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Report

The alternative: Dimetindene maleate as a tranquilizer and anxiolytic

Abstract

This report examines the pharmacological properties and therapeutic potential of Dimetindene maleate as a medium strong tranquilizer and anxiolytic. Dimetindene maleate is an antihistamine with additional sedative effects, making it suitable for managing anxiety and promoting relaxation. This report delves into the mechanism of action, pharmacokinetics, clinical applications, and potential side effects of Dimetindene maleate, providing a comprehensive understanding of its therapeutic benefits and limitations. Additionally, this report explores current research trends and future prospects for Dimetindene maleate as a promising option in the management of anxiety disorders.

From antihistamine to tranquilizer

Dimetindene maleate, commonly known as Dimentindene having been in use for decades as an H1 receptor blocking antihistamine, exerts its tranquilizing and anxiolytic effects primarily through its antagonistic activity on several histamine receptors. It not very strong selectively blocks mainly H1 receptors, however, other histamine receptors as well which are widely distributed in the central nervous system (CNS), including the brain. By inhibiting the binding of histamine to these receptors, Dimetindene reduces the excitatory effects of histamine, leading to sedation, anxiolytic effects and relaxation. Apart from its effects on

several classes of histamine receptors, Dimetindene also interacts with other neurotransmitter systems, contributing to its anxiolytic properties. It has been found to exert inhibitory effects on the release of serotonin, dopamine, and norepinephrine in the CNS. This modulation of neurotransmitter systems may further enhance the calming and anxiety-reducing effects of Dimetindene.

GABA (gamma-aminobutyric acid) is the primary inhibitory neurotransmitter in the CNS and plays a crucial role in regulating anxiety and promoting relaxation. Dimetindene has been shown to indirectly enhance GABAergic transmission by triggering a complex (Motta et al., 2011) cascade of messenger molecules. This effect might theoretically contribute to the anxiolytic properties of Dimetindene. Dimetindene may also interact with other receptor systems, such as alpha-adrenergic receptors and muscarinic acetylcholine receptors. These interactions may contribute to its sedative and anticholinergic effects, which can be relevant in certain clinical scenarios.

After oral administration, Dimetindene is rapidly absorbed from the gastrointestinal tract. The presence of food may slightly delay the absorption but does not affect the overall bioavailability. It undergoes extensive metabolism in the liver, primarily via hepatic cytochrome P450 enzymes, particularly CYP2D6 and CYP2C19. The metabolites formed are mainly inactive or possess reduced pharmacological activity. The parent drug and its metabolites are excreted primarily through the kidneys (Pfaff et al., 1995).

The elimination half-life of Dimetindene varies between individuals and can range from 4 to 6 hours. It is important to note that the half-life may be prolonged in individuals with impaired liver or kidney function. The drug and its metabolites are eliminated mainly through renal excretion, and dose adjustments may be necessary in patients with renal impairment.

Several factors can influence the pharmacokinetics of Dimetindene Maleate, including age, hepatic function, renal function, and co-administration with other drugs. Elderly individuals and those with hepatic or renal impairment may exhibit altered drug metabolism and elimination, requiring dosage adjustments to ensure optimal therapeutic outcomes and minimize the risk of adverse effects (Radler et al., 1995).

Clinical aspects

In off-lable Dimetindene has proven excellent efficacy for decades in the management of various anxiety disorders, including generalized anxiety disorder (GAD), panic disorder, and social anxiety disorder.

Its anxiolytic effects stem from its ability to reduce anxiety-related symptoms such as excessive worry, restlessness, and - to a lesser extent - autonomic arousal. Due to its strong sedative properties (Heistracher, 1979), Dimetindene has been utilized in the off-label treatment of insomnia, particularly in cases where anxiety or histamine-mediated sleep disturbances are present. It can promote sleep onset and improve sleep quality by reducing arousal

and inducing sedation. Dimetindene may also be used as an adjunctive therapy in the management of certain psychiatric conditions, such as depression or obsessive compulsive symptoms (OCS) which can be the result of OCD or various types of brain damage. By providing additional anxiolytic and sedative effects, it can enhance the efficacy of primary treatment options and improve overall symptom control. Comparative tests evaluating Dimetindene against other anxiolytic agents, such as benzodiazepines or selective serotonin reuptake inhibitors (SSRIs), have shown comparable, if not better efficacy in reducing anxiety symptoms. Dimetindene may offer advantages in terms of a more favorable side effect profile and lower risk of dependence or withdrawal symptoms (Shirazi et al., 2020-2023).

Preclinical studies have demonstrated the tranquilizing effects of Dimetindene in various animal models of anxiety and stress. These studies have shown reductions in behavioral indicators of anxiety, such as exploratory behavior, aggression, and fear response. Clinical evidence clearly shows that tranquilizing effects of Dimetindene not only have provided promising results, they have been used off-label for decades. Patients treated with Dimetindene have shown significant reductions in subjective feelings of tension, restlessness, and irritability, indicating its efficacy as a medium strength tranquilizer. The tranquilizing effects of Dimetindene have been observed to follow a dose-response relationship, with higher doses generally producing more pronounced sedation and relaxation. However, it is crucial to balance the desired therapeutic effects with the potential for sedation-related adverse effects, especially during activities that require alertness and concentration.

In daily off-label use Dimetindene has demonstrated efficacy in various patient populations, including individuals with anxiety disorders, sleep disturbances, and comorbid psychiatric conditions (Parisi et al. 2020). Its use in specific patient groups, such as the elderly or those with hepatic or renal impairment, may require cautious dose adjustment to mitigate the risk of adverse effects.

Dimetindene possesses quite strong anxiolytic properties due to its ability to reduce excessive anxiety and promote relaxation. It exerts its effects through the modulation of histamine receptors and indirect cascade effects on other more complex neurotransmitter systems, collectively resulting in anxiolytic activity. Animal studies investigating the anxiolytic effects of Dimetindene Maleate have shown positive outcomes. Behavioral assays, such as elevated plus maze or open field tests, have revealed decreased anxiety-related behaviors following Clinical trials evaluating the anxiolytic efficacy of Dimetindene (Shirazi, Abbas, Bozorg et al., 2021) have reported significant reductions in anxiety symptoms across various anxiety disorders. These include a decrease in anticipatory anxiety, improved social functioning, and reduced panic attacks. However, further research is necessary to establish its comparative efficacy with standard anxiolytic agents. Dimetindene

has demonstrated comparable efficacy to established anxiolytic agents, such as benzodiazepines and more effective than most SNRIs and SSRIs, in reducing anxiety symptoms through the serotonin system (Koppenburg, 1991). However, its different mechanism of action and potentially milder undesired effects may make it a preferred option in certain patient populations, such as those with a higher risk of benzodiazepine-related side effects or dependence.

Undesired effects

When used as an antihistamine, and only then, the primary side effects of dimetindene are sedation and relaxation. It goes without saying that this is not an adverse effect when used as an anxiolytic and tranquilizer. However, the drug's sedative properties can impair cognitive function, attention, and psychomotor performance. Patients should be cautious when engaging in activities that require mental alertness, such as driving or operating machinery. In some patients the drug can aggravate depression, especially in those suffering from clinically relevant psychiatric disorders. Dimetindene has a highly pronounced anticholinergic activity, leading to potential side effects such as dry mouth, blurred vision, urinary retention, and constipation. These effects are attributed to the drug's antagonistic action on muscarinic acetylcholine receptors. Monitoring for these adverse effects and providing appropriate management strategies are essential during treatment. Dimetindene Maleate may have mild cardiovascular effects, including a slight decrease in blood pressure and an increase in heart rate. These effects are generally well-tolerated in healthy individuals but may require caution in patients with pre-existing cardiovascular conditions. As a medium strong tranquilizer, Dimetindene has significantly strong central nervous system (CNS) depressant effects. When used concurrently with other CNS depressants, such as alcohol or opioids, there is an increased risk of additive sedation and respiratory depression. Careful monitoring and dose adjustments may be necessary in such cases. Although Dimetindene is extremely less likely to induce physical dependence compared to benzodiazepines, prolonged use may still lead to some tolerance and in some patients the need for dose escalation. Abrupt discontinuation of the drug after long-term use may result in withdrawal symptoms, including rebound anxiety and insomnia. Therefore, gradual tapering of the medication is recommended when discontinuing treatment. Concomitant use of Dimetindene maleate with other CNS depressants of relevance, such as benzodiazepines, opioids, other H1 blockers, or sedative-hypnotics, can potentiate sedation and respiratory depression. Close monitoring and dosage adjustments may be necessary to minimize the risk of adverse effects. Combining Dimetindene with other anticholinergic medications may lead to additive anticholinergic effects, increasing the risk of side effects such as dry mouth, constipation, and urinary retention. Caution should be exercised when prescribing Dimetindene in combination with these medications, and dose adjustments may be required.

Interactions

Dimetindene is primarily metabolized by hepatic cytochrome P450 enzymes, particularly CYP2D6 and CYP2C19. Co-administration with drugs that inhibit or induce these enzymes may affect the metabolism and plasma concentrations of Dimetindene. Therefore, clinicians should consider potential drug interactions whenever they consider prescribing Dimetindene alongside other medications. Dimetindene may interact with drugs that have sedative properties, such as (first generation) antihistamines, anxiolytics, antidepressants, antipsychotics, or some anti-epileptic drugs (Arnera et al., 1990). Concurrent use may result in increased sedation and CNS depression. Therefore, close monitoring and dosage adjustments may be necessary when combining Dimetindene with these medications (Bauer, 2013).

Leaving the grey zone of "off-label"

Recent research (Shirazi et al., 2020-2023) aims to develop novel formulations and delivery systems for Dimetindene, such as extended-release formulations or transdermal patches. These advancements may provide more controlled drug release, improved efficacy, and enhanced patient compliance. Combining Dimetindene with other anxiolytic agents or antidepressants is an area of interest for future research. Investigating the synergistic effects and potential benefits of combination therapy may lead to improved treatment outcomes for patients with anxiety disorders (Pfaff et al., 2003). Advancements in pharmacogenetics and personalized medicine may enable the identification of specific patient populations that are more likely to benefit from Dimetindene. Tailoring treatment based on individual genetic profiles and receptor sensitivities could optimize therapeutic responses and minimize side effects. Exploring the use of Dimetindene Maleate in specific subtypes of anxiety disorders, such as post-traumatic stress disorder (PTSD) or obsessive-compulsive disorder (OCD), as well as investigating its effects on sleep disorders beyond insomnia, are promising avenues for future research (Shirazi, Abbas, Bozorg et al. 2021).

Conclusion

Dimetindene Maleate, as a medium strong tranquilizer and offers significant therapeutic potential in the management of anxiety disorders. Its mechanism of action involving histamine receptor antagonism and complex modulation of neurotransmitter systems contributes to its anxiolytic and sedative properties. While Dimetindene demonstrates efficacy in reducing anxiety symptoms, it is important to consider potential side effects, including sedation, anticholinergic effects, and CNS depression. Proper patient selection, dose adjustments, and monitoring can help maximize benefits and minimize risks. Ongoing research and future prospects for Dimetindene focus on novel formulations, combination therapy, targeted approaches, and exploring its use in specific anxiety subtypes. With further investigation, Dimetindene may continue

to be a highly valuable option in the armamentarium of anxiety management. Acknowledging the great potential of Dimetindene as a medium strong tranquilizer and potent anxiolytic, it is crucial to emphasize the importance of individualized treatment plans and comprehensive assessments before initiating therapy.

Healthcare professionals should consider factors such as the severity of anxiety symptoms, comorbidities, potential drug interactions, and patient preferences when determining the appropriateness of Dimetindene Maleate for a specific individual. Furthermore, it is essential to maintain open and honest communication with patients regarding the benefits and potential side effects of Dimetindene. Patients should be educated about the sedative effects of the medication and advised to exercise caution when engaging in activities that require alertness. Monitoring for adverse effects, especially in vulnerable populations such as the elderly or those with impaired hepatic or renal function, is essential to ensure patient safety. To put it into a nutshell, Dimetindene represents a medium strong tranquilizer and anxiolytic with demonstrated efficacy in the management of anxiety disorders. Its pharmacological properties, including histamine receptor antagonism and complex modulation of neurotransmitter systems contribute to its anxiolytic and sedative effects. By understanding the mechanism of action, pharmacokinetics, clinical applications, and potential side effects of Dimetindene, healthcare professionals can make informed decisions regarding its use and provide optimal care to patients with anxiety disorders. Continued research and exploration of this medication may lead to further advancements, improving its therapeutic potential and expanding treatment options for individuals experiencing anxiety-related symptoms.

Conflict of interests

None declared.

Remark

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