

THE TREATMENT OF PROLACTINOMA DURING PREGNANCY

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REZUMAT

În cazul femeilor cu macroprolactinom cu extindere infraselară sau inferioară, tratamentul cu bromocriptină a fost sugerat pentru restaurarea fertilității. După momentul concepției, terapia este discontinuată și reinițiată doar dacă simptomele date de creșterea tumorală reapar. La femeile cu macroprolactinoame mai mari, alegerea tratamentului optim este mai dificil de determinat. Unii sugerează reducerea maximă a mărimii tumorii prin tratament medical înaintea sarcinii. După momentul concepției, tratamentul cu bromocriptină poate fi stopat, sau continuat și în timpul sarcinii, în funcție de agresivitatea tumorii. Dacă simptomele de creștere tumorală reapar, tratamentul poate fi început din nou. Dacă tratamentul medical eșuează, se recomandă intervenția chirurgicală. Alăptarea este posibilă la femeile cu prolactinoame.

ABSTRACT

In women with micro- or small infrasellar or inferiorly extending macroprolactinomas, treatment with bromocriptine has been suggested to restore fertility. Following conception, therapy is discontinued, and reinitiated only if symptoms of tumor growth develop. In women with larger macroprolactinomas, the optimal choice of treatment is more difficult to determine. One should advocate the patient to aim at maximal tumor size reduction by medical treatment prior to pregnancy. Following conception, treatment with bromocriptine may be stopped or continued during pregnancy, depending on the aggressiveness of the tumor. If symptoms of tumor re-growth develop in the former, therapy may be reinitiated. If medical treatment fails, surgery is recommended. Breast feeding is possible in women with prolactinomas.

Prolactinomas are generally classified according to size. Microprolactinomas are less than 10 mm in size, whereas macroprolactinomas are at least 10 mm in size. Macroprolactinomas can be intrasellar or can extend into the extrasellar neighborhood and invade the dura, sphenoid bone, cavernosus sinuses, the suprasellar cisterns, and the adjoining parts of the brain. Prolactinomas larger than 4 cm in diameter and/or with massive extrasellar extension may be termed "giant prolactinomas". The clinical features of prolactinomas are composed of the endocrine effects due to the hyperprolactinemic state, and local tumor mass effects.¹

Observation may be an option in patients with microprolactinomas in the absence of any relevant

clinical symptoms. In all other patients with prolactinomas, medical therapy is the initial treatment of choice. Transphenoidal surgery remains an option in patients with resistance to, or intolerance to dopamine agonists.

Medical therapy is employed as primary therapy of prolactinomas in most centers now. It is based on the use of dopamine agonists. Whereas bromocriptine (a lysergic acid amide), lisuride (an aminoergoline), pergolide (a clavine alkaloid), and cabergoline (an ergoline derivative) are all ergot alkaloids, quinagolide is a nonergot compound. Worldwide, the most experience has been with bromocriptine.

In an analysis of over 6000 pregnancies, bromocriptine has not been found to increase the risk of spontaneous abortions, ectopic or multiple pregnancies, trophoblastic disease, or congenital malformations, when treatment is stopped at the first sign of pregnancy.² Long-term follow-up of children born from mothers taking bromocriptine in this fashion did not reveal any ill effects. Experience is naturally more limited for cabergoline, with no

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increased risk of preterm, ectopic, or multiple birth deliveries, or malformations being observed in 265 pregnancies. Most centers still prefer bromocriptine to restore fertility, although pregnant women may be reassured when taking cabergoline prior to conception. The rising estrogen levels during pregnancy have a marked stimulatory effect on the normal lactotrophs. Hypertrophy and hyperplasia result in an up to 1.5-fold increase in pituitary size. Such increase in size may also occur with prolactinomas, mostly in the second and third trimesters. In a metaanalysis of 19 publications², 1.2% of 363 pregnant women with microprolactinomas and 24% of 82 pregnant women with macroprolactinomas had symptoms of tumor enlargement (headaches and/or visual disturbances). In 69 women with macroprolactinomas treated with surgery or radiotherapy prior to pregnancy, the risk of symptomatic tumor enlargement was considerably attenuated, being 4% in that compilation. Bromocriptine has been used successfully during pregnancy to reduce symptomatic tumor enlargement, with no side effects on the infant, but experience is limited so far.

In women with micro- or small infrasellar or inferiorly extending macroprolactinomas, treatment with bromocriptine has been suggested to restore fertility. Following conception, therapy is discontinued, and reinitiated only if symptoms of tumor growth develop. In women with larger macroprolactinomas, the optimal choice of treatment is more difficult to determine. One should advocate the patient to aim at maximal tumor size reduction by medical treatment prior to pregnancy. At least, responsiveness of tumor size to medical treatment should be established. One possibility would be then to use bromocriptine to restore fertility. Following conception, treatment with

bromocriptine may be stopped or continued during pregnancy, depending on the aggressiveness of the tumor. If symptoms of tumor re-growth develop in the former, therapy may be reinitiated. If medical treatment fails, surgery is recommended. Surgery carries an 1.5-fold risk of fetal loss in the first trimester, and a 5-fold increased risk thereafter. However, it does not increase the risk of malformations. Furthermore, it has to be considered that continued treatment with bromocriptine has not been studied in a sufficiently large number of patients for safety to the developing fetus. Therefore, a more conservative approach would be to perform a surgical debulking prior to pregnancy, thereby greatly reducing the risk of symptomatic tumor enlargement during pregnancy. This may be an option especially in patients with tumors unresponsive in size to medical treatment. Bromocriptine may still be required to normalize PRL levels and restore fertility. Periodic PRL levels are of limited benefit for follow-up during pregnancy. Whereas PRL levels rise during pregnancy in normal women, they do not always do so in women with prolactinomas, even during tumor enlargement. In patients with macroprolactinomas, once or twice monthly visual field testing is recommended. Postpartum PRL levels and tumor size may be reduced compared with values before pregnancy, possibly due to minor infarctions in the tumor. Breast feeding is possible in women with prolactinomas.

REFERENCES

1. Molitch ME. Disorders of prolactin secretion. *Endocrinol Metab Clin North Am* 2001 30; 585-610.
2. Bronstein MD, Salgado LR, de Castro Musolino NR. Medical Management of Pituitary Adenomas: The Special Case of Management of the Pregnant Woman. *Pituitary* 2002; 5: 99-107.