CABERGOLINE

Use

Cabergoline is used to treat hyperprolactinaemic amenorrhoea, and galactorrhoea. Use can also, occasionally, be justified to suppress lactation after childbirth.

Pharmacology

Bromocriptine is a derivative of ergot that functions as a dopamine D_2 agonist. It was first used to treat patients with Parkinson's disease in 1974 (but is now only used for this purpose in patients who suffer a fluctuant response when treated by levodopa alone). It was once widely used to suppress lactation (see web archive) but side effects resulted in a general switch to the use of Cabergoline in the late 1980s.

Carbergoline is a closely related drug that it well absorbed when given by mouth, metabolised in the liver with a half life of 2–4 days, and excreted largely in the bile. It is a potent, long-lasting inhibitor of prolactin secretion that has now become the most widely used drug in the management of hyperprolactinaemia. Indeed a single dose twice a week will restore ovulation in most women with hyperprolactinaemic amenorrhoea. Although the manufacturers (and the MHRA – the UK regulatory agency) have both recommended that treatment should be avoided during pregnancy, and for a month before women try to conceive, there is no evidence of teratogenicity, little evidence that low dose treatment causes the fibrotic heart valves changes sometimes seen in patients with Parkinson's disease, and a real possibility that withdrawal could prevent ovulation or result in vision-threatening increase in size if the tumour is already large. Low dose treatment during lactation has not caused a problem in patients with a prolactinoma, and the baby ingests, on a weight-related basis, less than 1% of the maternal dose. It is, however, often possible to stop treatment during lactation because prolactinomas usually only grow slowly at this time.

Effect on lactation

Milk formation during late pregnancy occurs under the combined stimulus of oestrogens, prolactin (placental lactogen) and progesterone. Insulin and cortisol may also have a role. Oestrogens antagonise the effects of prolactin, and lactation is stimulated when oestrogen levels fall after delivery.

Oestrogens were once used widely to suppress lactation in the puerperium, but they were found to be relatively ineffective, and to increase the risk of potentially life threatening thromboembolism. Trials undertaken between 1972 and 1984 showed 2·5 mg of bromocriptine twice a week for 2 weeks to be a more effective alternative. However most drug trials only looked at the immediate effect of drug treatment and there is some evidence that, although bromocriptine reduces pain, engorgement and milk production one week after delivery more than a breast binder, the situation is reversed two weeks later.

Over the next ten years reports started to appear of mothers having seizures, strokes, heart attacks and sudden severe hypertension while taking bromocriptine to suppress lactation. While it is difficult to know whether these problems were caused by the use of bromocriptine problems were, however, reported with sufficient frequency for the manufacturers to stop recommending the use of bromocriptine to suppress lactation in 1994. Since discomfort is only a transient problem there can seldom be a case for using ***any*** drug to suppress lactation in most mothers, but drug use can still be justified in certain situations. Continued milk production can certainly cause acute anguish to a few mothers coping with a stillbirth or early neonatal death. Here cabergoline is probably the drug of choice (even though it gets little mention in the recent Cochrane review). It seems to be relatively free from the problems associated with the use of bromocriptine to suppress lactation, although that could be because it has not, as yet, been as widely used. However, post-treatment rebound certainly seems less marked. If either drug is used for this purpose, treatment should certainly be stopped at once if the mother experiences any severe headache or visual disturbance.

Use to suppress lactation

A single 1 mg dose of cabergoline by mouth is usually enough to suppress lactation immediately after delivery. If lactation has already been established, give four 250 mg doses at 12 hour intervals.

Supply

500 microgram scored tablets of cabergoline are available (costing £3·70 each), as are 2·5 mg tablets of bromocriptine (costing 18p each).

References

See also the relevant Cochrane reviews ©

European Multicentre Study Group for Cabergoline in Lactation Inhibition. Single dose cabergoline versus bromocriptine in inhibition of peurperal lactation: randomised, double-blind, multicentre study. *BMJ* 1991;**302**:1367–71. [RCT]

Rains CP, Bryson HM, Fitton A. Cabergoline. *Drugs* 1995;**49**:255–79. [SR]

Caballero-Gordo A, Lopez-Nazareno N, Calderay M, *et al.* Single-dose inhibition of puerperal lactation. *J Reprod Med* 1991:**36**:717–21.

Webster J. A comparative review of the tolerability profiles of dopamine agonists in the treatment of hyperprolactinaemia and inhibition of lactation. *Drug Safety* 1996;**14**:228–38.

Caballero GA, Caballero DJL. Caberbolina: Nuevo dopaminérgico a dosis única en la inhibición de la lactación. *Acta Ginecológica* 1996;**53**:172–9. [RCT]

Dutt S, Wong F, Spurway JH. Fatal myocardial infarction associated with bromocriptine for postpartum lactation suppression. *Aust NZ J Obstet Gynaecol* 1998;**38**:116–9.

Colao A, Abs R,Barcena DG, *et al.* Pregnancy outcomes following carbergoline treatment: extended results from a 12 year observational study. *Clin Endocrinol (Oxf)* 2008;**68**:66–71.

Martin NM, Tan T, Meeran K. Dopamine agonists and hyperprolactinaemia. [Editorial] *BMJ* 2009;**338**:554–5. [*BMJ* 2009;338:b381.]

March 2009 [rewrite]