Cabergoline is an effective treatment for clinically non-functioning pituitary adenomas

Greenman Y1,5, Cooper O6, Yaish I1, Robenshtok E4,5, Sagiv N1, Jonash KT3,5, Mallick J7, Gertych A7, Shimon I4,5, Ram Z5,5, Melmed S6, Stern N1,3

1Institute of Endocrinology and Metabolism, 2Department of Neurosurgery, and 3Neuroradiology Unit, Tel Aviv Sourasky Medical Center; 4Institute of Endocrinology and Metabolism, Rabin Medical Center; 5Sackler Faculty of Medicine, Tel Aviv University. 6Pituitary Center, and 7Pathology Department, Cedars Sinai Medical Center.

OBJECTIVES

• To evaluate the role of DA therapy in patients with NFPA residual tumors after surgery
• To examine whether there is a correlation between response to DA treatment and D2R tumors expression
• To evaluate predictive factors associated with tumors response

METHODS

• Retrospective analysis of prospectively collected data was conducted at two pituitary referral centers with different standard practices for post-operative management of NFPA: DA therapy or conservative follow up.
• Patients were treated (cabergoline 2 mg/week) upon detection of residual tumor on postoperative MRI (preventive treatment - PT group, N=55), or when tumor growth was detected during follow-up (remedial treatment -RT group, N=24). The control group received no medication and comprised 60 patients.
• Dopamine receptor 2 (D2R) expression was examined by immunohistochemistry, D2R long and short isoform mRNA expression was measured by quantitative RT-PCR.

RESULTS

Post-op treatment of NFPA with DA decreases tumor remnant growth

Control group (60) Treatment group (79) p value
Sex F/M 21/39 33/46 NS
Age 57.3 ±14 57.8 ±13 NS
Maximal diameter (pre-op) 26.2±10.9 28.5±11.5 NS
Invasiveness 58.3% 57% NS
Visual field defects 58.3% 52% NS
Macroadenoma (post-op) 63.6% 84% 0.014
High prolactin 31.8% 34.4% NS
Follow up (y) 6.3±5.2 8.8±6.5 0.018

Shrinkage 0% 29.2% 38.2%
Stable 46.7% 29.1% 49.1%
Growth 53.3% 41.7% 12.7%
Tumor control (shrinkage + stabilization) 46.7% 58.3% 87.3%
P<0.0001 for all comparisons

No association between D2R expression and response to treatment

Immunostaining for D2R

Multivariate analysis for tumor progression

\[ X^2 \quad p \quad HR \quad 95\% CI \]

| Medical Center | Treatment | 9.95 | 0.0016 | 0.32 | 0.16-0.65 |
| Post op micro/ macro | Macro | 0.06 | 0.8 | 0.91 | 0.43-1.89 |
| Sex | Male | 5.15 | 0.023 | 2.29 | 1.12-4.68 |
| Age | 8.61 | 0.003 | 0.96 | 0.94-0.98 |

CONCLUSIONS

Dopamine agonist therapy is associated with decreased prevalence of residual tumor enlargement in patients with NFPA, particularly when treatment is instituted prophylactically after surgical resection.