



# Could Hormone Remission be Achieved in Prolactinomas with Surgery?



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Submission: May 24 2018; Published: July 18, 2018

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## Abstract

We retrospectively analyzed 33 prolactinoma cases. Endoscopic endonasal transsphenoidal (EET) surgery can be used as an effective method for microprolactinoma treatment to achieve rapid biochemical and clinical remission. In some macroprolactinomas (<24mm) EET surgery is effective (90% cases)

**Keywords:** Pituitary adenoma; Prolactinoma; Endoscopic endonasal transsphenoidal surgery; Biochemical remission

## Introduction

Dopamine agonists (DA) are recognized as an effective medical treatment since the beginning 1970s<sup>[1,2]</sup> Normoprolactinemia was achieved in 59% when using bromocriptine<sup>[3]</sup>. Normal PRL level can be achieved in 80-90% when using DA. Relevant systemic side effects, including vomiting, nausea, dizziness, headache have been reported in about one third of patients treated with DAs<sup>[4,5]</sup>. DAs have a significant effect on other dopamine, serotonin androgenic receptors, which leads to severe neurological disorders such as postural hypotension or dyskinesia, psychosis, or mania, which provoke compulsive states<sup>[6,7]</sup>. In some cases these possible complications assume surgery over prolactinomas.

## Material and Methods

This study included 33 patients who underwent primary pituitary surgery over prolactinomas with no prior DA treatment

(19 female, 14 male; age ranged, 20–67 years). Microprolactinomas 10 cases, macroprolactinomas 19 cases, giant prolactinoma 4 cases. Endoscopic endonasal transsphenoidal (EET) surgery was performed by single neurosurgeon. Plasma PRL levels were obtained before surgery, and then on the 1<sup>st</sup> day, 1<sup>st</sup> week, 1<sup>st</sup> month, 3<sup>rd</sup> month and then every 6<sup>th</sup> months after surgery. Catamnesis 1-5 years MRI check-up was performed before surgery and then on 3, 6 and 12 month, then on yearly basis.

## Results and Discussion

Median preop PRL serum level for all patients was 530 ng/mL (ranging, 65–1440 ng/mL) Cavernous sinus invasion was observed in 16 (48,5%) cases after surgery. Biochemical remission of PRL level back to normal was in 10 cases with microprolactinomas (100%), in 10 (53%) cases of macroprolactinomas after surgery. No DA therapy after surgery in those with normal PRL

<sup>1</sup>Thorner MO, McNeilly AS, Hagan C & Besser GM. Long-term treatment of galactorrhea and hypogonadism with bromocriptine. *BMJ* 1974 2 419–422.

<sup>2</sup>Werder K, Fahlbusch R, Landgraf R, Pickardt CR, Rjosk HK & Scriba PC. Treatment of patients with prolactinomas. *Journal of Endocrinological Investigation* 1978 1 47–58

<sup>3</sup>Webster J, Piscitelli G, Polli A, Ferrari C, Ismail I & Scanlon M. For the Cabergoline Comparative Study Group. *New England Journal of Medicine*, 1994 904–909

<sup>4</sup>Molitch ME (1999) Medical treatment of prolactinomas. *Endocrinol Metab Clin North Am* 28(1):143–169

<sup>5</sup>Diagnosis and treatment of hyperprolactinemia: An endocrine society clinical practice guideline, 2011

<sup>6</sup>14. Noronha S, Stokes V, Karavitaki N & Grossman A. 2010. Treating prolactinomas with dopamine agonists: always worth the gamble?. *Endocrine In press* 10.1007/s12020-015-0727-2

<sup>7</sup>16. Ali S, Klahr K & Freudenreich O. 2015. Management of psychosis associated with a prolactinoma: case and review of the literature. *Psychosomatics* 51 2010. 370–376. 10.1016/S0033-3182(10)70718-0.

serum level. Follow up lasted 1-5 years. Postoperative complications such as CSF leak, meningitis, additional oculomotor disorder or visual impairment have not been established. No mortality. Biochemical and clinical remission was achieved after EET surgery with no DA therapy: microadenomas - 100% cases, macroprolactinomas - 53% (macroprolactinomas with size less than 24mm - 90% cases). Visual disturbances and visual field defects improved in all cases over macro and giant prolactinomas.

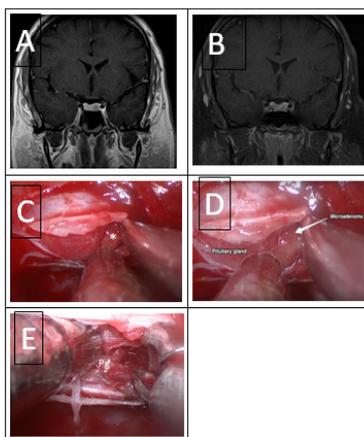
EET surgery over micro and macroprolactinomas (tumor should be removed in capsule) achieves biochemical and clinical remission within a short period of time. Though EET surgery over microprolactinomas gives 100% remission rate, in cases of macroprolactinomas EET surgery gives 53% remission rate. Macroadenomas give recurrence after surgery in 6 months period. We noticed that the size starting from 24mm and more would

likely to lead to recurrence. Meanwhile macroprolactinomas less than 24mm give 90% remission. Cavernous sinus invasion is predicting factor over recurrence.

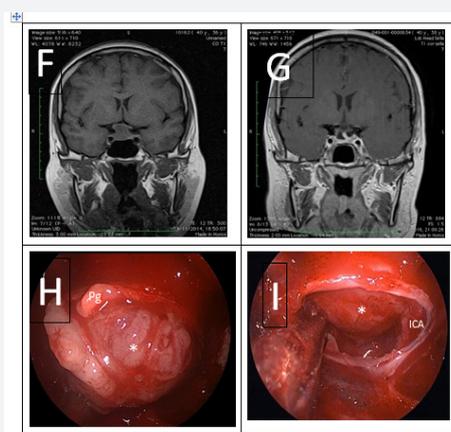
### Conclusion

Biochemical remission could be achieved surgically especially in microprolactinomas in 100% cases.

Biochemical remission might be achieved surgically in macroprolactinomas with size less than 24 mm (90% cases), cavernous sinus invasion (Knosp 0-2) is the prognostic factor. Ophthalmic symptoms regression is achieved in 100% patients and faster in cases macro and giant adenoma in comparison to DA therapy. Menses normalized in 100% cases of microprolactinomas and in 86% cases in macroadenomas with size less than 24mm.



**Case 1:** Women 30 y.o. presenting with amenorrhea, galactorrhea. Preoperative T1 weighted image with dynamic Gd contrast (A) demonstrate hypointensive lesion 7x5x6mm. PRL level of 1164 ng/ml. Endoscopic endonasal resection of microadenoma. Intraoperative images are presented (C-E). Images C, D show intraoperative endoscopic view of microprolactinoma (\*) and pituitary gland on the left side. Image E shows intraoperative endoscopic view microprolactinoma total removal and pituitary gland (Pg). Coronal and sagittal postoperative T1 weighted image with dynamic Gd contrast (B) after surgery. Following surgery, the patient's prolactin level returned to normal. Patient got pregnant 3 months after surgery. Catamnenis 2 years. No DA after surgery.



**Case 2:** Women 37 y.o. presenting with dysmenorrhea, galactorrhea. Preoperative T1 weighted image (F) demonstrate hypertensive lesion with suprasellar extension 13x18x17mm, Knosp 1. PRL level of 850 ng/ml. Patient underwent EET resection over macroadenoma. Intraoperative images are presented (H, I). Image G shows intraoperative endoscopic view of macroprolactinoma (\*) and part of pituitary gland (Pg) superiorly. Image H shows intraoperative endoscopic view of the macroprolactinoma total removal, diaphragm with pituitary (\*) and medial wall of left cavernous internal carotid artery (ICA). Postoperative MRI with dynamic Gd contrast G showed total resection of the tumor with suprasellar cistern decompression. Prolactin level returned to normal within 3 months. Catamnenis 4 years. No DA therapy after surgery.



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DOI: [10.19080/JETR.2018.03.555622](https://doi.org/10.19080/JETR.2018.03.555622)

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