ENOXIMONE

[ARCHIVED MONOGRAPH]

Use

Intravenous enoximone is sometimes used in the short term management of heart failure that fails to respond to other forms of treatment. Milrinone (q.v.) is an easier drug to administer.

Pharmacology

Enoximone (patented in 1980) is a selective phosphodiesterase inhibitor which acts mainly on the myocardium as an inotrope. It is, however, also a mild vasodilator. Long term oral use seems to be associated with an increase in mortality in adults with congestive failure, and the drug is now only used in the short term intravenous management of patients in whom a low cardiac output persists despite treatment with a catecholamine such as dobutamine (q.v.). Preoperative monitoring has certainly shown enoximone to be of short term benefit in restoring myocardial function after by-pass surgery. It seems to work by increasing the intracellular concentration of cyclic AMP. This could explain why the drug's effectiveness seems to be enhanced by the simultaneous use of a catecholamine to stimulate the cardiac β-receptors. Enoximone is excreted in the urine, but is also partially metabolised in the liver. The half life is much the same in infancy as it is in adult life, but varies widely, being 1-4 hours in healthy volunteers and twice this in patients in heart failure, and even longer where renal function is poor. The volume of distribution is also high (V_D 3·6 l/kg), making it important to employ an initial loading dose. Use could be hazardous in patients with outlet obstruction or hypertrophic cardiomyopathy (as with any inotrope). There is no published evidence relating to the use of enoximone in pregnancy, and it is not known whether the drug is excreted into breast milk. There is no animal evidence of teratogenicity. The manufacturers have not yet endorsed the use of enoximone in children.

Treatment

Give 600 micrograms/kg of enoximone over 15 minutes (0·24 ml of a solution made up as described below for each kilogram the baby weighs). Continuing this same infusion at a rate of 0·24 ml/kg per hour then provides a maintenance infusion of 10 micrograms/kg per minute. Maintenance doses of up to 20 micrograms/kg per minute have sometimes been used for short periods, but drug accumulation could be a hazard where there is renal failure. The benefits seen at the start of treatment seem to wane with time. Treatment following corrective cardiac surgery is seldom continued for more than 1 or 2 days. Prepare a fresh solution once every 24 hours.

Propylene glycol toxicity

Enoximone contains 41·3% w/v of propylene glycol, and sustained high dose administration is known to have caused severe hyperosmolality. Some propylene glycol is metabolised by the liver, but much is excreted unmetabolised in the urine. Renal failure would, therefore, increase the risk of toxicity

Propylene glycol is widely used as a solvent in IV drugs, and is also a component of many topical pharmaceutical creams. While it is relatively non-toxic, excess intake can certainly be harmful. The first sign of accumulation is usually an otherwise unexplained rise in osmolality. Symptoms have included stupor, seizures and lactic acidosis. Arrhythmias have developed in animals.

Supply and administration

20 ml ampoules containing 5 mg/ml cost £15. Dilute immediately before use with an equal volume of water for injection to obtain a solution containing 2·5 mg/ml, and prepare a fresh solution once every 24 hours. Enoximone should not be co-infused with any other drug. It is incompatible with dextrose, and dilution with 0·9% sodium chloride imposes a relatively large obligatory sodium load on the baby. The manufacturers are not even prepared to say that it is safe to infuse enoximone through a terminal Y connector into a line containing glucose because solubility problems cause rapid crystal formation. Troublesome crystal deposition can even narrow, and occasionally block, a narrow IV line even when the drug is infused in saline. Make sure that the solution is still a clear yellow colour prior to administration. Keep ampoules at below 20ºC (they are conveniently stored at 4ºC).

References

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