EFFICIENCY OF CABERGOLINE SUPPRESSIVE THERAPY IN YOUNG PATIENTS WITH PROLACTINOMA

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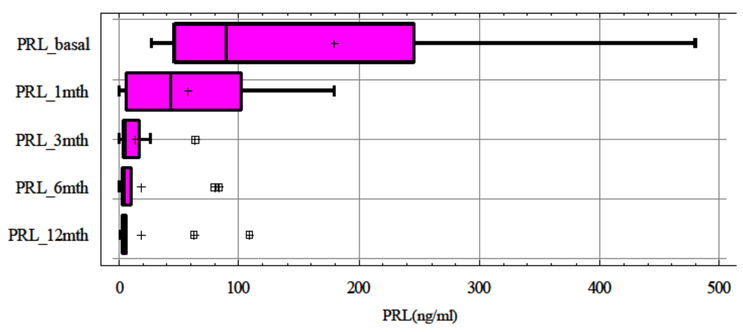
Objectives:

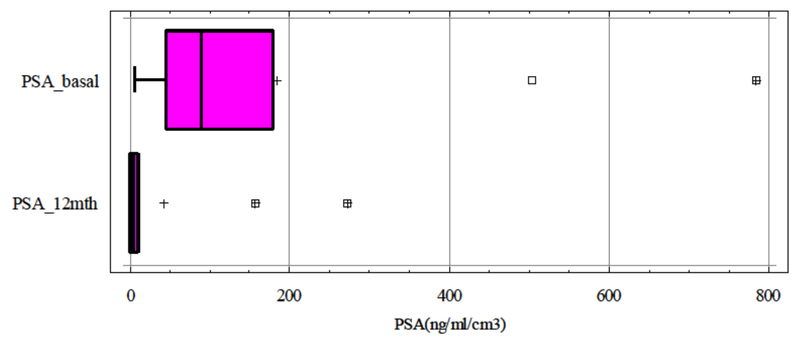
The aim: to study the clinical and hormonal peculiarities of PROL (prolactinoma), manifesting in people under the age of 18 and monitoring the effectiveness of suppressive CAB (Cabergoline, Dostinex) therapy during 12 months period.

Methods:

The total study included 11 patients with PROL, manifesting in childhood.
The clinical examination included: medical history, anthropometry, objective examination (including ophthalmological, neurological, cardiological), physical and pubertal development (Tanner stage) estimation, blood pressure measurement.
Blood samples for PRL (prolactin), GH (Growth hormone), IGF-1 (insulin-like growth factor-1), LH (luteinizing hormone), FSH (follicle stimulating hormone), T (total testosterone), E2 (estradiol), TSH (thyrotropin), fT4 (free thyroxine), cortisol were taken in fasting state and were measured using commercial kits («ELISA» DRG Diagnostics, USA).
There were also examined 54 healthy volunteers (25 males and 29 females) aged 15-19 to determine the range of normal PRL blood values.
Pituitary adenoma was verified by MRI (Tomograph Siemens Magnetom Impact with the magnetic field of 1T). Microadenoma diagnosed with pituitary tumor diameter ≤ 10 mm; macroadenoma - 11-30 mm and giant adenoma > 30 mm.
Pituitary volume (cm3) was calculated according to Di-Chiro-Nelson, using the correction coefficient 1.33.
It were assessed TSA (total secretory activity, ng/ml), PaSA (partial secretory activity, ng/ml/cm3) and SpTG (the speed of tumor growth, cm3/yr).
Target PRL levels in patients with PROL during suppressive therapy CAB was 5 normal percentile. Data analysis: ANOVA, multivariate and univariate regression analysis were performed. Data are given as average, standard error, Median, Min, Max mean. All analyses were conducted using "Statgraphics Plus for Windows 7.0» (Manugistic Inc. USA). A P-value of less than 0.05 was considered significant.

Results:





Normal values of the PRL blood levels of healthy children of both sex aged 15-19 were determined and percentile diagrams were plotted.
Among the **11 patients with PROL** diagnosed in childhood (Me = 16.0 yrs) [Min. 12,0 - Max. 18.0] there were 9 girls and 2 boys. MikroPROL was in 7 girls (average age of first diagnosis: ME = 17.5 yrs), makroPROL - 4 patients (2 girls and 2 boys) (average age of first diagnosis: ME = 16.0 yrs) among them 1 girl and 1 boy (12 and 16 years old) had a gigantic PROL. **Clinical:** Neurological symptoms were observed in 11 patients (100%); 7 - moderately severe hypotension, 8 girls in late puberty - menstrual disorders (opsomenorrhea and secondary amenorrhea); galactorrhea of II stage was found in 3 girls and 2 boys; in 3 children – delay of growth (GH-deficient) and sexual maturation.
At initial examination PRL blood levels was (174.8 ± 49,4) ng/ml (Me = 89.6 ng/ml) [Min. 27,6 - Max. 470.0]: macroPROL - Me = 52.3 ng/ml [Min. 27,6 - Max. 470.0]; microPROL - Me = 200.0 ng/ml [Min. 46,4 - Max. 480.0].
Before treatment PaSA in the whole group was: Me = 81.3 ng/ml/cm3 [Min. 6,2 - Max. 783.0]; in group with macro - and giant PROL - Me = 47.1 ng/ml/cm3 [Min. 6,2 - Max. 90.8]; with microPROL - Me = 98.9 ng/ml/cm3 [Min. 45,3 - Max. 783,3] ($p < 0,05$).
SpTG was Me = 0.8 cm3/yr [Min. 0,2 - Max. 32.0]. Univariate regression analysis showed that the average therapeutic CAB dose was: Me = 1.0 mg/week [Min. 0,2 - Max. 2.0] mg/week; the average cumulative dose - Me = 44.2 mg/yr [Min. 12 - Max. 104.0] mg/yr.
A statistically significant reduction of PRL levels after 1 month of therapy was found, but **the most positive effect was achieved after 3 months therapy (n=9).**
The high efficiency of high start doses of CAB were confirmed by MRI: after 12 months of therapy the decreasing of the pituitary volume by 50% or more was marked in 5 patients, in 2 patients - by 30-49%, and 2 girls became pregnant.

Conclusions:

1) It was found that clinical and hormonal peculiarities of PROL in patients below the age of 18 is the rapid tumor growth and formation of a macro- and giant adenoma in a short time.
2) Prescription of high start doses of CAB is safe and effective in treatment of PROL in children:
- **as evidenced by the absence of side effects, the normalization of the pituitary-gonadal axis and growth hormone function,**
- **rapid sustained reduction in the concentration of PRL level to 5 percentile norm age in most patients (90.1%),**
- **statistically significant reduction of PaSA in all patients, decrease of pituitary tumors by 50% or more in 54.5% patients.**

3) Reducing high-proliferative effect in children with mikroPROL and high SpTG is achieved by applying the average therapeutic dose of CAB 1.0 mg / week, with an average cumulative dose of 44.2 mg / year [Min. 36,1 - Max. 84.2].

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