

Stress, Anxiety, Depression:- A Complete Overview

Avani N. Joshi ¹, Kalpita D. Thakkar ², Vivek J. Jetani ³, Arshi A. Hasmani ⁴, Zahirabbas Z. Dhebar ⁵

¹Assitant Professor, Department of Pharmacy, Gyanmanjari Pharmacy College ²Student, Bachelor of Pharmacy, Gyanmanjari Pharmacy College ³Student, Bachelor of Pharmacy, Gyanmanjari Pharmacy College

⁴Student, Bachelor of Pharmacy, Gyanmanjari Pharmacy College

⁵Student, Bachelor of Pharmacy, Gyanmanjari Pharmacy College

Submitted: 01-05-2023 Accepted: 08-05-2023

ABSTRACT

In this modern contemporary era due to the modern lifestyle issues people have been going through chronic mental illness ailments such as anxiety disorders , depression , major depression , separation anxiety, social phobia, agoraphobia, mixed anxiety, etc. These issues are not only prevailing in the young adults, but also in the children and young pubescents. Moreover, it is quite important that these mental ailments are managed in the conventional manner. There are multiple drugs such as Pregabalin, the Tricyclic antidepressants, Buspirone, Benzodiazepines, etc which help in treating not only Generalized anxiety disorder but also treating other chronic mental ailments . Furthermore it has been proved that Not only pharmacotherapy but also Psychotherapy is used to treat the disorders of mental illness .In

addition to this, the cognitive behavioral therapy is quite useful in the treatment of generalized anxiety disorder. The anxiety disorders come with ample of comorbid complications such as panic disorders as well as the bipolar disorders. In order to deal well with the disorders of anxiety both the patients as well as the clinical therapist must work in a cooperative manner. The people who undergo conditions of stress, anxiety disorders, mood stability disorders, etc need extra emotional support and attention to their problems. Depression is a disorder that can lead a person turn into socially awkward introvert and can affect their healthy work life balance.

KEYWORDS:-Anxiety, Stress, Generalized Anxiety disorder, Depression, agoraphobia.

INTRODUCTION



Figure 1: Symptoms of Deoression



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

The majorly found mental ailments are entitled as Anxiety disorders. The prevalence of Anxiety disorders if more in females than in males by two or three times [1]. Anxiety disorders are one of the most chronic ailments amongst all the other illness, which tend to have a major impact on the lives of the patient [2].Furthermore, anxiety disorders can be categorised according to the International classification of diseases[3], that consists of not only the disorders of phobia but also panic disorders, agoraphobia, social phobia, specific phobia, generalised anxiety disorder, separation anxiety, mixed anxiety, depression etc ...[4].Moreover, the separation anxiety disorder can be classified by the tenacious and excessive anxiety which can be associated along with the separation of the patient with their near and dear ones [5,6]. The disorders of anxiety can be closely related with multiple conditions that are comorbid with the anxiety disorder itself. Moreover, the patients suffering from the anxiety disorders have an increased risk of further complications over the time. The term sequential comorbidity can be entitled for the situations where the anxiety disorders further lead to separation and panic

anxiety as well [7] . Not only this but there is more with the anxiety disorders, they may elevate the risk of developing other complicated ailments for instance depression, or its co related disorders [8]. The initial diagnosis as well as the treatment of the anxiety disorders may also potentially lead to a step that may be responsible effectively against the other mental ailments as well as the somatic disorders. This association which is in between the diagnosis and precautions, must be examined well for controlled series of trials . The anxiety disorders are those amongst the so called entitled as chronic and complex genetic ailments that are characterized by the complex pathogenetic interactions of both the environmental and other multiple variants of genes at the various loci of chromosomes . In addition to this the first degree relatives of the patient are most likely to acquire panic disorders, on comparison to others. Moreover the occurrence of the disease within some families in excess of what would be expected from the occurrence in the population can also be observed in not only the generalized anxiety disorders but also some specific phobias.

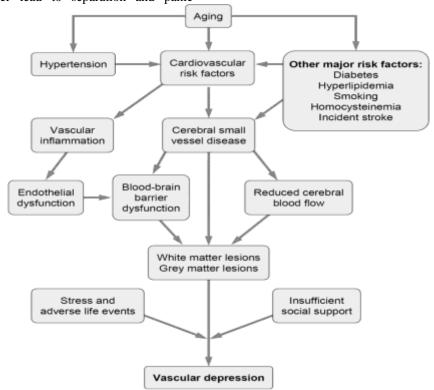


Figure 2: Pathophysiology of depression

Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

Life events for anxiety disorders:

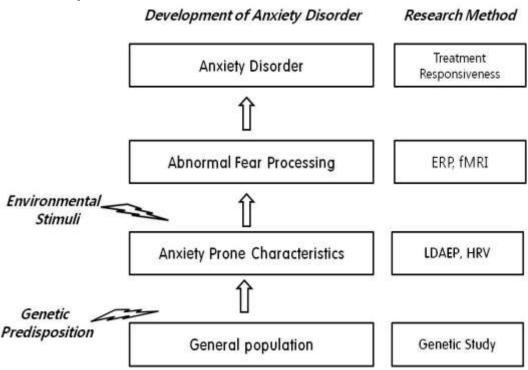


Figure 3: Pathophysiology of Anxiety Disorder

The degree of participation of the factors that are genetic in the development has a couple of life events [9]. For instance,

- Maltreat and failed to look after
- Sexual violence
- Disquieting injuries [10]
- Death of the near or dear ones
- Divorce or brutal separation
- Financial insecurities and problems [11]

The two therapies which include the pharmacotherapy and psychotherapy must be offered to the patient that is marked up to be equivalently effective . In addition to , in some cases, the psychotherapy alone is preferred on assessment in case of some specific phobias, where the drugs are not indicated in the treatment. For major types of anxiety disorders, the therapies that are cognitive behavioral therapy are mostly recommended [12]. Nevertheless, the therapies which are psychodynamic can be recommended to be offered when the cognitive behavioral therapies have proved to be not so effective [13]. However the cognitive behavioral therapy depends upon the particular type of the specific anxiety disorder that is supposed to be treated, In addition to this the patient must feel secured that its quite harmless

situation. In this particular situation, the best kinds of the expected outcomes can be achieved when the patient is under the supervision of the respective concerned therapist[14]. Furthermore, during the course of supervision it must be made sure that the patient is experiencing the habituation of the response to the anxiety, in order to eradicate the underlying fears[15]. Several stages for instance the stages of not only stress but also the stages of anxiety as well as tension and excitation etc can be cured by the means of the acute treatment using the Benzodiazepines . Moreover the Benzodiazepines are found to be effective for the treatment of panic disorders, social phobia, generalized anxiety disorders etc ...In addition to this they are also effective for treating the agoraphobia . However, it has been proved that they also tend to possess multiple side effects .Henceforth the usage of these must be terminated after a longer period of time .Major side effects include chronic complications such as attempt to suicides, cardiac arrest, cardiovascular diseases, contraindications etc, upon the observation of these adverse effects the drug must be discontinued [16]

Treatments:

While not only the cognitive behavioral therapy but also the psychotherapy and



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

pharmacotherapy therapy are given the first priority as the treatments to the anxiety disorders, there are other multiple clinically practiced treatment options such as

- Psychotherapy by the metacognitive means [17]
- Acceptance and commitment therapy[18]
- The techniques that based on mindfulness [19]
- Non invasive stimulation techniques [20]
- Exercises and physical activities [21]

Apart from the therapies of drugs there are specific guidelines for the clinical practice based treatment such as

- Counselling
- Psycho education about what is anxiety and its disorders
- Instructions for the exercises that allow anxiety confronting situations and the real life based situations
- Usage of the manuals which are responsible for self help

In the cases of anxiety disorders both the patients as well as the physicians must work as the joint effort is a necessity [22]. When the major ailments of mental illness are classified, depression is the major diagnostic category, which is amongst the disorders of the mood stability, comprising the dysthymia which can be defined as the low mood occurring for at least two years along with other two major signs and symptoms of depression, cyclothymia which is a mood stability disorder that causes the highs and lows and shifting of moods, as well as the bipolar disorders which are the disorders which are associated with the mood episodes that have swings which ranges from depressive lows to manic highs [23]. There is a series of multiple symptoms that indicate the signs of depression, for instance depressed and a very low mood, fatigue, low on energy, inability to feel pleasure, etc ...[23]Moreover various other signs and symptoms such as sleep disturbance as well as psychomotor disturbances, feelings of guilt , self doubt , low self confidence , tendency to attempt suicide, continuous appetite and food intake habits, irregular body weight, pessimism, etc can also be seen under special circumstances . Moreover it has been proven that the depression and mood stability disorder conditions are more prone to females than makes, the mathematical ratio expression of the females to males is as high as 5:2. Majorly, the depression course is marked to be recurrent, where the patients go through the time intervals with the episodes of signs and

symptoms and the stages of recovery periods . However, there are some patients having the chronic course of depression[24].Furthermore the most common depression manifestation can be considered as the depression that is prolonged for a time interval of about more than one year of duration [25]. In addition to this, the patients who are undergoing depression, tend to have an increased risk of the death which is premature than the other cases [26]. According to the studies which are epidemiological the patients have a huge risk of heart ailments, decreased life expectancy, because the depression itself is a major risk factor that leads to cardiovascular diseases, which yields to an increased risk of myocardial infection, other chronic ailments and also psychiatric disorders [27]. The mild yet so chronic manifestation of depression can be considered as the personality disorder which is a type of mental ailment that makes a person very rigid with a unhealthy thinking ability .which can also be further classified a distinct mood disorder dvsthvmia [28].Structured psychotherapy patterns for instance not only the cognitive behavioral therapy but also the interpersonal types play an important role for the outcomes which are positive as the sole treatment for the cases which are ,mild and not severe, along with the combination of the antidepressants in the cases which are slightly moderate or crucially severe [29]. Furthermore, the monoamine oxidase inhibitors as well as the tricyclic drugs have been potentially proven to be more effective as the antidepressants. Moreover, the antidepressants are group of the heterogenous drugs which on the primary basis acts on increasing the monoamines availability at the synaptic cleft[30]. In addition to this the development and synthesis of new drugs such as the selective serotonin reuptake inhibitors which have least number of side effects but at the same time they are much more effective than the already available drugs which are also tricyclic[31]. The major depression is the disorder which is a familial disorder that has the potency which can be carried a threefold increased risk in the first degree relatives on comparing the risk rate with the other general population . However the depressive disorders have been classified as the disorders which are genetically complex just like the cardiac diseases, cancer, diabetes mellitus, hypertension etc..[32].

The mood stability disorders such as the bipolar ailment or the major depression can be considered as the ailments which are the most commonly found psychiatric disorders of the



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

modern contemporary era in the society currently. According to a statistical data study it has been concluded that people undergo the bipolar disorders as well as the major depression at least one or even more times in their entire life tenure [33]. Although a complete amalgamation of multiple genetic factors can be responsible for being involved in the depression development because the defect in even a single gene can be potential to usually fail to induce the multifaceted expression of symptoms and signs of major depression [34]. The stress which is chronic is a crucial component in the depression, although it does not mark to function as a factor which is not only sufficient but also necessary factor. According to this perspective, The hypothalamic -pituitary-adrenal axis, is a crucial and basic neuroendocrine circuit that helps in not only stress management but also it has been a major concern of research topic for depression [35]. The information that is present on the brain as well as the neural circuitry is supposed to be responsible for the expression as well as the development of an ailment which is a crucial plan of action for a better diagnose of the ailment and to specifically interpret the obtained observations from the cellular, molecular as well as the experiments of the tissues which are in a clinically pertinent context .Although the regions of the brain are identified in the involvement of the mood regulatory actions as well as the emotions and also the definite information on the central neural circuits which maybe responsible for the disorders of the mood that is yet incomplete generally due to the anatomical lesions in the patients who are suffering and who have been less consistently found relative to the other disorders that are neurological for instance some neurodegenerative disorders [36].

However, not only the neuropathological but also the neuroradiological studies have proven the associations of corelations between the structural abnormalities as well as the disorders of mood in the brain . For instance, the glial reduction that was seen in the anterior cingulate gyrus as well as the neuropathological studies of the patients of the mood disorders [37]. The age of the initiation of the disorders of anxiety may differ from different disorders. Majorly the specific phobia as well as the separation anxiety disorders may start to initiate since the childhood days from the mean age of about 7 years which if further followed by the social anxiety disorders that starts from 13 years, furthermore, agoraphobia without the panic attacks that initiates from 20 years and the age of the

initiation of panic disorders is 24 years [38].Moreover the generalized anxiety disorders may also possibly start in the later phases of the life tenure [39].In addition to this the disorders of anxiety may tend to be present potentially run for a more longer and chronic course which tend to possess the fluctuating the symptoms in different severity between the time intervals of relapse and remission in the generalized anxiety as well as the agoraphobia and a more chronic course in the social phobia [40]. The ongoing approach of the etiological factors of the anxiety disorders may be an amalgamation of psychosocial factors for instance adversity in the childhood period, stress, genetic vulnerability, stress, that me potentially manifest in not only the neuropsychological but also the neurobiological dysfunctions [41].

Initially the obsessive compulsive disorders as well as the post traumatic stress disorders were mentioned in the classified categories of anxiety disorder however, they are now a part of the mental disorders [42]. In the hospitals, clinics, outpatient departments etc ...most of the patients who are willing to seek the help that helps them in the conventional management from the social phobia, agoraphobia as well as the generalized anxiety disorders [43] it isn't necessary to treat all the anxiety disorders with mild transient and the non associated impairment in the not only occupational but also the social functions [44]. Despite of that the treatment can be indicated whenever the patient shows remarkable distress or if at all the patient suffers from the conditions such as the suicidal attempt idea in mind, abuse of alcohol, and also the secondary depression. Furthermore, the anxiety disorders can mostly be cured on the outpatient means[45]. However the hospitalization indication may include the attempt to suicide, not giving any response by the patient to any sort of the treatment, or else the comorbidity that is corelated and relevant for instance major depression, disorders of the personality, as well as the substance abuse[46].In addition to this, the different patients with different anxiety disorders may tend to mark up different degrees of the utilization of the healthcare [47]. In contradiction to this the patients that undergo the agoraphobia usually are scared that they may have to suffer from a chronic somatic disability for instance the myocardial infraction and they might also require an immediate as well as the spontaneous medical help. Moreover the patients of simple phobias usually have an instinct that the may be able to

Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

cope the disability and also may potentially think of it as a normal situation that it is normal to be scared from things such as a spider or sometimes the fear of dogs as well . There is a verification about the substantial undertreatment of the disorders [48]. The people suffering from the ailments must receive the education and knowledge about the psychoeducation, that imparts them with the knowledge of the diagnosis, etiological factors as well as the disease mechanism of action, also the vivid approaches that have to be followed in order to cure the ailments . Moreover the plan of action for the treatment of the disorders must be an amalgamation pharmacotherapy, of the psychotherapy, as well as the other interventions that are necessary that can be chosen after carefully considering the factors of the individuals, for instance the preference mode of the patient, history of the patient which briefs about the initially preferred modes of treatments, severity of the illness, comorbid conditions, for example the disorders of the personality, rate of suicide attempt , locally available modes of treatment options and financial aspects its costs, as well as various other aspects [49]. Although , multiple studies have proved that the efficacy of the medications of the generalized anxiety disorders, agoraphobias, as well as the social phobias but the treatment options that include the studies for the specific types of phobias are lesser comparatively that also suggest the efficacy of the paroxetine [32].

Pregabalin the calcium modulator:-

The drug pregabalin can be considered as the calcium modulator that is marked up to act at the alpha 2 Gama subunit of the calcium channels that are voltage gated . Moreover this particular drug has the ability which is entitled as the sedative properties . In addition to this , Pregabalin can eradicate the disorders of sleep that is a part of the anxiety disorders . The drug pregabalin does not subject to the hepatic metabolism henceforth , its not acting with the inhibitors . However when this drug is discontinued there have been instances where the patients tend to suffer from not only substance abuse but also with the withdrawal syndromes [50].

The traditional antidepressants; Tricyclic:-

The antidepressants that are traditional also entitled as the tricyclic antidepressants , both the imipramine and the clomipramine are equally effective as the second generation antidepressants in the conventional management of the ailment of anxiety disorders . However , they must be strictly used with cautions making sure the concerns of the patients suicide , the reason being potential fatal toxicity that occurs on the overdose of the drug [51].

The drug Buspirone:-

Figure 4: Structure of Buspirone

The drug Buspirone is a receptor of 5-hydroxytryptamine 1A agonist that has a remarkable improvement in the generalized anxiety

disorders. Although its superiority hasn't been proved well by all the possible studies [52].

Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

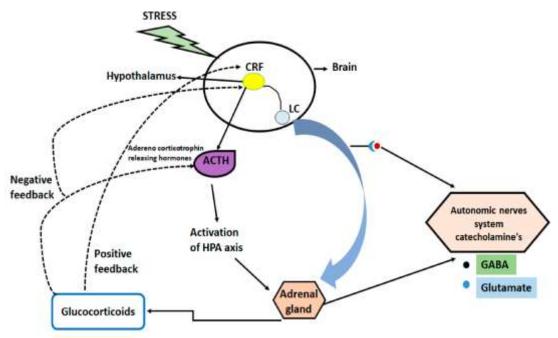


Figure 5: Mechanism of Buspirone

Benzodiazepines to treat anxiety disorders:-

Figure 6: Structure of Benzodiazepines

Benzodiazepines are supposed to have the effects that are anxiolytic start their mechanism of action as soon as they are applied by either oral or parenteral modes . However a major drawback of the benzodiazepines is that it may cause some severe cases of increased insomania as well as the increment in jitters [53].Regardless of what

considering the fact that the treatment using this drug is directly effective on the central nervous system of the body, its responsible for the central nervous system depression , that yields to several conditions, for instance fatigue, impairment in the abilities to drive, more reaction time and various other side effects [54].



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

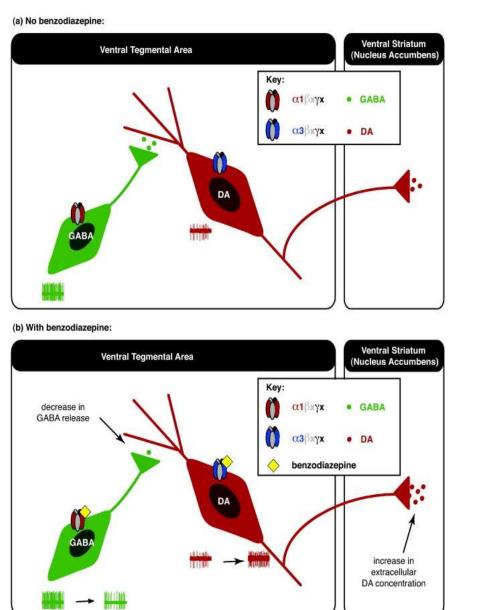


Figure 7: Mechanism of Benzodiazepines

The reversible inhibitor Moclobemide:-

The drug Moclobemide can be considered as the reversible as well as the selective monoamine oxidase inhibitor A. It is majorly used in the treatments concerned with social phobia [55].

The Antidepressant agomelatine:-

This drugs is supposed to act on the receptors MT1 and MT2 which easily cures the generalized anxiety disorders [56].

The newest antidepressant :-

The new variation in the categories of the antidepressants vortioxetine, has marked up an highly effective impact on the generalized anxiety disorders [57].

The principles of general treatment :-

The people who are suffering from these ailments must be made aware about the side effects that may be a possible outcome , as well as the safety warnings and instructions . Moreover if the patients are well aware about the adverse effects



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

they may cope the improvement compliance earlier[58]. In most of the cases the people who are suffering from the anxiety disorders, they are scared of the psychotropic drugs because of the adverse side effects. In addition to this in the cases of agoraphobia when the drugs tend to cause increased jitters, usually the patients prefer to discontinue the antidepressant drugs [59].

Treating the generalized anxiety disorders in elder patients:-

On comparison the people who have crossed the age of approximately 65 years have a lesser risk of developing any anxiety disorders, However, the generalized anxiety disorder is always an exception. According to the studies it has been proven the efficacy of drugs for instance duloxetine, venlafaxine, pregabalin as well as the quetiapine etc in the people of age round about 65 or more [45].

While treating the generalized anxiety disorders in the older patients, that fact that the drug interactions may cause severe side effects in the body must be taken into consideration. The adverse effects maybe an amalgamation of anticholinergic effects, orthostatic hypotension risk cardiovascular mishaps, falling risk etc...[60]

Treatment of anxiety disorders in patients during the childhood and adolescents;

The psychotherapy:-

In the patients of younger age rather than the generalized anxiety disorders, the other ailments such as specific phobias, agoraphobia, etc are more common. In order to conventionally manage the generalized anxiety disorders in the younger patients, the efficacy has been showed by drugs like fluoxetine, sertraline, duloxetine etc...in order to treat the social phobia the drugs like venlafaxine and paroxetine can be used [61].

Moreover the studies have remarkably proved that the drug fluoxetine is the best proven drug which can be most preferred for treating the anxiety disorders in children and adolescents [62].

Treatment for the women who are pregnant as well as breastfeeding:-

For the females who are pregnant , if the anxiety disorders are kept untreated , it's a major threat to the development of the unborn child[63]. There can also be an increased risk of cardiovascular malfunctions because of the usage of antidepressants during their first trimester [64]. Moreover the antidepressant usage can lead to multiple situations like spontaneous abortions , deliveries which are earlier than the given time , still births , dysfunctions of metabolism as well as endocrine systems , respiratory distress etc... [65]



Figure 4: Psychotheraov

It has been found that along with the anxiety disorders, the people who are suffering need some supportive talks and an extra attention towards their problems which make them emotional .Moreover, there are patients who tend to require some formal psychological treatment interventions that can be mostly done on the outpatient basis[66]. Treating the anxiety disorders, by the means of cognitive behavioral therapy, is more effective than any other treatments [67].In order to treat the anxiety disorders not only the

pharmacotherapy but also the psychotherapy have been found the most effective [68].

Henceforth, Depression as well as the major anxiety disorders can also affect the day to day functioning of the person for instance it is also associated with the factors like downscale in the productivity at the respective workplace [69], risk of being majorly absent at work or even the problem like social dysfunction [70].



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

REFERENCE

- [1]. Wittchen HU, Jacobi F, et.al., "The size and burden of mental disorders and other disorders of the brain in Europe 2010. National Library of Medicine", September 2010;21(9):655-79. Doi: 10.1016/j.euroneuro.2011.07.018
- [2]. WHO: "Depression and Other Common Mental Disorders: Global Health Estimates." Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO (http://apps.who.int/iris/bitstream/Handle/10665/254610/WHO-MSD-MER-2017.2 eng.pdf;jsessionid=829EAD6A4E0473EB DE28F4FD23B8D556?sequence=1) (last Accessed on 22 August 2018).
- [3]. Dilling, Horst, Mombour, W, Schmidt, M. H & World Health Organization . (1991). "InternationaleKlassifikationpsychischerSt örungen : ICD-10", Kapitel V (F, klinischdiagnostische Leitlinien / hrsg. Von H. Dilling, W. Mombour und M. H. Schmidt. Huber. https://apps.who.int/iris/handle/10665/382
- [4]. WHO:ICD 11.https://icd.who.int/dev11/l-m/en. (last accessed on 22 August 2018)

21

- [5]. Silove D, Alonso J, et.al., "Pediatric-Onset and Adult-Onset Separation Anxiety Disorder Across Countries in the World Mental Health Survey." National Library of Medicine, july 2015;172(7):647-56. Doi: 10.1176/appi.ajp.2015.14091185.
- [6]. Baldwin DS, Gordon R, et.al., "The separation of adult separation anxiety disorderv", National Library of Medicine, August 2016;21(4):289-294. Doi: 10.1017/S1092852916000080.
- [7]. Kossowsky J, Pfaltz MC, et.al., "The separation anxiety hypothesis of panic disorder revisited: a meta-analysis", National Library of Medicine, july 2013;170(7):768-81. Doi: 10.1176/appi.ajp.2012.12070893.
- [8]. Grant BF, Goldstein RB, et.al., Epidemiology of DSM-5 Alcohol Use Disorder: Results From the "National Epidemiologic Survey on Alcohol and Related Conditions III", National Library of Medicine, August 2015;72(8):757-66. Doi: 10.1001/jamapsychiatry.2015.0584.
- [9]. Gottschalk MG, Domschke K. "Novel developments in genetic and epigenetic

- mechanisms of anxiety", National Library of Medicine, January 2016;29(1):32-8. Doi: 10.1097/YCO.00000000000000219.
- [10]. Klauke B, Deckert J, et.al., Life events in panic disorder-an update on "candidate stressors", National Library of Medicine, August 2010;27(8):716-30. Doi: 10.1002/da.20667.
- [11]. Schiele MA, Domschke K, "Epigenetics at the crossroads between genes, environment and resilience in anxiety disorders", National Library of Medicine, March 2018;17(3):e12423. Doi: 10.1111/gbb.12423.
- [12]. Leichsenring F, Salzer S, et.al., "Psychodynamic therapy and cognitive-behavioral therapy in social anxiety disorder: a multicenter randomized controlled trial", National Library of Medicine, July 2013;170(7):759-67. Doi: 10.1176/appi.ajp.2013.12081125.
- [13]. Bandelow B, Wiltink J, Alpers GW, et al.: "Deutsche S3-Leitlinie Behandlung von Angststörungen".

 www.awmf.org/uploads/tx szleitlinien/05

 10281 S3_Angstst%C3%B6rungen_201405_2.pdf (last accessed on 13 August 2018)
- [14]. Gloster AT, Wittchen HU, et.al., "Psychological treatment for panic disorder with agoraphobia: a randomized controlled trial to examine the role of therapist-guided exposure in situ in CBT", National Library of Medicine, June 2011;79(3):406-20. Doi: 10.1037/a0023584.
- [15]. Diemer J, Mühlberger A, et.al., "Virtual reality exposure in anxiety disorders: impact on psychophysiological reactivity", National Library of Medicine, August 2014;15(6):427-42. Doi: 10.3109/15622975.2014.892632.
- [16]. Soyka M., "Treatment of Benzodiazepine Dependence", National Library of Medicine, March 2017;376(12):1147-1157. Doi: 10.1056/NEJMra1611832.
- [17]. Normann N, van Emmerik AA, et.al., "The efficacy of metacognitive therapy for anxiety and depression: a meta-analytic review", National Library of Medicine, May 2014;31(5):402-11. Doi: 10.1002/da.22273.



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

- [18]. Gloster AT, Sonntag R, et.al., "Treating Treatment-Resistant Patients with Panic Disorder and Agoraphobia Using Psychotherapy: A Randomized Controlled Switching Trial", National Library of Medicine, February 2015;84(2):100-109. Doi: 10.1159/000370162.
- [19]. Rodrigues MF, Nardi AE, et.al., "Mindfulness in mood and anxiety disorders: a review of the literature. Trends Psychiatry Psychother", National Library of Medicine, July 2017;39(3):207-215. Doi: 10.1590/2237-6089-2016-0051.
- [20]. Zwanzger P, Fallgatter AJ, et.al., "Anxiolytic effects of transcranial magnetic stimulation—an alternative treatment option in anxiety disorders?", National Library of Medicine, June 2009;116(6):767-75. Doi: 10.1007/s00702-008-0162-0.
- [21]. Ströhle A., "Sports psychiatry: mental health and mental disorders in athletes and exercise treatment of mental disorders", National Library of Medicine, August 2019;269(5):485-498. Doi: 10.1007/s00406-018-0891-5.
- [22]. Archer J, Bower P, et.al., "Collaborative care for depression and anxiety problems", National Library of Medicine, October 2012;10:CD006525. Doi: 10.1002/14651858.CD006525.
- [23]. Zis AP, Goodwin FK., "Major affective disorder as a recurrent illness: a critical review", National Library of Medicine, July 1979;36(8 Spec No):835-9. Doi: 10.1001/archpsyc.1979.01780080009002.
- [24]. Olsson GI, von Knorring AL. "Adolescent depression: prevalence in Swedish highschool students", National Library of Medicine, May 1999;99(5):324-31. Doi: 10.1111/j.1600-0447.1999.tb07237.x.
- [25]. Kerr, T., Schapira, K., et.al., "The Relationship between Premature Death and Affective Disorders", APA Psycnet, January 2018; 115(528), 1277-1282. Doi:10.1192/bjp.115.528.1277
- [26]. Harris EC, Barraclough B., "Excess mortality of mental disorder", National Library of Medicine, July 1998;173:11-53. Doi: 10.1192/bjp.173.1.11.
- [27]. Pratt LA, Ford DE, et.al., "Depression, psychotropic medication, and risk of myocardial infarction", National Library of Medicine, December

- 1996;94(12):3123-9. Doi: 10.1161/01.cir.94.12.3123.
- [28]. Akiskal HS., "Dysthymia and cyclothymia in psychiatric practice a century after Kraepelin", National Library of Medicine, January 2001;62(1-2):17-31. Doi: 10.1016/s0165-0327(00)00347-5.
- [29]. Nobel Foundation. Nobel Lectures Physiology or Medicine, 1901–1970 (Elsevier, Amsterdam, 1970).
- [30]. Bunney WE Jr, Davis JM., "Norepinephrine in depressive reactions. A review", National Library of Medicine, December 1965;13(6):483-94. Doi: 10.1001/archpsyc.1965.01730060001001.
- [31]. Schildkraut JJ, Gordon EK, et.al., "Catecholamine metabolism in affective disorders. I. Normetanephrine and VMA excretion in depressed patients treated with imipramine", National Library of Medicine, December 1965;3(4):213-28. Doi: 10.1016/0022-3956(65)90003-8.
- [32]. Lander ES, Schork NJ., "Genetic dissection of complex traits". September 1994;265(5181):2037-48. Doi: 10.1126/science.8091226.
- [33]. Kessler RC, Berglund P, et.al., "Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication", National Library of Medicine, June 2005;62(6):593-602. Doi: 10.1001/archpsyc.62.6.593.
- [34]. Burmeister M., "Basic concepts in the study of diseases with complex genetics", National Library of Medicine, March 1999;45(5):522-32. Doi: 10.1016/s0006-3223(98)00316-3.
- [35]. de Kloet ER, Joëls M, et.al., "Stress and the brain: from adaptation to disease", National Library of Medicine, June 2005;6(6):463-75. Doi: 10.1038/nrn1683.
- [36]. Ongür D, An X, et.al., "Prefrontal cortical projections to the hypothalamus in macaque monkeys", National Library of Medicine, November 1998;401(4):480-505.
- [37]. Rajkowska G, Miguel-Hidalgo JJ, et.al., "Morphometric evidence for neuronal and glial prefrontal cell pathology in major depression", National Library of Medicine, May 1999;45(9):1085-98. Doi: 10.1016/s0006-3223(99)00041-4.



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

- [38]. Kessler RC, Berglund P, et.al., "Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication", National Library of Medicine, June 2005;62(6):593-602. Doi: 10.1001/archpsyc.62.6.593.
- [39]. Angst J, Gamma A, et.al., "The generalized anxiety spectrum: prevalence, onset, course and outcome". National Library of Medicine, February 2009;259(1):37-45. Doi: 10.1007/s00406-008-0832-9.
- [40]. Bandelow B, Baldwin D, et.al., "Biological markers for anxiety disorders, OCD and PTSD a consensus statement. Part I: Neuroimaging and genetics", National Library of Medicine, August 2016;17(5):321-65. Doi: 10.1080/15622975.2016.1181783.
- [41]. Bandelow B, Baldwin D, et.al., "Biological markers for anxiety disorders, OCD and PTSD: A consensus statement. Part II: Neurochemistry, neurophysiology and neurocognition", National Library of Medicine, April 2017;18(3):162-214. Doi: 10.1080/15622975.2016.1190867.
- [42]. Wittchen HU, Kessler RC, et.al., "Generalized anxiety and depression in primary care: prevalence, recognition, and management", National Library of Medicine, 2002;63 Suppl 8:24-34.
- [43]. Bandelow B, Michaelis S. "Epidemiology of anxiety disorders in the 21st century", Taylor & Francis, 2015;17(3):327-335.
- [44]. .Bandelow B, Sher L, et.al., "Guidelines for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder in primary care", National Library of Medicine, June 2012;16(2):77-84. Doi: 10.3109/13651501.2012.667114.
- [45]. Bandelow B, Lichte T, et.al., "The German guidelines for the treatment of anxiety disorders", National Library of Medicine, August 2015;265(5):363-73. doi: 10.1007/s00406-014-0563-z.
- [46]. Baldwin DS, Anderson IM, et.al., "Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology",

- National Library of Medicine, May 2014;28(5):403-39. Doi: 10.1177/0269881114525674.
- [47]. Regier DA, Narrow WE, et.al., "The de facto US mental and addictive disorders service system. Epidemiologic catchment area prospective 1-year prevalence rates of disorders and services", National Library of Medicine, February 1993;50(2):85-94. Doi:
 - 10.1001/archpsyc.1993.0182014000700.
- [48]. Alonso J, Lépine JP; et.al., "Overview of key data from the European Study of the Epidemiology of Mental Disorders (ESEMeD)", National Library of Medicine, 2007;68 Suppl 2:3-9.
- [49]. Benjamin J, Ben-Zion IZ, et.al., "Double-blind placebo-controlled pilot study of paroxetine for specific phobia", National Library of Medicine, April 2000;149(2):194-6. Doi: 10.1007/s002130000372.
- [50]. Baldwin DS, Ajel K, et.al., "Pregabalin for the treatment of generalized anxiety disorder: an update", National Library of Medicine, 2013;9:883-92. doi: 10.2147/NDT.S36453.
- [51]. Thanacoody HK, Thomas SH, "Tricyclic antidepressant poisoning: cardiovascular toxicity", National Library of Medicine, 2005;24(3):205-14. Doi: 10.2165/00139709-200524030-00013.
- [52]. Stahl SM, "Don't ask, don't tell, but benzodiazepines are still the leading treatments for anxiety disorder", National Library of Medicine,2002 Sep;63(9):756-7. Doi: 10.4088/jcp.v63n0901.
- [53]. Schweizer E, Rickels K, et.al., "The effect of personality on withdrawal severity and taper outcome in benzodiazepine dependent patients", National Library of Medicine, May 1998;28(3):713-20. Doi: 10.1017/s0033291798006540.
- [54]. Stein DJ, Ahokas AA, et.al., "Efficacy of agomelatine in generalized anxiety disorder: a randomized, double-blind, placebo-controlled study", National Library of Medicine, October 2008;28(5):561-6. Doi: 10.1097/JCP.0b013e318184ff5b.
- [55]. Stein DJ, Ahokas A, et.al., "Agomelatine prevents relapse in generalized anxiety disorder: a 6-month randomized, double-blind, placebo-controlled discontinuation



Volume 8, Issue 3 May-June 2023, pp: 58-70 www.ijprajournal.com ISSN: 2249-7781

- study", National Library of Medicine, July 2012;73(7):1002-8. Doi: 10.4088/JCP.11m07493.
- [56]. Stein DJ, Ahokas A, et.al., "Agomelatine in generalized anxiety disorder: an active comparator and placebo-controlled study", National Library of Medicine, April 2014;75(4):362-8. Doi: 10.4088/JCP.13m08433.
- [57]. Stein DJ, Ahokas A, et.al., "Efficacy and safety of agomelatine (10 or 25 mg/day) in non-depressed out-patients with generalized anxiety disorder: A 12-week, double-blind, placebo-controlled study", National Library of Medicine, May 2017;27(5):526-537. Doi: 10.1016/j.euroneuro.2017.02.007.
- [58]. Fu J, Peng L, et.al., "The efficacy and safety of multiple doses of vortioxetine for generalized anxiety disorder: a meta-analysis", National Library of Medicine, April 2016;12:951-9. Doi: 10.2147/NDT.S104050.
- [59]. Durham RC, Chambers JA, et.al., "Long-term outcome of cognitive behaviour therapy clinical trials in central Scotland", National Library of Medicine, November 2005;9(42):1-174. Doi: 10.3310/hta9420.
- [60]. Schuurmans J, van Balkom A, et.al. "Latelife anxiety disorders: a review", National Library of Medicine, August 2011;13(4):267-73. Doi: 10.1007/s11920-011-0204-4.
- [61]. Farah s., Hussain, et.al., "pharmacologic Treatment of pediatrics Anxiety Disorders", HHS Public access, June 2016; 3(2): 151–160. doi: 10.1007/s40501-016-0076-7
- [62]. Hetrick SE, McKenzie JE, et.al., "Newer generation antidepressants for depressive disorders in children and adolescents", National Library of Medicine, November 2012;11(11):CD004851. Doi: 10.1002/14651858.CD004851.pub3.
- [63]. .Huybrechts KF, Palmsten K, et.al., "Antidepressant use in pregnancy and the

- risk of cardiac defects", National Library of Medicine, June 2014;370(25):2397-407. Doi: 10.1056/NEJMoa1312828.
- [64]. Oyebode F, Rastogi A, et.al., "Psychotropics in pregnancy: safety and other considerations", National Library of Medicine, July 2012;135(1):71-7. Doi: 10.1016/j.pharmthera.2012.03.008.
- [65]. Bandelow B, Lichte T, et.al., "The diagnosis of and treatment recommendations for anxiety disorders", National Library of Medicine, July 2014;111(27-28):473-80. Doi: 10.3238/arztebl.2014.0473.
- [66]. Bandelow B, Reitt M, et.al., "Efficacy of treatments for anxiety disorders: a meta-analysis", National Library of Medicine, July 2015;30(4):183-92. Doi: 10.1097/YIC.0000000000000078.
- [67]. Patterson B, Boyle MH, et.al., "The use of waitlists as control conditions in anxiety disorders research", National Library of Medicine, December 2016;83:112-120. Doi: 10.1016/j.jpsychires.2016.08.015.
- [68]. James AC, James G, et.al., "Cognitive behavioural therapy for anxiety disorders in children and adolescents", National Library of Medicine, June 2013;(6):CD004690. Doi: 10.1002/14651858.CD004690.pub3.
- [69]. Broadhead WE, Blazer, et.al., "Depression, disability days, and days lost from work in a prospective epidemiologic survey", National Library of Medicine, November 1990;264(19):2524-8.
- [70]. Briley M, Moret C, "Improvement of social adaptation in depression with serotonin and norepinephrine reuptake inhibitors", National Library of Medicine, October 2010;6:647-55. Doi: 10.2147/NDT.S13171.