Dopamine agonists in prolactinomas

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The objectives of the treatment of hyperprolactinemia are the suppression of excessive hormone secretion and its clinical consequences (in particular infertility, sexual dysfunction and osteoporosis), tumor removal and relief of any disturbance in vision and cranial nerve function, preservation of the residual pituitary function and, if possible prevention of disease recurrence or progression. For over 20 years bromocriptine has been the standard drug for hyperprolactinemia. It not only inhibits PRL synthesis and secretion but reduces cellular DNA synthesis and tumor growth. Suppression of PRL levels and tumor shrinkage after bromocriptine therapy, at doses of 2.5-5 mg/day, is observed in 80% of prolactinomas. Side effects (nausea, dizziness and hypotension) are a limiting factor in continuing the treatment in 5-10% of patients. Moreover, complete or partial resistance to bromocriptine treatment is observed in a minority of patients. Both quinagolide and cabergoline, two selective D2 receptor agonists, were proven to be effective in some resistant patients. In particular, recent evidence suggests that weekly administrations of cabergoline treatment are more effective and better tolerated than bromocriptine: stable normoprolactinemia was achieved in 83% of patients treated with cabergoline compared to 59% of those treated with bromocriptine; ovulatory cycles or pregnancies were recorded in 72% of women treated with cabergoline and in 52% of those treated with bromocriptine. Cabergoline at weekly low doses successfully reduced macroprolactinoma size in most patients. A further advantage is that cabergoline induced significantly less frequent, less severe and shorter-lived side effects (particularly nausea and vomiting) than bromocriptine. Neither bromocriptine, cabergoline nor quinagolide have been associated with any teratogenic effect on foetal development or on pregnancy outcome. Very recently we also demonstrated a very high success rate of cabergoline withdrawal in both macro- and microprolactinomas: approximately 65% of patients remained normoprolactinemic 5-yr after cabergoline withdrawal. These results indicate the need of periodic treatment interruptions at least in patients not showing tumor remnants at MRI.