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BENZODIAZEPINES: ARE CLONAZEPAM BETTER THAN LORAZEPAM AND ALPRAZOLAM, A COMPARATIVE REVIEW ARTICLE

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ABSTRACT

Anxiety is a common occurrence in humans, and it appears in a variety of anxiety disorders, making it an essential clinical focus. Recent advances in nosology, epidemiology, and psychobiology have resulted in a better understanding of anxiety disorders. Advances in medicine and psychotherapy for these diseases have given patients reasonable hope for symptom alleviation and functional improvement. Prescription medications known as benzodiazepines are frequently used to treat anxiety because they slow down neural transmissions between the brain and body and enhance the activity of a brain neurotransmitter called GABA.In the benzodiazepine class of drugs, Clonazepam, Lorazepam, and Alprazolam are frequently prescribed for their sedative, anxiolytic (anti-anxiety), anticonvulsant, and muscle relaxant effects; however, each drug has unique qualities that make it appropriate for a variety of therapeutic uses.All three medications have the risk of tolerance, dependency, and withdrawal symptoms. Because of these hazards, they are typically recommended for brief periods of time. The purpose of this review article is to compare the effects of Clonazepam, Alprazolam and Lorazepam.

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INTRODUCTION

The Latin term "anxietas" (to choke, throttle, bother, and upset) is the root of the English word "anxiety," which refers to a range of behavioral, affective, and cognitive reactions to perceived risk. It's common for humans to feel anxious. When anxiety is controlled, it can help people respond adaptively and predictably to difficult or stressful situations. When anxiety levels are too high, people become unstable and develop dysfunctional states [1]. The highest estimated prevalence rate of all psychiatric disorders, neurotic disorders, was found to be 20.7% (18.7-22.7) after a meta-analysis of 13 psychiatric epidemiological studies (Reddy and Chandrashekhara) with a total sample size of 33,572 subjects who met the following criteria: door-to-door survey, all age groups included, and prevalence rate for urban and rural being available [2]. Females had a considerably higher prevalence of all neurotic illnesses (32.2% vs. 9.7%, P < 0.01). Anxiety disorders were projected to impact 3.6% of the world's population in 2015 [3]. Depression affects over 280 million people worldwide. The World Mental Health Survey (WMHS) indicates that anxiety disorders affect anywhere from 3% to 19% of people in different countries during their lifespan. Based on data from the WMHS 2005, the 12-month prevalence of anxiety disorders in India was estimated to be 3.41% [4].

Anxiety affects people of all ages, but it is particularly prevalent in older adults [5]. Anxiety is a state of tension, anxiety, or worry brought on by perceived or actual threats. Fear sets off the body's stress reaction, commonly referred to as the fight, flight, or freeze response. This may include changes in respiration or heart rate, as well as cognitive, physical, and behavioral aspects. By increasing blood and oxygen flow to the muscles, this reaction can aid humans in escaping or avoiding danger. But anxiety can also be experienced by people for non-dangerous items like: significant occurrences or choices, speaking in public, societal circumstances. It's not always the case that anxiety indicates a mental health issue. Many people experience occasional feelings of anxiety. However, anxiety may indicate an anxiety disorder if it becomes excessively frequent, out of proportion to the circumstance, or lasts after the crisis has passed. The Anxiety and Depression Association of America (ADAA) estimates that 40 million or more Americans suffer from an anxiety disorde r [6]. In the nation, it is the most prevalent kind of mental disorder. But only36.9% of those suffering from anxiety disorders are given therapy. A usual emotion that many individuals go through is anxiety. When this emotion gets extreme or out of proportion to what triggers it, an anxiety disorder develops. A person suffering from acute anxiety may go through a panic episode, which is characterized by a sharp sensation of terror or panic that peaks and then passes. Anxiety can be exacerbated by alcohol, caffeine, stress, and sleep deprivation

Anxiety symptoms can be minimized by some drugs, which helps to control the illness. Some may take drugs continuously, while others may use them to facilitate the start of therapy. Medications that a doctor might recommend include the following:

A) Antidepressants: Despite the fact that they also treat depression, several antidepressants have been shown to reduce anxiety. Examples include citalopram, fluoxetine, and serotonin reuptake medications. It takes a few weeks for them to start functioning.

B) Beta-blockers: Although they don't completely eliminate anxiety, these medications do lessen its bodily manifestations, such an accelerated heartbeat. They can be taken in short bursts or just in rare instances when something makes people anxious.

C) Benzodiazepines: These medications instantly relieve anxiety, but they also have a high potential for addiction or dependence. Consequently, physicians only recommend them for brief periods of time. Often used as Valium, diazepam is a benzodiazepine.

Benzodiazepines: The classic anxiolytics, benzodiazepines, were first made available in the early 1960s. Before benzodiazepines were developed ten years ago, meprobamate and barbiturates were frequently used to treat anxiety and discomfort. Barbiturates, on the other hand, might be fatal in an overdose, and these drugs were linked to dependence. Benzodiazepines were dubbed "one of the greatest inventions of the twentieth century" since they are far safer than barbiturates and meprobamate (Healy 2002). It is therefore not surprising that they sprang to prominence as the most often prescribed class of psychotropic drugs globally in the middle of the 1970s (Balter 1974) [7].

Benzodiazepines are sedatives that minimize the physical symptoms of anxiety, such as stiff muscles. These medications also promote relaxation and produce speedy results [8]. Peak blood levels occur about 1-2 hours after a person consumes their dose. People may experience the affects sooner than this. Although benzodiazepines can be quite beneficial for short-term difficulties, doctors rarely prescribe them because they lose effectiveness over time and can be addictive.
Due to these concerns, experts recommend that doctors do not advise continuous usage of benzodiazepines for more than 6 months. Some people may use benzodiazepines to treat short-term anxiety. People who are afraid of flying, for example, may take them before to taking off. Off-label, it could assist with tics and bipolar disorder. Side effects may include tiredness, disorientation, and sadness. Short-term use of these drugs is typically safe and effective, but long-term usage can result in tolerance, dependency, and other side effects. The sedative-hypnotic, anxiolytic, anticonvulsant, and skeletal muscle relaxation properties of benzodiazepines are due to their binding to GABAA receptor subtype in the limbic system, thalamus, and hypothalamus. They also bind to an allosteric site of the GABAA–Cl receptor complex, which increases the frequency of the opening of the chloride channels. Moreover, benzodiazepines enhance the affinity of GABA (gammaaminobutyric acid) for GABAA receptors and potentiate the inhibitory effects of GABA throughout the nervous system. These effects of GABAmediated actions account for the sedative–hypnotic [9]. Benzodiazepines are classified into several categories, each with its own set of applications, which are- alprazolam (Xanax), clonazepam (Klonopin), diazepam (Valium), lorazepam (Ativan), midazolam (Versed)Xanax, Klonopin, Valium, Ativan, and Versed are examples of benzodiazepines. Benzodiazepines are widely used to treat anxiety disorders and other associated conditions. The Food and Drug Administration has approved eight benzodiazepine compounds for this use. Though clonazepam is classified as an anticonvulsant, it is also prescribed for this use [10].

Taking too much benzodiazepine is harmful, and combining it with alcohol or other narcotics can be lethal. Benzodiazepines affect the cellular activity of neurons that cause stress and anxiety reactions. The Food and Drug Administration (FDA) approved them for the treatment of:

Insomnia, generalized anxiety condition. Possible diagnoses include social anxiety disorder, seizures (e.g. epilepsy), and panic disorder.

Clonazepam: Clonazepam is a potent long-acting benzodiazepine that acts as a GABA-A receptor agonist and increases serotonin production.[11]

Clonazepam oral tablet is a prescription medicine sold under the brand name Klonopin. It's also accessible as a generic medication.

Clonazepam is available in two forms: oral tablets and oral disintegrating tablets.Clonazepam is used to treat panic disorders. It is also used to control seizures.

Clonazepam may be used as part of a combined treatment. This means that it may need to be taken alongside other medications.

The most commonly documented side effect of Clonazepam is sedation [12][13] The release of dopamine may be inhibited by clonazepam [14].

Clonazepam works by boosting the action of gamma aminobutyric acid. This molecule transmits impulses throughout a person's neurological system. If a person's GABA levels are insufficient, their body may become stimulated. This could cause them to experience panic attacks or seizures.

Adults (18–64 years old) with panic disorder usually start with 0.25 mg twice a day. After three days, doctors can raise the dosage to 0.5 mg, with a daily maximum of 4 mg. A progressive dosage reduction of no more than 0.125 mg per three days is recommended.

Children under the age of 18 should not use clonazepam, and older adults may develop side effects because of the drug's slower metabolism. To stop the body from accumulating too much medication, doctors could advise a lower dosage or a modified dosing schedule.

When taken orally, clonazepam is rapidly and completely absorbed; peak plasma concentrations are typically reached in 1–4 hours; the mean volume of distribution is large, estimated at 3 l/kg; 85% of plasma proteins bind to the drug; it is necessary to assume that clonazepam crosses the placental barrier and has been found in maternal milk; and the mean elimination half life is lengthy, at roughly 30 hours (18–60 hours) [15].

Clonazepam is an FDA-approved medication used to treat panic and seizure disorders. It has anxiolytic and anticonvulsant qualities [16][17]

Clonazepam, as a central nervous system depressant, shares common adverse effects with other benzodiazepine drugs, primarily manifesting as sedation and motor impairment.

Alprazolam: The most widely prescribed psychotropic drug in the United States is alprazolam, also marketed under several trade names.
It is typically prescribed to treat anxiety and panic disorders. After oral administration, alprazolam is rapidly absorbed, reaching its peak plasma concentration in one to two hours. Oral alprazolam has an average 80–100% bioavailability [18].

Alprazolam increases the risk of respiratory depression, low blood pressure, and death when used alongside CNS depressants, particularly opioids [19]. Hepatic microsomal oxidation biotransforms alprazolam into its major metabolites, 4 and αhydroxyalprazolam, which are further broken down by cytochrome P450 (CYP) 3A4 (Greenblatt and Wright, 1993).

Alprazolam should not be administered to patients who are at a higher risk of suicide or who are abusing alcohol, opioids, or other sedative medications because it is much more toxic than other benzodiazepines in overdose situations. Avoid grapefruit and grapefruit juice as well since they contain furanocoumarins, which inhibit CYP3A4 and raise alprazolam levels in the blood [20].

Alprazolam comes in the following strengths: 0.25 mg, 0.5 mg, 1 mg, and 2 mg for regular release and oral disintegrating tablets; 0.5 mg, 1 mg, 2 mg, and 3 mg for extended-release tablets. Additionally, oral solutions of 0.5 mg/5 mL and 1 mg/10 mL of alprazolam are offered [21][22].

A more recent benzodiazepine that is being utilized increasingly frequently in overdose situations is alprazolam [23][24].

Oral tablets with the brand name Xanax are given for specific anxiety conditions. Alprazolam is the active ingredient in Xanax.

The FDA has approved Xanax for the following adult conditions: panic disorder, generalized anxiety disorder, and agoraphobia (the fear of being in situations from which it may be difficult to escape).

Upon dissolving, Xanax tablets release all of the drug, as they are instant release tablets. Xanax mild side effects include the following:

loss of memory, constipation ,hypotension, or low arterial pressure, dry mouth fatigue, feeling lightheaded or dizzy, issues with coordination or balance, difficulty focusing, difficulty speaking clearly, shifts in appetite, and shifts in weight, mild allergic response.

Lorazepam: The FDA has approved the drug lorazepam, which is intended to treat adult status epilepticus, cure anxiety-related sleeplessness, and prepare patients for anesthesia [25].

Master and Kajaria carried out the first Indian investigation into the use of benzodiazepines in anxiety disorders.This double-blind study compared the effectiveness of lorazepam and diazepam in treating anxiety-related neuroses in sixty outpatients. It was determined that while both Lorazepam and Diazepam are useful anxiolytics, Lorazepam produces a clinically meaningful response sooner [26]. For brief periods of time, doctors can prescribe benzodiazepines like lorazepam to treat anxiety symptoms or insomnia brought on by anxiety. Lorazepam produces a calming effect by interfering with the neurotransmitter system, which is the brain's chemical messenger system [27].

When injected intravenously (IV), lorazepam is primarily used to treat acute episodes of agitation and anxiety [28]. Sedation is the main side effect of Lorazepam [29].

RESULTS

It has long been debatable whether or not to treat anxiety disorders using benzodiazepines. It has split medical professionals into two groups: those who emphasize the drawbacks of using them and steer clear of them, and those who still prescribe them but do so grudgingly or even covertly. Despite efforts to promote antidepressants as first-line pharmacological treatment for anxiety disorders, studies show that benzodiazepines are still the most commonly used medications for these conditions in the USA (55–94% of patients treated with benzodiazepines for anxiety disorders; Stahl, 2002) (Bruce 2003; Vasile 2005). Several European nations have also reported using benzodiazepines often (Smolders 2007; Demyttenaere 2008). Benzodiazepines share more similarities than differences, with the duration of action being the key distinguishing factor. They are usually classified as shortacting (up to 6 hours), intermediate-acting (6-12 hours), and long-acting (more than 12 hours).Alprazolam and Lorazepam are short acting while Clonazepam is Long acting.Short-acting benzodiazepines (such as alprazolam) must be taken three to four times per day, which is not particularly convenient. As a result, they may not be appropriate for long-term use. They may be more effective for immediate, one-time relief of anxiety or distress. These benzodiazepines should probably be avoided if there are concerns about usage, because there is a correlation, however inconclusive (e.g., Pradel 2010), between short duration of action and predisposition to abuse. Intermediate-acting (e.g., oxazepam) and long-acting benzodiazepines (e.g., diazepam, clonazepam) are best taken once or twice day and are typically recommended for long-term treatment. Long-acting benzodiazepines can build up in the body, especially if administered before previous doses have been cleared. Excessive drowsiness, known as "hangover sedation," can occur, particularly in the elderly [30] Clonazepam has a slower onset than Alprazolam, which is followed by Lorazepam. Alprazolam has the shortest half-life, whereas Clonazepam has the longest half-life, followed by Lorazepam. The three drugs with the longest half-lives are Clonazepam, Lorazepam, and Alprazolam.

DISCUSSION

After reviewing many articles we discovered that all three benzodiazepines—clonazepam, alprazolam, and lorazepam—have different main applications as well as different rates of onset and duration of action. Because of its intermediate onset and long-lasting effects, clonazepam is best suited for the long-term management of anxiety, panic disorders, and seizure disorders. This makes it an excellent choice for chronic illnesses that require consistent control. While it has a shorter half-life and a higher chance of dependence and withdrawal, alprazolam is preferred for its extremely early onset, which relieves acute anxiety and panic episodes. With its quick onset and moderate duration, lorazepam is a flexible alternative that works well for premedication for surgery or the treatment of acute seizures as well as short-term anxiety alleviation.

CONCLUSION

The conversation above makes it quite evident that clonazepam, which has a more favorable side effect profile than alprazolam or lorazepam and requires a lower dosage, may be a suitable medicine for treating anxiety disorder in patients using concurrent antidepressants. We hypothesize that alprazolam is more dangerous when taken excessively than other benzodiazepines. While clonazepam is often used to treat anxiety, lorazepam has a greater preference for the GABA-A receptor and is typically utilized for sedation. Concerns about the improper long-term use of these Benzodiazepines highlight the significance of teamwork between primary care physicians, nurses, pharmacists, and clinicians. Adopting resources such as databases from the Controlled Substance Prescription Monitoring Program (CSPMP) can help prevent misuse and encourage safe medication practices.

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