

Role of Phenzelzine in Depression

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Abstract

Phenzelzine is the drug used to treat patients suffering from atypical depression or treatment resistant depression. The present article will review the different approaches in the treatment of atypical depression and the role of phenzelzine. Phenzelzine is not the drug of choice in treatment of mild or moderate depression because of its adverse effects profile. It is the drug used in treatment of severe depression. Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), chromium, and cognitive therapy are the options for treatment of mild or moderate depression because of their safety profile. Despite advances in agents for treatment of depression, treatment for atypical depression remains dependent upon older agents for the greatest efficacy.

Introduction

Phenzelzine is a monoamine oxidase inhibitor (MAO inhibitor) which is used in the treatment of severe depression or treatment resistant depression. The major drawback associated with the use of phenzelzine is rare instances of acute liver injury^[1].

Clinical Indications

Phenzelzine is an FDA-approved drug for the management of depression in adults. Off label, the drug may be used for the management of treatment-resistant depression, panic disorder, and social anxiety disorder. Phenzelzine is also specifically useful for young women who have depression and mood disorders. Research has not established the safety and efficacy for children or adolescents.

MAO-inhibitors such as phenzelzine can treat a variety of diseases including bulimia nervosa, PTSD, pain secondary to angina, atypical facial pain, migraine, and even ADD (attention deficit disorder). Phenzelzine has also been found to help lower weight in patients with obesity and potentially help the L1 cell-mediated response for the neural generation, axon regrowth and sprouting, and myelination^[1,2].

Mechanism of Action

Phenzelzine is a nonselective monoamine oxidase A and B inhibitor (MAOI): phenzelzine irreversibly blocks serotonin, norepinephrine, and dopamine from being broken down, allowing these neurotransmitters to have a more prolonged effect on their accompanying receptors. Phenzelzine usually takes up to 2 to weeks to start showing some benefit. If by 6 to 8 weeks, therapy has not achieved the intended results, a higher dosage will be necessary^[3-5].

Dose and Route of Administration

Phenzelzine can only be administered orally via tablet form. Patients must avoid foods and beverages containing tyramine, tryptophan, and/or caffeine to prevent phenzelzine drug-interaction. The starting dose is 15 mg/ day, which may be increased to 3 doses of 15 mg/day, making a total of 45 mg/day. The highest allowable concentration of phenzelzine is up to 90mg/day for adults and geriatrics.

If a patient has a depressive disorder, the recommended initial dose is 5 mg PO/day over a 2 to 6 week period to determine if the anti-depressive effect has occurred; if not, dose adjustment may be necessary.

Patients with hepatic or severe renal impairment must avoid monoamine oxidase inhibitors to prevent toxicity or worsening of the condition^[6].

Adverse Drug Effects

Although phenelzine's intended use is to block serotonin from being broken down, it can also have adverse effects on the GABA and melatonin receptors and thus can potentiate insomnia. The inhibition of norepinephrine from break down can also affect the vascular smooth muscles. A profound decrease in blood pressure leading to orthostatic hypotension may also occur in patients taking phenelzine. To treat the orthostatic hypotension caused by phenelzine, a patient must avoid consumption of caffeine and drink up to 2 liters of water/day to prevent dehydration. Constipation, dry mouth, change in weight, anorgasmia, nausea, and weight gain are well-known side effects of this drug^[7-9].

Phenelzine may also cause drowsiness or dizziness; thus, the clinician should exercise caution in patients operating machinery or driving. Patients diagnosed with asthma must use discretion due to the drug's effect on sympathetic neurotransmission^[10].

Contraindications

Phenelzine's worst, even potentially life-threatening reaction, is a hypertensive crisis that occurs when taking this drug is taken with tyramine-containing foods such as cheese and wine. Phenelzine must stop two weeks before the patient ingests any tyramine-containing substances to avoid an adverse reaction^[11-12].

This drug cannot be combined with tramadol because seizures may be potentiated. Also, phenelzine may not be combined with sympathomimetic drugs (e.g., amphetamines, cocaine, methylphenidate) because it can cause a hypertensive crisis with a headache, intracranial bleeding, and even the potential of death occurring.

The combination of MAOI with a tricyclic/tetracyclic antidepressant, such as amoxapine, is possible because it has 5HT_{2A} protective properties. The most common side effects are weight gain and orthostatic hypotension when using this combination.

Phenelzine is contraindicated with these substances and medications: SSRI, SNRI, clomipramine, St. John's Wort, MDMA (ecstasy), cocaine, methamphetamine, meperidine, tramadol, methadone, and fentanyl, non-subcutaneous sumatriptan, chlorpheniramine, brompheniramine, dextromethorphan, and procarbazine due to the high risk of serotonin syndrome^[13].

Phenelzine is especially contraindicated for pregnant women as a Category C risk because of the potential of fetal malformation during the first trimester. Also, while breastfeeding, if a baby becomes sedated or irritable, then the drug needs to be discontinued immediately. Phenelzine contraindications include individuals with renal impairment and hepatic impairment due to drug toxicity. Phenelzine administration is permissible in patients with cardiac abnormalities, but close monitoring is required^[14-15].

Phenelzine and Treatment Resistant Depression

A clinician must be cautious when giving phenelzine to children under the age of 16 because it can increase the risk of suicide or bipolar disorder.

If the depression is resistant to all other antidepressants, an MAOI can be combined with D-amphetamine or methylphenidate or lithium and mood-stabilizing anti-convulsive to augment the best response.

Children require monitoring in-person to assess if the proper achievement of the antidepressant effects of phenelzine.

The onset of the antidepressant effects of phenelzine takes 2-3 weeks to begin. There is no need to taper off phenelzine because the effects naturally wear off within the same 2 to 3 week time period.

If orthostatic hypotension does occur, the dosing can split to four times/day to lower the concentration of the drug administered each dose. The hepatic function and renal function must be monitored at each clinic visit to prevent liver or kidney toxicity^[16].

Overdose Toxicity and its Management

For patients who overdose on phenelzine, the symptoms can range from agitation to comatose status. Sympathetic overflow effects can also be observed, such as hypertension, tachypnea, tachycardia, and dilated pupils. There may be observable involuntary movements of the face and jaw.

If phenelzine overdose is suspected, dialysis and acidification of the urine must take place immediately. Chlorpromazine is another option if a hypertensive crisis secondary to suspected phenelzine overdose^[5,8].

Effects on Lactation and Breastmilk

Phenelzine can elevate serum prolactin in some patients^[17] and has caused galactorrhea in nonpregnant, nonnursing patients^[18].

Conclusion

Monoamine oxidase is an enzyme that is responsible for degradation of norepinephrine and serotonin. Phenelzine acts in the human body by inhibition of enzyme monoamine oxidase inhibitor, therefore increases the level of norepinephrine and serotonin in brain which is responsible for its antidepressant effect. Phenelzine is now not commonly used drug of presence of antidepressants such as the tricyclic antidepressants and the selective serotonin reuptake inhibitors which are having better efficacy and safety profile as compared to phenelzine. Common adverse effects associated with phenelzine are drowsiness, dizziness, headache, insomnia, tremor, dry mouth, nausea, increased appetite, weight gain and sexual dysfunction. Phenelzine also has food as well as drug interactions. Therefore Phenelzine is now reserved only for the patients suffering from treatment resistant depression.

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