

RIBAVIRIN = Tribavirin (former BAN)

Use

Treatment with ribavirin may reduce the severity of bronchiolitis due to respiratory tract viral infection if started within 3 days of the onset of lower respiratory tract symptoms. Combined treatment with interferon alfa (q.v.) controls viraemia and slows disease progression in children with chronic hepatitis C infection.

Pharmacology

Ribavirin (first synthesised in 1972) is a stable, white, synthetic nucleoside with in vitro antiviral properties against the respiratory syncytial virus, and some adenoviruses as well as the influenza, parainfluenza and measles viruses. A significant amount of drug is absorbed systemically after aerosol administration and the concentration in respiratory secretions is particularly high. Ribavirin is teratogenic and embryolethal and should never be given to pregnant patients; the manufacturers even advise against it being administered by staff who are pregnant. There is some evidence that it can be mutagenic in cell culture, and may (with chronic exposure), induce benign glandular tumours. Its clinical use is therefore currently limited to high-risk children (children with congenital heart disease, existing bronchopulmonary dysplasia or immunodeficiency) with proven lower respiratory tract viral infection. There is only one study suggesting that use speeds recovery in ventilator-dependent infants and little evidence that it reduces the time it takes for patients to stop shedding live virus particles. The only common adverse effect in children with standard treatment is conjunctivitis, but little is known about possible long term morbidity or toxicity. While widespread American experience suggests that ribavirin is safe used in this way, most clinicians in Europe believe that further evidence of efficacy is needed. Nine small controlled studies have now been done, but the total number of children studied (291 in all) remains inadequate to establish the utility of this form of treatment.

Perinatal Hepatitis C infection

When viral RNA can be detected in the mother's blood on PCR testing during pregnancy, there is about a 5% risk of the baby becoming infected, and this increases if the woman also has HIV. There is, however, no reason to undertake Caesarean delivery or advise the woman not to breast feed unless there is HIV. One study suggests that delaying membrane rupture as long as possible once the woman goes into labour may minimise the risk of transmission. If the woman is anti-HCV positive but viral RNA is not detectable it is very rare for the baby to become infected. When infection occurs during rather than before birth viral RNA may take 2–3 months to become detectable in the baby but, if it does appear, this indicates active infection and merits referral to a supra-regional liver centre. Other babies should be watched until they become anti-HCV negative. The prognosis for those babies who do become actively infected is variable. It looks as though complete viral elimination occurs in a quarter, but a minority develop progressive disease meriting treatment with ribavirin and interferon alfa (q.v.) to stop liver fibrosis eventually progressing to frank cirrhosis.

Treatment

Nebulised administration: Administer 60 mg/ml of ribavirin for 2 hours 3 times a day using a small particle aerosol generator (SPAG) for 3 to 7 days, preferably using a modified Easy Vent[®] CPAP device. Early treatment *may* be appropriate in high-risk children with a proven viral lower respiratory tract infection to try and reduce the chance of their needing ventilator support. There is no good evidence that use shortens the duration of treatment in children already ill enough to be receiving respiratory support, and such use can easily cause the ventilator to become clogged.

Oral administration: Children with progressive chronic hepatitis C infection have been treated with 15 mg/kg of ribavirin by mouth once a day for 6 or even 12 months. While such treatment is of little benefit on its own, combined treatment with subcutaneous interferon alfa-2b (q.v.) frequently abolishes all detectable evidence of viraemia during treatment and for at least 6 months after treatment stops, especially in patients with genotype 2 or 3 infection. The dose of interferon used has usually been 3 million units/m² of the standard preparation three times a week, or 15 micrograms/kg of the pegylated (polyethylene glycol-conjugated) product once a week. Such treatment has **not** yet been attempted in children less than a year old.

Supply and administration

Ribavirin comes in 100 ml vials containing 6 g of lyophilised drug costing £116 per vial. For nebulised administration dissolve the powder with 100 ml of sterile water for injection free of all preservatives. Any of the reconstituted solution not used within 24 hours of preparation should be discarded.

References

See also the relevant Cochrane reviews ©

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