

PROSTAGLANDIN E₂ = Dinoprostone (rINN)

Use

Prostaglandin E₂ gels and vaginal tablets now widely used to initiate and augment labour. Both Prostaglandin E₁ and E₂ can be used to maintain patency of the ductus arteriosus pending surgery in babies with a duct-dependent congenital heart defect.

Pharmacology

Prostaglandin E₁ and E₂ are potent vasodilators originally isolated from prostate gland secretions that inhibit platelet coagulation and stimulate uterine contractility. Prostaglandin E₂ was first synthesised in 1970 and is still occasionally used to terminate pregnancy by extra-amniotic administration, while tablets, gels, pessaries are now very widely used to ripen the cervix and/or initiate labour at term. Misoprostol (q.v.), an analogue of prostaglandin E₁, is also sometimes used to initiate labour, and is more widely used to control postpartum bleeding, although the manufacturers have not yet sought permission to market the drug for use in this way. Caution must be employed before using prostaglandins and oxytocin simultaneously because each drug potentiates the effect of the other.

Prostaglandins were first used experimentally to sustain ductal patency in 1975, and continuous IV infusions are now frequently employed in the early preoperative management of babies with duct-dependent congenital heart disease. Prostaglandin E₁ (alprostadil) is the licensed preparation, but a similar dose of Prostaglandin E₂ is equally effective and eight times as cheap. Because of rapid inactivation during passage through the lung, the half life during IV infusion is less than a minute, and no loading dose is necessary. Monitor oxygen saturation. Respiratory depression and apnoea are common with high dose treatment (some texts still recommend a dose that is much higher than necessary) and may occur, even with the dose recommended here, especially in the cyanosed or preterm baby. High dose treatment causes vasodilatation and hypotension, and has rarely caused diarrhoea, irritability, seizures, tachycardia, pyrexia and metabolic acidosis. Watch for hypoglycaemia. Continued IV use for more than 5 days can cause gastric-outlet obstruction due to reversible antral hyperplasia, and long term use can cause hyperostosis of cortical bone.

Sustained oral administration is still sometimes used in a few centres, but it is rarely employed in the UK now because delay is not thought to render surgery any less technically difficult. Start with 25 micrograms/kg by mouth once an hour and double this if necessary. Some babies manage with treatment every 3–4 hours, but many need a dose every two hours to remain stable.

Treatment

Maternal: 1 mg of vaginal gel (2 mg if the cervix is unfavourable) inserted high into the posterior fornix, or a 3 mg vaginal tablet similarly positioned is now the most widely used method of inducing labour. A second dose of either can be given, if necessary, after 6–8 hours. An infusion of 0.25 to 1 microgram per minute is now only rarely used to initiate labour, but is still occasionally employed to induce labour after fetal death.

Neonatal: Start with a 10 nanograms/kg per minute IV infusion through a secure line (0.6 ml/kg per hour of a solution made up as described below) and then use oxygen saturation to adjust this dose up, or down, as necessary. Always use the lowest effective dose: a 40 nanograms/kg per minute dose is rarely needed.

Preventing neonatal apnoea

Use the minimum effective dose of prostaglandin. If high dose treatment is necessary the risk of apnoea can be reduced by giving IV aminophylline (q.v.). Caffeine (q.v.) would probably be equally effective.

Compatibility

Prostaglandin E₂ (dinoprostone) is very unstable in solution, and should never be infused with any other drug. In contrast it may be acceptable to add prostaglandin E₁ (alprostadil) (terminally) when absolutely necessary, into a line containing dobutamine and/or dopamine, heparin, midazolam, morphine or ranitidine, although the manufacturers remain reluctant to endorse this advice.

Supply and administration

One 0.75 ml IV ampoule of prostaglandin E₂ (containing 1 mg/ml) costs £8.50. Note that 10 mg/ml ampoules are sometimes stocked for use in termination of pregnancy. To give an infusion of 10 nanograms/kg per minute, add 0.5 ml of dinoprostone from a 1 mg/ml ampoule to 500 ml of 10% dextrose saline to produce a solution containing one microgram of dinoprostone per ml, and infuse this at a rate of 0.6 ml/kg per hour. A less concentrated solution of dextrose or dextrose saline can be used where necessary. Store ampoules at 4°C, and prepare a fresh IV solution daily. A sugar-free oral solution with a one week shelf life can be prepared on request. Vaginal gels and tablets are widely used to induce labour; the two are *not* strictly bioequivalent, but a 3 mg tablet is cheaper than 2 mg of gel (£10 v. £18).

References

- See also the Cochrane reviews of obstetric use ©
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