Original Article

The Comparision of Outcome of Microscopic Versus Endoscopic Trans-sphenoidal Surgery for Pituitary Adenoma

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Objective: To compare the efficacy of endoscopic transsphenoidal surgery with microscopic transsphenoidal surgery among patients who were operated for pituitary adenomas.

Methods: This randomized control trial was carried out in Neurosurgery Department, Sir Ganga Ram Hospital Lahore from September 2011 till September 2015. Sample size of 140 (70 in each group) was estimated and non-probability purposive sampling technique was used. Patients of pituitary adenomas were randomly selected for each of the procedure and an informed consent was taken. Two groups of patients were made. Group A patients underwent endoscopic surgery for pituitary tumor and Group B patients were operated by microscopic technique. After 48 hours of surgery, patients where be evaluated for radiological evidence of respectability and visual recovery by undergoing post-operative MRI and visual assessment by ophthalmologist. All the informations were entered in a structured performa. The data was analyzed by using SPSS version 25. All qualitative variable like gender, outcome in terms of complete resection and visual field defects were presented by frequency and percentage. Quantitative data like age was presented by mean and standard deviation. The groups were compared for outcome using chisquare test. P values were considered statistically significant if < 0.05.

Results: Out of 140 pituitary adenoma patients, 45% had microadenomas, while 55% macroadenomas. Mean patients age was 35±10 years. 57% patients were female. Among our study population, 29.2% patients had visual field defects at the time of presentation. Among 70 patients whose pituitary tumors were resected by endoscopic technique, 70% got complete resection of tumour, while among 70 patients whose pituitary tumors were resected by microscopic surgical technique, only 48% got complete tumor resection. (p=0.003). Among 41 patients who had visual field defects, 21 underwent endoscopic resection and 100% (i.e. all 21) patients showed improvement in visual field defects postoperatively. While 20 patients with visual field defects underwent microscopic resection, where 80% patients showed improvement in visual field defects postoperatively (p=0.04).

Conclusions: Our study concluded that endoscopic trans-sphenoidal surgery for pituitary adenoma is much more efficacious than microscopic trans-sphenoidal surgery, as determined by respectability of the tumor and correction or improvement in visual field defects postoperatively. Complete resection will be of value as it will correct other sign and symptoms and hence morbidity and mortality in operated patients as well.

Keywords: Pituitary adenoma, Trans-sphenoidal surgery. Microscopic resection, Endoscopic resection, Complete resection, Visual field defects.

Introduction

Pituitary adenomas arise primarily from the anterior pituitary gland (adenohypophysis)[1] whereas posterior pituitary adenomas known as neurohypophyseal tumors are very rare.[2,3] On the basis of size, these tumors are classified as microadenomas if less than 1cm and macroadenomas if more than 1cm.[4,5] Schloffer was the first who resected pituitary tumor via transsphenoidal surgery in 1907. [6] Major complications of transsphenoidal pituitary surgery include CSF Leak, intracranial major vessels injury, endocrine abnormalities and few minor nasal complications.[7] Two modes are utilized for this transsphenoidal excision: one conventional microscopic and second newly advented endoscopic. Microscopic approach provides direct access to the floor of the sella with minimal dissection of the posterior nasal mucosa or septectomy.[8] While in endoscopic approach, after posterior septectomy a high-speed drill is used to create a wide opening in the rostrum for the endoscope and instruments. After tumor removal, cavity is inspected for residual tumor. using 308 and 458 angled endoscopes.[9,10] Jankowski Was who first time introduced endoscopic approach for pituitary tumor in 1992.[11] Literature suggests that

endoscopic approach provides broader surgical field, better outcome, lesser operative time, and lower complication rate comparted to microscopic trans-sphenoidal approach.[12-14]

The novel approach for pituitary adenoma surgery in the tertiary care centres of our country is the microscopic transsphenoidal one while in the rest of the world with the introduction of newer transsphenoidal endoscopic approach the management of pituitary tumours has been changed grossly. When judging any new surgical technique, it must be compared with the current gold standard based on important key indicators (outcome variables). If we hypothesize that endoscopy is safer than microscopy in some aspects like tumor respectability, as the previous literature showed. It was pertinent to conduct a study comparing these two procedures and to direct the resources to more efficacious one, and from patient's aspect if it is proved then patients can always opt for more safe and efficacious procedure. Hence the objective of our study was to compare the efficacy of endoscopic transsphenoidal surgery with microscopic transsphenoidal surgery for pituitary adenomas among patients who presented at Neurosurgery Department, Sir Ganga Ram Hospital Lahore, Pakistan.

Methods

This randomized control trial was carried out in Neurosurgery Department, Sir Ganga Ram Hospital Lahore from September 2011 till September 2015. Sample size of 140 (70 in each group) was estimated using 95% confidence level, 80% power of test with an excepted efficacy in terms of complete resection in 49.2% in microscopic group and 70.6% in endoscopic group. For sampling, non-probability purposive technique was used. Both genders, age more than 10 years, and both types of pituitary adenomas, microadenomas < 1cm and macroadenoma >1cm, as assessed on MRI, were the inclusion criterias. While patients diagnosed as having craniopharyngiomas, recurrent pituitary adenoma operated before by transs- phenoidal approach, and patients with complete vision loss were excluded from study

Preoperative data such as age sex, presenting symptoms and visual status was evaluated. Before surgery all patients underwent neuroradiological assessment which includes CT, MRI and CT Angio/ MR Angio, while ophthalmological evaluation consists of fundoscopy, visual acquity and perimetry if patient is seemed to be having visual field defects. Patients were randomly selected for each of the procedure and an informed consent was taken. Two groups of patients were made. Group A patients underwent endoscopic surgery for pituitary tumor and Group B patients were operated by microscopic technique. After 48 hours of surgery, patients where be evaluated for radiological evidence of respectability and visual recovery by undergoing post-operative MRI and visual assessment by ophthalmologist.

During Postoperative period visual assessment was done in patients who previously had visual field defects as per perimetry and results in terms of measurable decibel of light required to stimulate retina were recorded. Outcome was assessed based on the following parameters i.e complete resection of tumour, improvement in visual field defects. No radiological evidence of residual tumor after 2 days of surgery (as per Post op MRI) defined the complete resection of tumor. If any evidence of residual tumor present than it would be incomplete resection. Improvement in the visual fields defect (if present pre operatively) was considered if there was one db increase or more in light to stimulate retina after surgery from baseline assessed by perimetry (Humphrey visual field analyzer 30-2 program) method after 2 days of surgery. All the informations were entered in a structured performa.

The data was analyzed by using SPSS version 25. All qualitative variable like gender, outcome in terms of complete resection and visual field defects were presented by frequency and percentage. Quantitative data like age was presented by mean and standard deviation. The groups were compared for outcome using chi-square test. p-values were considered statistically significant if < 0.05.

Results

Out of total of 140 patients suffering pituitary adenoma, 70(50%) patients underwent endoscopic trans-sphenoidal resection while 70(50%) underwent microscopic trans-sphenoidal resection. 60(43%) patients were male while 80 (57%) patients were female. Mean age of the patients was 35±10 years. 45% of the total number of patients (63 out of 140) presented with microadenomas (i.e.<1cm), while 55% patients (77 out of 140) were having macroadenomas (i.e.>1cm) **(Fig-1).** Among our study population, 29.2% (41 out of 140) patients were having visual field defects at the time of presentation **(Fig-2).**

59.3% (n=83) patients of total population had complete tumour resection, while 40.7%(n=57) patients had incomplete tumour resection. Among 70 patients whose pituitary tumor was resected by endoscopic technique, 70% (n=49) got complete resection of tumour, while among 70 patients whose pituitary tumor was resected by microscopic surgical technique, only 48% (n=34) got complete tumor resection. The complete resectibility of tumor was achieved significantly more via endoscopic technique as compared to microscopic technique (p=0.003) **(Table-1)**. Among 41 patients who had visual field defects, 21 underwent endoscopic resection and 100% (i.e. all 21) patients showed improvement in visual field defects postoperatively. While 20 patients with visual field defects underwent microscopic resection, where 80% (i.e. 16 out of 20) patients showed improvement in visual field defects postoperatively.

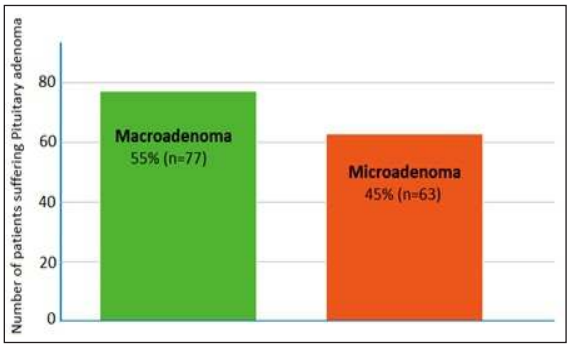

Fig-1: Types of pituitary adenomas among our studied patients.

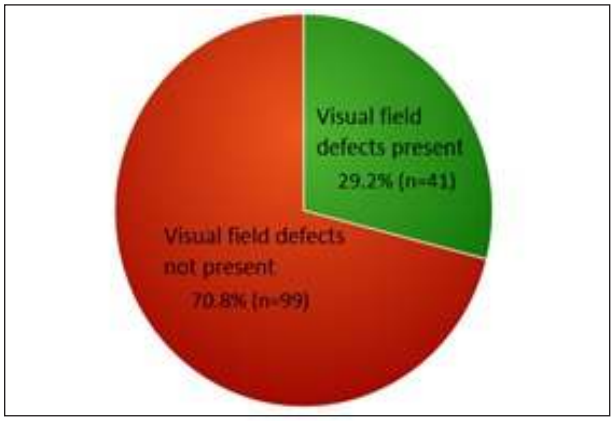

Fig-2: Prevalence of visual field defects in patients who presented with pituitary adenoma.

This improvement in visual field defects after endoscopic resection was significantly higher in comparison to that after microscopic resection technique (p=0.04) **(Table-2).**

Discussion

The aim of the study was to compare the outcome of the two surgical technique i.e. endoscopic and microscopic, for the resection of pituitary adenoma. The present study aimed at comparing outcome in terms of completeness of resection and improvement in visual field defects if any present, as analyzed by clinical evaluation and preoperative visual field assessment by perimetry. A recent increase in use of endoscopic transsphenoidal technique in past decade has made it very essential to get its comparison

Table-1: Comparison of outcome (resectibility) of endoscopic pituitary surgery vs microscopic pituitary surgical technique (n=140).

Surgical Technique	Resection Achieved		Total	P-value
	Complete	Incomplete		
Endoscopic	70% (n=49)	70% (n=49)	70	
Microscopic	48% (n=34)	52% (n=36)	70	0.003
Total	59.3%% (n=83)	40.7% (n=57)	140	

Table-2: Comparison of outcome (improvement in visual field defects) of endoscopic pituitary surgery vs microscopic pituitary surgical technique (n=41).

Surgical Technique	Resection Achieved		Total	P-value
	Complete	Incomplete		
Endoscopic	100% (n=21)	0% (n=0)	21	
Microscopic	80% (n=16)	20% (n=04)	20	0.04
Total	90.2% (n=37)	9.8% (n=04)	41	

with the traditional technique of using microscope so that evidence-based advantages of either technique can be established rather than having theoretical knowledge. In our center, 55% of the patients were having macroadenoma while 45% were having microadenomas on presentation, this frequency is different from hospital of Italy where majority of the patients were having macroadenomas[15] There was female predominance with male to female ratio of 0.75:1,this was also observed in study conducted in a hospital in Shanghai, China.[16] Mean age of patients presenting to our center having pituitary adenomas was 35±10 years which was also comparable to the same study conducted in china. Disease control or resectability of the tumour as judged by presence or absence of residual tumour on post-operative MRI , it was observed that 59% i.e. n=83 total population of our patients got complete resection of tumour operated with either endoscopic or microscopic assisted technique. About 70% of our patients undergoing endoscopic transsphenoidal pituitary surgery (group A) got complete resection of tumour while with microscopic surgical technique (Group B) we got 48% patients having complete resection. This was gross difference in outcome what we observed in our study in terms of resectability with p value of 0.003 (highly significant). This is one of an important parameter to compare the efficacy of any procedure with other and most national and international studies compare the outcome of two procedure based on resectability which is easy to measure as radiological evidences are easily available by having postoperative MRI. In an international study of pituitary adenoma,[12] complete tumor excision was achieved in 64.71% patients in endoscopic trans-sphenoidal surgery group, but in only 46.15% patients in microscopic group. In another study of 2272 patients with pituitary adenoma, Aijun Li and colleagues[13] found significantly higher rate of gross tumor removal (P = 0.009) and lower risk of septal perforation (P = 0.014) with Endoscopic transsphenoidal technique in comparison to microscopic approach. A 15 studies literature review[14] concluded more effectiveness, less complication rate & shorter post-operative hospital stay associated with endoscopic trans-sphenoidal approach compared with microscopic surgery. In a similar meta-analysis by Leonie H. A. Broersen,[17] of 97 articles with 6695 pituitry adenaoma patients underoing resection, percentage of patients in remission after endoscopic surgery (76.3 %) was higher as compared to percentage of patients in remission after microscopic surgery (59.9%). Jared D.Ament et all concluded that Endoscopic transsphenoidal surgery is cost-effective compared to microscopic transsphenoidal surgery.[18] Deyan Popov D[19] said that endoscopic group had higher levels of remission in comparison to the microscopic group (81.8% vs. 70.9%). Rodrigo V. S. Bastos and colleagues[20] found the lower rate of postoperative complications in endoscopic transsphenoidal surgery as compared to microscopic transsphenoidal surgery. Hamideh Akbari[21] concluded that endoscopic Transsphenoidal Surgery (ETS) is superior to Microscopic Transsphenoidal Surgery (MTS). Gross total resection (GTR) was observed in the 81.2% of the patient in the ETS group. In the MTS group, GTR was observed in 15.8%. In the present study we analyzed another outcome variable i.e. visual field improvement in patients presenting with visual field defects due to macroadenomas. All patients presented to our centre with macroadenomas were having visual field defects both clinically and confirmed on preoperative ophthalmological assessment as per perimeter. Among n=41 patients having visual field defects due to pituitary adenomas, n=20 were operated using endoscopic surgical technique .100% of the patients got improvement in their visual field defect as compare to 80% n=16 of the patients operated microscopically as shown by clinical and post-operative visual field assessment by perimetery. This is again a reliable parameter to study and analyze and hence establishing the fact that which procedure is better than other based on clinical evidences. Although number of patients in current study is too small to have a reliable comparison b/w surgical technique but still results are very convincing. When we compare with international data, a Canadian study conducted in University of Toronto showed Complete normalization of preoperative visual defects in 50% of the patients treated endoscopically and 39% had gradual improvement[22.] Mortini et al. reported complete recovery in 40% and improvement in 50% of patients underwent treated microscopically[23], while another study conducted in Bellaria Hospital Italy, showed visual improvement in 58.4% of patients underwent endoscopic technique of pituitary surgery[24.] In our data, endoscopic surgical technique seems to superior than microscopic approach with significant difference and p value of 0.04. Our comparison results are very much like a study conducted in china where two surgical technique were compared and statistically significant difference of $p<0.05$ was found based

the above and other outcome variables.[16]

One limitation to this study is that we didn't compare complication rate among two groups which need to be elaborated further because any technique to be adopted should be studied in detail in terms of its prons and cons. Complications like postoperative pain and CSF rhinorrhea which are most common one and along with that recurrence of tumour. These are very important to study so that we should be confident enough about any of the technique to be adopted but due to short study period we couldn't get the post-operative complication rate in two groups it need long follow up , some complications are immediate but many are long term complications which need long follow up to be elaborated .further studies should be encouraged in our setting so that surgeons should be confident about the efficacy of either procedure i.e microscopic or endoscopic. Traditionally, microscopic technique is widely used in our setting because less expertise are available for endoscopic technique but to be in pace with international recommendations we should opt this technique and should be applied widely.

Conclusion

Our study concluded that endoscopic trans-sphenoidal surgery for pituitary adenoma is much more efficacious than microscopic trans-sphenoidal surgery, as determined by resectability of the tumor and correction or improvement in visual field defects postoperatively. Complete resection will be of value as it will correct other sign and symptoms and hence morbidity and mortality in operated patients as well.

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References

1. Larkin S, Ansorge O. Pathology And Pathogenesis Of Pituitary Adenomas And Other Sellar Lesions. [Updated 2017 Feb 15]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-.
2. Viaene AN, Lee EB, Rosenbaum JN, Nasrallah IM, and Nasrallah MP. Histologic, immunohistochemical, and molecular features of pituicytomas and atypical pituicytomas. Acta Neuropathologica Communicationsvolume 2019; 7(69):1-11.
3. Fang H, Lu G, YinW, Yingying J, Yi L,Zhenwei Y et al. Clinical and imaging features of granular cell tumor of the neurohypophysis, A restrospective analysis. Medicine 2019; 97(9):1-6.
4. Kopczak A, Renner U, Karl Stalla G. Advances in understanding pituitary tumors. F1000Prime Rep. 2014;6:5.
5. Yatavelli RKR, Bhusal K. Prolactinoma. [Updated 2018 Nov 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-.
6. Schmidt RF, Choudhry OJ, Takkellapati R, Eloy JA, Couldwell WT, and Liu JK. Hermann Schloffer and the origin of transsphenoidal pituitary surgery. Neurosurg Focus. 2012;33(2):E5.
7. Prete A, Corsello SM, Salvatori R. Current best practice in the management of patients after pituitary surgery. Ther Adv Endocrinol Metab. 2017;8(3):3348.
8. Li HY, Feng CY, Zhang C, et al. Microscopic surgery for pituitary adenomas to preserve the pituitary gland and stalk. Exp Ther Med. 2017;13(3):10111016.
9. Shama BS, Sawarkar DP, Suri A. Endoscopic pituitary surgery: Techniques, tips and tricks, nuances, and complication avoidance. Neurol India 2016;64:724-36.
10. Hansasuta A, Pokanan S, Punyawai P, Mahattanakul W. Evolution of Technique in Endoscopic Transsphenoidal Surgery for Pituitary Adenoma: A Single Institution Experience from 220 Procedures. Cureus. 2018;10(1):e2010.
11. Theodros D, Patel M, Ruzevick J, Lim M, Bettegowda C. Pituitary adenomas: historical perspective, surgical management and future directions. CNS Oncol. 2015;4(6):411429.
12. Prajapati HP, Jain SK, Sinha VD. Endoscopic versus Microscopic Pituitary Adenoma Surgery: An Institutional Experience. Asian J Neurosurg. 2018;13(2):217221.
13. Li A, Liu W, Cao P, Zheng Y, Bu Z, et al. Endoscopic Versus Microscopic Transsphenoidal Surgery in the Treatment of Pituitary Adenoma: A Systematic Review and Meta-Analysis. World Neurosurg. 2017;101:236-246.
14. Gao Y, Zhong C, Wang Y, et al. Endoscopic versus microscopic transsphenoidal pituitary adenoma surgery: a meta-analysis. World J Surg Oncol. 2014;12:94.
15. Frank G, Pasquini E, Farneti G, Mazzatenta D, Sciarretta V, Grasso V, et al. The endoscopic versus the traditional approach in pituitary surgery. Neuroendocrinology. 2006;83(3-4):240-8.
16. Cheng X R, Tian L H,Gao W W. A comparison between Endoscopic transspenoidal surgery and Traditional transspenoidalmicrosurgery for functioning pituitary adenomas.The journal of international medical research2011;39:1985-1993.
17. Broersen, L.H.A., Biermasz, N.R., van Furth, W.R. et al. Endoscopic vs. microscopic transsphenoidal surgery for Cushing's disease: a systematic review and meta-analysis. Pituitary 2018;21(5): 524-34.
18. Ament JD, Yang Z, Khatchadourian V, Strong EB, Shahlaie K. Cost- Effectiveness of Endoscopic Versus Microscopic Transsphenoidal Surgery for Pituitary Adenoma. World Neurosurgery 2018; 110: 496-503.
19. Deyan Popov D, Hadzhiyanev A, Bussarsky A, and Ferdinandov D. Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery in a single center. Biomedical Research 2018;29(14): 2971-74.
20. Bastos RVS, Silva CMDM, Tagliarini JV, Zanini MA, Romero FR, et al. Endoscopic versus microscopic transsphenoidal surgery in the treatment of pituitary tumors: systematic review and meta-analysis of randomized and non-randomized controlled trials. Archives of Endocrinology and Metabolism 2016; 60(5): 411-419.
21. Akbari H, Malek M, Ghorbani M, Hashemi SMR, Khamseh ME, Ali Zare Mehrjardi AZ, et al. Clinical outcomes of endoscopic versus microscopic trans-sphenoidal surgery for large pituitary adenoma, British Journal of Neurosurgery 2018; 32(2):206-209.
22. Dehdashti AR, Ganna A, Karabatsou K, Gentili F. Pure endoscopic endonasal approach for pituitary adenomas: early surgical results in 200 patients and comparison with previous microsurgical series. Neurosurgery 2008;62:10061015.
23. Mortini P, Losa M, Barzaghi R. Results of transsphenoidal surgery in a large series of patients with pituitary adenoma. Neurosurgery2005; 56:12221233.
24. Sadler TW. Langman's medical embryology. 8th edition. Philadelphia: Lippincott Williams&Wilkins; 2000.