Treatment of Adverse Effects

Withdrawal of hydralazine or dosage reduction reverses many of the adverse effects. Peripheral neuropathy has been reported to be alleviated by pyridoxine. If overdosage occurs the benefit of gastric decontamination is uncertain, but activated charcoal may be given if the patient presents within 1 hour of ingestion. Symptomatic and supportive treatment, including plasma expanders for shock and a beta blocker for tachycardia, should be given as necessary. Hypotension may respond to placing the patient in the supine position with the feet raised. If possible, pressor drugs should be avoided. If a pressor is necessary, one should be chosen that will not cause tachycardia or exacerbate arrhythmias; adrenaline should not be used.

Precautions

Hydralazine is contra-indicated in patients with severe tachycardia, dissecting aortic aneurysm, heart failure with high cardiac output, cor-pulmonale, or myocardial insufficiency due to mechanical obstruction, for example aortic or mitral stenosis or constrictive pericarditis. Hydralazine is also contra-indicated in patients with idiopathic SLE and related disorders. Hydralazine-induced vasodilatation produces myocardial stimulation. It should therefore be used with caution in patients with ischaemic heart disease since it can increase angina and it should not be given after myocardial infarction until the patient's condition has stabilised. Patients with suspected or confirmed ischaemic heart disease should be given hydralazine under cover of a beta blocker, which should be started a few days before hydralazine, in order to prevent myocardial stimulation. If given to patients with heart failure they should be monitored for orthostatic hypotension and tachycardia during the initial stages of therapy, preferably in hospital. If treatment with hydralazine is to be stopped in patients with heart failure it should generally be withdrawn gradually. Hydralazine should be used with caution in patients with cerebrovascular disorders. The dose of hydralazine should be reduced or the dosage interval prolonged in patients with hepatic or renal impairment. Complete blood counts and antinuclear antibody determinations should be carried out about every 6 months during long-term therapy. Urine analysis (for microhaematuria and proteinuria) is also recommended.

Interactions

The hypotensive effect of hydralazine may be enhanced by other drugs with a hypotensive action. Severe hypotension may occur if hydralazine and diazoxide are given together. However, some interactions with antihypertensives may be beneficial: thiazide diuretics also counteract the fluid retention caused by hydralazine, and beta blockers diminish the cardiac-accelerating effects

OVERDOSAGE:

Overdose can occur due to accidental administration of excessive doses, miscalculations, or misuse. Factors increasing the risk include lack of proper medical supervision, incorrect dosing, or patient-specific variables such as impaired renal or hepatic function. In some cases, overdose may result from attempts to self-medicate or misuse the medication outside of medical guidance.

Symptoms of Hydralazine Overdose

The clinical presentation of an overdose can vary depending on the amount ingested and individual patient factors. Common symptoms include:

- Severe hypotension (low blood pressure)
- Reflex tachycardia (rapid heartbeat)
- Palpitations
- Flushing and sweating
- Headache and dizziness
- Nausea and vomiting
- Weakness and fatigue

In severe cases, overdose may lead to shock, arrhythmias, or even coma. Immediate recognition of these symptoms is vital for prompt intervention.

There is no specific antidote for hydralazine overdose. Therefore, treatment focuses on symptomatic management and preventing complications. Hospitalization is often required for close monitoring and intervention.

Prevention and Precautions

Preventing overdose involves proper dosing, patient education, and careful monitoring during administration. Healthcare providers should adhere to recommended guidelines and adjust doses based on patient-specific factors. Patients should be informed about the importance of following medical instructions and reporting any adverse symptoms immediately.

PREGNANCY.

For reports of thrombocytopenia and a lupus like syndrome occurring in neonates after maternal treatment with hydralazine during pregnancy, see Effects on the Blood and Lupus Erythematosus respectively, under Adverse Effects, above.

PREGNANCY AND BREST FEEDING.

Hydralazine concentrations were found to be similar in maternal and umbilical M cord blood in a study of 6 women being treated with hydralazine for pronounced hypertension during pregnancy. Hydralazine was determined in the breast milk of 1 mother, but amounts detected were unlikely to produce clinically relevant concentrations in the infant.

Storage: - Store Protect from light, at a temperature no exceeding 30°C

Improper Storage may deteriorate the product

Medicine: - Keep out of reach of children.

Presentation: - 10x1 ml ampoule in tray such tray in carton with insert.

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For the use of Registered Medical Practitioner or Laboratory or Pharmacy

℞ Hydralazine Hydrochloride Injection USP

AMERICAN HYDRALZIN 20

Injection

FOR IV INFUSION USE ONLY

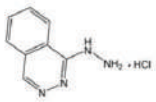
Composition: -

Each ml Contains: -

Hydralazine Hydrochloride	USP	20 mg
Water for Injection	IP	q.s.

DESCRIPTION: -

Hydralazine Hydrochloride Injection USP is an antihypertensive available in a 1 mL amopule for intravenous administration. Hydralazine Hydrochloride USP is a white to off-white, odorless crystalline powder. It is soluble in water, slightly soluble in alcohol, and very slightly soluble in ether. It melts at about 275°C, with decomposition, and has a molecular weight of 196.64. Molecular Formula $C_8H_8N_4HCl$, and its structural formula is:



Hydralazine Hydrochloride

PHARMACOLOGY

PHARMACOKINETICS

Hydralazine hydrochloride injection is a potent vasodilator primarily used in the management of hypertension and hypertensive emergencies. Understanding its pharmacokinetics is essential for optimizing therapeutic efficacy and minimizing adverse effects. This detailed overview covers the absorption, distribution, metabolism, and excretion (ADME) of hydralazine hydrochloride when administered via injection.

Absorption As an injectable formulation, hydralazine hydrochloride bypasses the gastrointestinal tract, leading to immediate bioavailability. When administered intravenously, the drug rapidly enters systemic circulation, providing quick onset of action typically within 10 to 20 minutes. Intramuscular or subcutaneous routes result in slower absorption, with peak plasma concentrations occurring within 30 to 60 minutes. The bioavailability of hydralazine via injection is considered complete, ensuring predictable plasma levels.

Distribution: - Hydralazine exhibits extensive distribution throughout body tissues. It has a moderate volume of distribution, approximately 1.6 L/kg, indicating significant tissue penetration. The drug binds to plasma proteins at a rate of about 10-20%, which influences its free (active) concentration. Hydralazine crosses the blood-brain barrier and placental barrier, raising considerations for central nervous system effects and fetal safety during pregnancy.

Metabolism: - The primary metabolic pathway for hydralazine involves hepatic acetylation, converting the drug into inactive metabolites. The rate of acetylation varies among individuals due to genetic polymorphisms, classifying patients as slow or fast acetylators. Slow acetylators tend to have higher plasma concentrations and prolonged drug effects, which can increase the risk of adverse reactions such as drug-induced lupus erythematosus. The hepatic metabolism also involves conjugation processes, further facilitating renal excretion.

Excretion: - Hydralazine and its metabolites are predominantly eliminated via the kidneys. Approximately 80-90% of the administered dose is excreted in the urine within 24 hours. The elimination half-life of hydralazine ranges from 2 to 8 hours, depending on individual metabolic rates and renal function. Impaired renal function can prolong drug clearance, necessitating dosage adjustments to prevent accumulation and toxicity.

USES AND ADMINISTRATION

Hydralazine is a direct-acting vasodilator that acts mainly on the arterioles. it reduces blood pressure and peripheral
resistance but produces fluid retention. Tachycardia and an increase in cardiac output occur mainly as a reflex response to the reduction in peripheral resistance. Hydralazine tends to improve renal and cerebral blood flow and its effect on diastolic pressure is more marked than on systolic pressure.
Hydralazine may be given intravenously in hypertensive crises. It is also used with isosorbide dinitrate in the management of heart failure. For further discussion of this use of hydralazine,The dose of hydralazine should be reduced or the dosage interval prolonged in patients with hepatic or renal
impairment. In hypertension.
In hypertensive crises, hydralazine hydrochloride is given by intravenous or intramuscular injection.
a dose of 5 to 10 mg is given by slow intravenous injection, repeated, if necessary, after 20 to 30 minutes.
Alternatively, a continuous intravenous infusion is given in an initial dose of 200 to 300 micrograms/minute; the usual maintenance dose range is 50 to 150 micrograms/minute. In the USA,
higher doses are used; a dose of 20 to 40 mg is given by rapid intravenous or intramuscular injection, repeated as necessary.

ADVERSE EFFECTS:

Adverse effects are common with hydralazine, particularly tachycardia, palpitations, angina pectoris, severe headache, and gastrointestinal disturbances such as anorexia, nausea, vomiting, and diarrhoea. These adverse effects, and flushing, dizziness, and nasal congestion, which occur less often, may be seen at the start of treatment, especially if the dose is increased quickly. They generally subside with continued treatment. Other less common adverse effects include orthostatic hypotension, fluid retention with oedema and weight gain, conjunctivitis, lachrymation, tremor, and muscle cramps. Hydralazine may deplete pyridoxine in the body, and can produce peripheral neuropathy with numbness and tingling of the extremities. Occasionally, hepatotoxicity, blood dyscrasias, haemolytic anaemia, difficulty in urinating, glomerulonephritis, constipation, paralytic ileus, depression, and anxiety occur.
Hypersensitivity reactions including fever, chills, pruritus, and rashes have been reported, and eosinophilia may occur. Antinuclear antibodies may develop after prolonged use of large doses, and a condition resembling SLE may occur. The incidence is greater in slow acetylators, patients with renal impairment, women, and patients taking more than 100 mg of hydralazine daily. The symptoms usually disappear when the drug is withdrawn; some patients may require treatment with corticosteroids. Acute over dosage may produce hypotension, tachycardia,
myocardial ischaemia, arrhythmias, shock, and coma.