universities, provide information on psychotropic drug usage among students in relation to psychological distress, previously scarcely described in the literature. The prevalence of psychotropic drug use was mainly in line with results of previous studies[44,45] . Both female and male students typically used antidepressants daily, while selective serotonin reuptake inhibitors and hypnotics were used more sporadically, which is according to clinical guidelines[46,47] . Female students were more frequent users of antidepressants than males , selective serotonin reuptake inhibitors (12vs. 42.9% last month) and hypnotics (13vs. 46.4% last month), while the opposite was reported for tricycle antidepressant (6 vs. 21.4%). Overall, these results align with previous research on gender differences in mental health and help-seeking [48,49]. In contrast, within cases (HSCL cut-off at ≥ 2.0) patterns of psychotropic drug use were very similar in males and females, and they were about twice as likely to take any of the psychotropic drug classes, compared to controls (HSCL <2.0).

This study describes a student population where approximately one quarter of the respondents showed a moderate to severe symptom load of anxiety and depression, and a previous study has concluded that both the level and increasing prevalence of psychological distress among Iraq students is worrying [50]. We found that the prevalence of psychotropic drug use varied between genders and classes of psychotropic medications.Previous studies have emphasised that sleep problems among students are prevalent and increasing [51], and insomnia prevalence is considerably higher in university students compared to the general population[52]. Therefore, continued monitoring of hypnotics use among students is warranted, with special focus on antidepressant use and effects in this population.

This study describes a prevalence of performance-enhancing drug use, including stimulants the last month, of 89.3% and 10.7% among females and male students, respectively. We cannot conclude whether these drugs were illicit or misused drugs. However, a previous study described that a substantial

proportion of the Basrah students have tried illicit drugs, and females more so than males [52]. A meta-analysis described the misuse of stimulant medications among students as a prevalent and growing problem[53]. Altogether, these results confirm the need of continued monitoring prevalence of psychotropic drug use among students and highlight the need of safeguarding the correct use of psychotropics, in addition to ensuring patient safety strategies in this population. Previous studies of young adults with mental health conditions have confirmed that females are more likely to receive treatment than males [54, 55]. In this study, the self-reported receipt of mental health treatment was examine among students of first year, second year, third year, fourth year, fifth year and final year were 7.1%, 3.6%, 21.4%, 28.6%, 3.6% and 35.7% respectively. 89.3% were had no Years of Failure, 3.6% had one year of failure and 7.1% had more than one year of failure. 67.9% of the drug user students were Satisfied with their college but most of the user (71.4%) were worried of their future life. The proportion of participants those using the psychotropic drug was associated with birth order most of them 1(17, 60.7%) were the middle son in their family. 82.1% of drug user were living with parents and 17.9% were missing one parent. (10.7%) of the drug user had a bad relationships with their families and friends. Regarding the type of psychotropic medicines used, the most common medications included sedatives and hypnotics (46.4%), selective serotonin-reuptake inhibitor (SSRIs) (42.9%) followed by tricyclic antidepressants (21.4%),and atypical antipsychotic (7.1%)

In our study, however, the use of psychotropic drugs among female and male students with psychological distress was different in the psychotropic drugs classes . Evidently, help-seeking involves opportunities for diagnosis and treatment, and implies positive association to medication usage. However, several factors are known to affect the use of mental healthcare among young adults, e.g., type and severity of mental health problem, stigma, mental health literacy, socioeconomic position, healthcare organisation and infrastructure [48, 56] , that would subsequently influence possibilities for detection of treatment needs. Furthermore, help-seeking among students is generally low, varies between university and college campuses, and across student characteristics [57, 58, 59]. Accordingly, a high unmet need for treatment of mental disorders among students has been recognised [54,60] Further research regarding psychotropic drug use among students with mental health

problems is warranted, and should involve longitudinal studies, and examine gender differences of causal and treatment factors, as well as medication safety issues in this population. Furthermore, systematic strategies to increase detection of need for mental health treatment among university students is of great importance, and might need several interventions at different levels, including an interdisciplinary approach. Generally, health authorities and universities need to focus on student mental health, to reduce psychological distress among students, and encourage students to seek help when needed.

Strengths and Limitations

The main strength of this study is the high response rate more than 90% among sample of medical universities students ,also using a very accurate reference of studies in our research.

Limitations are mostly the number of people that participated in filling the form of our study and the potential selection bias regarding the prevalence measures and associations [61]. Often the only feasible method in large scale studies, self-reported symptom levels do not compare directly to diagnostic categories of these conditions. Similarly, the self-reported use of medication has obvious limitations compared to register data. The self-reported psychotropic drug usage was reported as daily or monthly prevalence, and are thereby not directly comparable to past-year prevalence commonly used in other pharmacoepidemiologic studies.

Conclusion

Depression is a serious condition that often can be effectively treated with available therapies. Side effects and drug interactions are barriers to successful treatment. Some side effects of antidepressants resolve with continued use while other side effects can be managed by dose reduction or adding other therapies. Appropriate management of side effects and avoidance of drugs that may interact with antidepressants may improve the success of antidepressant therapy.

References

[1]World Health Organization. Depression and other common mental disorders: Global health estimates. Licence: CC BY-NC-SA 3.0 IGO., 2017. URL http://apps.who.int/iris/bitstream/10665/254610/1/WHO- MSD-MER-2017.2-eng.pdf

[2] Lippincott Pharmacology 7 editions ,chapter 10

[3] Devane CL, Chiao E, Franklin M, Kruep EJ. Anxiety disorders in the 21st century: status, challenges, opportunities, and comorbidity with depression. American Journal of Managed Care, 2005 Oct; 11(Suppl. 12): S344-353.

[4] U.S. Department of HealtH & HUman ServiceS national institutes of Health niH publication no. 07-3561 revised 2007

[5]American Psychiatric Association. Practice guidelines for the treatment of patients with major depressive disorder.2nd ed. September 2007. Accessed January 22, 2010.

[6] Fava M, Cassano P. Mood disorders: Major depressive disorder and dysthymic disorder. In: Stern TA, Rosenbaum JF, Fava M, Biederman J, Rauch SL, eds. Massachusette General Hospital Comprehensive Clinical Psychiatry, 1st ed, Philadelphia, Pa: Mosby Elsevier; 2008:chap 29.

[7]Altshuler LL, Hendrich V, Cohen LS. Course of mood and anxiety disorders during pregnancy and the postpartum period. Journal of Clinical Psychiatry, 1998; 59: 29.

[8] Rohan KJ, Lindsey KT, Roecklein KA, Lacy TJ. Cognitive-behavioral therapy, light therapy and their combination in treating seasonal affective disorder. Journal of Affective Disorders, 2004; 80: 273-283.

[9]Tsuang MT, Bar JL, Stone WS, Faraone SV. Gene-environment interactions in mental disorders. World Psychiatry, 2004 June; 3(2): 73-83.

[10] Reynolds CF III, Dew MA, Pollock BG, Mulsant BH, Frank E, Miller MD, Houck PR, Mazumdar S, Butters MA, Stack JA, Schler- nitzauer MA,Whyte EM, Gildengers A, Karp J, Lenze E, Szanto K, Bensasi S, Kupfer DJ. Maintenance treatment of major depression in old age. New England Journal of Medicine, 2006 Mar 16; 354(11): 1130-1138.

[11] March J, Silva S, Petrycki S, Curry J,Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J. Treatment for Adolescents with Depression Study (TADS) team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. Journal of the American Medical Association, 2004; 292(7): 807-820.

[12] Anderson IM. Selective serotonin reuptake inhibitors versus tricyclic antidepressants: a meta-analysis of efficacy and tolerability. J Affect Disord. 2000 Apr;58(1):19-36.

[13] Thorstrand C. Clinical features in poisonings by tricyclic antidepressants with special reference to the ECG. Acta Med Scand. 1976;199(5):337-44. [PubMed]

[14] Hillhouse TM, Porter JH. A brief history of the development of antidepressant drugs: from monoamines to glutamate. Exp Clin Psychopharmacol. 2015 Feb;23(1):1-21. [PMC free article] [PubMed]

[15] Richelson E. Antimuscarinic and other receptor-blocking properties of antidepressants. Mayo Clin Proc. 1983 Jan;58(1):40-6. [PubMed]

[16] Gillman PK. Tricyclic antidepressant pharmacology and therapeutic drug interactions updated. Br J Pharmacol. 2007 Jul;151(6):737-48. [PMC free article] [PubMed]

[17] David DJ, Gourion D. [Antidepressant and tolerance: Determinants and management of major side effects]. Encephale. 2016 Dec;42(6):553-561.[PubMed]

[18] Drug interactions with selective serotonin reuptake inhibitors, especially with other psychotropics. Prescrire Int. 2001 Feb;10(51):25-31. [PubMed]

[19] Bérard A, Zhao JP, Sheehy O. Antidepressant use during pregnancy and the risk of major congenital malformations in a cohort of depressed pregnant women: an updated analysis of the Quebec Pregnancy Cohort. BMJ Open. 2017 Jan 12;7(1):e013372. [PMC free article] [PubMed]

[20] Gentile S. Tricyclic antidepressants in pregnancy and puerperium. Expert Opin Drug Saf. 2014 Feb;13(2):207-25. [PubMed]

[21] Lanza di Scalea T, Wisner KL. Antidepressant medication use during breastfeeding. Clin Obstet Gynecol. 2009 Sep;52(3):483-97. [PMC free article] [PubMed]

[22] Feighner JP. Mechanism of action of antidepressant medications. J Clin Psychiatry. 1999;60 Suppl 4:4-11; discussion 12-3. [PubMed]

[23] Xue W, Wang P, Li B, Li Y, Xu X, Yang F, Yao X, Chen YZ, Xu F, Zhu F. Identification of the inhibitory mechanism of FDA approved selective serotonin reuptake inhibitors: an insight from molecular dynamics simulation study. Phys Chem Chem Phys. 2016 Jan 28;18(4):3260-71. [PubMed]

[24] Preskorn SH. Clinically relevant pharmacology of selective serotonin reuptake inhibitors. An overview with emphasis on pharmacokinetics and effects on oxidative drug metabolism. Clin Pharmacokinet. 1997;32 Suppl 1:1-21. [PubMed]

[25] Perry PJ, Wilborn CA. Serotonin syndrome vs neuroleptic malignant syndrome: a contrast of causes, diagnoses, and management. Ann Clin Psychiatry. 2012 May;24(2):155-62. [PubMed]

[26] Graudins A, Stearman A, Chan B. Treatment of the serotonin syndrome with cyproheptadine. J Emerg Med. 1998 Jul-Aug;16(4):615-9. [PubMed]

[27] Baigel GD. Cyproheptadine and the treatment of an unconscious patient with the serotonin syndrome. Eur J Anaesthesiol. 2003 Jul;20(7):586-8. [PubMed]

[28] Horowitz BZ, Mullins ME. Cyproheptadine for serotonin syndrome in an accidental pediatric sertraline ingestion. Pediatr Emerg Care. 1999 Oct;15(5):325-7. [PubMed]

[29] McDaniel WW. Serotonin syndrome: early management with cyproheptadine. Ann Pharmacother. 2001 Jul-Aug;35(7-8):870-3. [PubMed]

[30] https://www.ncbi.nlm.nih.gov/books/NBK557395/

[31] Mason PJ Morris VA, Balcezak TJ. Serotonin syndrome. Presentation of 2 cases and review of the literature. Medicine (Baltimore). 2000 Jul;79(4):201-9. [PubMed]

[32] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Roccella EJ., National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003 May 21;289(19):2560-72. [PubMed]

[33] CNS spectrums 10, 732-747, 2005

[34] CNS spectrums 13 (S11), 15-21, 2008

[35] Inflammopharmacology29,75-90,2021

[36] Chonnam medical journal 54,101-112,2018

[37] https://accessemergencymedicine.mhmedical.com/content.aspx?sectionid=65097819&bookid=1163#1108432238

[38] Horst WD, Preskorn SH. Mechanisms of action and clinical characteristics of three atypical antidepressants: venlafaxine, nefazodone, bupropion.J Affect Disord. 1998 Dec;51:237-54.

[39] Hickie IB, Rogers NL. Novel melatonin-based therapies: potential advances in the treatment of major depression. Lancet. 2011 Aug 13;378(9791):621-31. [40]. Harmer CJ, Duman RS, Cowen PJ. How do antidepressants work? Newperspectives for refiningMay;4:409-418.

[41] Montgomery SA.Psychopharmacol. 1995

[42] Detyniecki K. Do Psychotropic Drugs Cause Epileptic Seizures? A Review of the Available Evidence. Curr Top Behav Neurosci. 2022;55:267-279.

[43] Zwar N, Richmond R. Bupropion sustained release. A therapeutic review of Zyban. Aust Fam Physician. 2002 May;31:443-7.

[44] Mccabe SE, West BT, Teter CJ, Boyd CJ. Trends in medical use, , and nonmedical use of prescription medications among college students from 2003 to 2013: connecting the dots. Addict Behav. (2014) 39:1176–182. 10.1016/j.addbeh.2014.03.008 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[45] Fond G, Bourbon A, Lançon C, Boucekine M, Micoulaud-Franchi JA, Auquier P, et al.. Psychiatric and psychological follow-up of undergraduate and postgraduate medical students: prevalence and associated factors. Results from the national BOURBON study. Psychiatry Res. (2019) 272:425–30. 10.1016/j.psychres.2018.12.174 [PubMed] [CrossRef] [Google Scholar]

[46] National Institute for Health and Care Excellence . Depression in Adults: Recognition and Management. NICE Clinical Guideline (CG90). (2009). Available online at: https://www.nice.org.uk/guidance/cg90 (accessed March 20, 2021).

[47] National Institute for Health and Care Excellence . Generalised Anxiety Disorder and Panic Disorder in Adults: Management (CG113). (2019). Available online at: https://www.nice.org.uk/guidance/cg113 (accessed March 20, 2021).

[48]Kovess-Masfety V, Boyd A, Van De Velde S, De Graaf R, Vilagut G, Haro JM, et al.. Are there gender differences in service use for mental disorders across countries in the European Union? Results from the EU-World Mental Health survey. J Epidemiol Community Health. (2014) 68:649–56. 10.1136/jech-2013-202962 [PubMed] [CrossRef] [Google Scholar]

[49]Boyd A, Van De Velde S, Pivette M, Ten Have M, Florescu S, O'neill S, et al.. Gender differences in psychotropic use across Europe: results from a large cross-sectional, population-based study. Eur Psychiatry. (2015) 30:778–88. 10.1016/j.eurpsy.2015.05.001 [PubMed] [CrossRef] [Google Scholar]

[50]Knapstad M, Sivertsen B, Knudsen AK, Smith ORF, Aarø LE, Lønning KJ, et al.. Trends in self-reported psychological distress among college and university students from 2010 to 2018. Psychol Med. (2019) 51:470–8. 10.1017/S0033291719003350 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[51]Sivertsen B, Vedaa O, Harvey AG, Glazier's N, Pallesen S, Aaro LE, et al.. Sleep patterns and insomnia in young adults: a national survey of Norwegian university students. J Sleep Res. (2019) 28:e12790. 10.1111/jsr.12790 [PubMed] [CrossRef] [Google Scholar]

[52]Jiang XL, Zheng XY, Yang J, Ye CP, Chen YY, Zhang ZG, et al.. A systematic review of studies on the prevalence of insomnia in university students. Public Health. (2015) 129:1579–84. 10.1016/j.puhe.2015.07.030 [PubMed] [CrossRef] [Google Scholar]

[52] Heradstveit O, Skogen JC, Edland-Gryt M, Hesse M, Vallentin-Holbech L, Lønning J, et al.. Self-reported illicit drug use among Norwegian university and college students.

associations with age, gender, and geography. Front Psychiatry. (2020) 11:1424. 10.3389/fpsyt.2020.543507 [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]

[53] Benson K, Flory K, Humphreys KL, Lee SS. Misuse of stimulant medication among college students: a comprehensive review and meta-analysis. Clin Child Fam Psychol Rev. (2015) 18:50–76. 10.1007/s10567-014-0177-z [PubMed] [CrossRef] [Google Scholar

[54] Bruffaerts R, Mortier P, Kiekens G, Auerbach RP, Cuijpers P, Demyttenaere K, et al.. Mental health problems in college freshmen: prevalence and academic functioning. J Affect Disord. (2018) 225:97–103. 10.1016/j.jad.2017.07.044 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[55] Brijnath B, Xia T, Turner L, Mazza D. Trends in GP prescribing of psychotropic medications among young patients aged 16-24 years: a case study analysis. BMC Psychiatry. (2017) 17:214. 10.1186/s12888-017-1375-2 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[56] Bjønness J. Gendered aspects of Danish students' non-medical use of prescription pharmaceuticals for enhancement purposes in the 'performance society'. Drugs Educ Prev Policy. (2019) 26:309–18. 10.1080/09687637.2019.1590530 [CrossRef] [Google Scholar]

[57] Barber M, Fairclough A. Verifiable cpd paper: a comparison of alcohol and drug use among dental undergraduates and a group of non-medical, professional undergraduates. Br Dent J. (2006) 201:581. 10.1038/sj.bdj.4814203 [PubMed] [CrossRef] [Google Scholar]

[58] Maier LJ, Liechti ME, Herzig F, Schaub MP. To dope or not to dope: neuroenhancement with prescription drugs and drugs of abuse among Swiss university students. PLoS ONE. (2013) 8:e77967. 10.1371/journal.pone.0077967 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[59] Tuv S, Strand M, Karinen R, Øiestad E, Christophersen A, Vindenes V. Effect and occurrence of synthetic cannabinoids. Tidsskr Norske Laegeforen. (2012) 132:2285–8. 10.4045/tidsskr.12.0471 [PubMed] [CrossRef] [Google Scholar]

[60] Lac A, Luk JW. Testing the amotivational syndrome: marijuana use longitudinally predicts lower self-efficacy even after controlling for demographics, personality, and alcohol and cigarette use. Prev Sci. (2018) 19:117–26. 10.1007/s11121-017-0811-3 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[61] Degenhardt L, Lynskey M, Hally W. Cohort trends in the age of initiation of drug use in Australia. Aust N Zeal J Public Health. (2000) 24:421–6. 10.1111/j.1467-842X.2000.tb01605.x [PubMed] [CrossRef] [Google Scholar]