The evaluation of seventy-five patients with prolactinoma: better results by drug therapy than surgery

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In this study, our objective was to evaluate clinical characteristics of patients with prolactinoma followed in our clinic and to determine the efficacy of surgical and medical therapies. Seventy-five patients with prolactinoma who had been followed between 1986-1993 were evaluated retrospectively. Fifty-seven patients were women (76%) and 18 were men (24%). Mean age was 29.2±7.9in women and 34.7±11.3 in men. Elevation of serum prolactin level over 150 mg/L and existence of pituitary mass were accepted as sufficient criteria for the diagnosis of prolactinoma. Symptoms and signs, CT and/or MRI findings, responses to therapy were recorded. The success of therapy were shown by normalization of serum prolactin levels. Surgical success rates were 26.0% for microadenomas and 11.7% for macroadenomas. The success with dopamine agonist therapy was much higher (87.5% for micro and 80% for macroadenomas). It is conculded that drug therapy is obviously better than surgery for the treatment of patients with prolactinoma.
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Key Words: Bromocriptine, Dopamine agonist, Prolactin, Prolactinoma

Hyperprolactinemia is a common laboratory finding in clinical endocrine practice and, if drug-induced hyperprolactinemia is excluded, its primary cause is prolactinoma (1). Prolactinomas are the most frequent pituitary tumors and comprise 40% of them (2). In this study, prolactinoma cases which had been followed in Hacettepe Medical School were retrospectively analysed.

PATIENTS AND METHODS

Seventy-five patients with prolactinoma who had been followed between the years of 1986-1993 were evaluated retrospectively. Mean duration of follow-up (SD) was 2.4±1.7 years (range: 1 to 7). The existence of pituitary mass and elevated serum prolactin level over 150 ug/L were accepted as sufficient criteria for the diagnosis of prolactinoma. Histopathological findings were not included in the study, because immunohistochemical studies had not been performed. Age and sex of patients, symptoms, physical signs, duration of symptoms, CT and/or MRI findings, responses to therapy were recorded. Tumors with a diameter higher than 10 mm were classified as macroadenomas and lower than 10 mm as microadenomas.

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RESULTS

Clinical data in patients with prolactinoma are shown in Table 1 and symptoms and signs of disease in women and in men are shown in Table 2.

Thirteen patients were treated only with bromocriptine, and 22 patients were treated only with surgery. Bromocriptine therapy was applied after surgery in 26 patients and after surgery + radiotherapy in 8 patients. Five patients were treated with surgery + radiotherapy without bromocriptine, and 1 patient was treated with radiotherapy + bromocriptine.

All of 13 patients treated only with bromocriptine had microadenoma. Two patients were lost during follow-up. Of the remaining 11 patients, serum prolactin levels returned to normal (<20 ug/L) in all (100%), symptoms improved in 10(90.9%), tumor disappeared in 4(36.3%) of them. The total number of patients treated with surgery was 61 (44 women, 17 men). Of these patients, 26 had microadenoma and 35 had macroadenoma. Three patients with microadenoma and one patient with macroadenoma were lost during follow-up. Serum prolactin levels were normalized and symptoms disappeared in 6 of 23 microprolactinoma

Table **1**. Clinical characteristics of prolactinoma patients.

	women	men
Number of patients	57 (76%)	18(24%)
Age	29.2±7.9 (16-57)	34.7±11.3 (18-55)
Number of microadenomas	39	1
Number macroadenomas	18	17
Most common symptom	amenorrhea	visual
Duration of symptoms (months)	45.3±37.5	7.7±26.2

Table 2. Symptoms and signs in prolactinoma patients

	Symptom/sign	%
Women: (n=57)	amenorrhea	94.7
	galactorrhea	78.9
	headache	59.6
	visual defects	8.7
	hirsutism	8.7
Men: (n-18)	visual defects	77.7
	headache	66.6
	impotence/loss of libido	55.5
	panhypopitutarism	16.6
	galactorrhea	11.1

patients (26.0%) and in 4 of 34 macroprolactinoma patients (11.7%). Of the patients with macroprolactinoma, 18 had visual disturbances and in 8 of them vision improved after surgery (44.4%). Postoperative panhypopituitarism developed in 1 patient with microadenoma (4.3%) and in 9 patients with macroadenoma (26.4%) (Table 3).

There were 34 patients (22 women, 12 men) treated with bromocriptine after surgical failure. These patients had been followed at least 3 months postoperatively before beginning bromocriptine. They were symptomatic and their serum prolactin levels were still above normal at the beginning of bromocriptine therapy. Thirteen of them had microadenoma and 21 had macroadenoma. Eight patients with macroadenoma were given radiotherapy after surgery as well. Of the microprolactinoma patients, serum prolactin levels returned to normal in 10(76.9%) and symptoms improved in 9(69.2%) by bromocriptine therapy. Two patients with macroprolactinoma were lost during follow-up. Of the remaining 19 patients, serum prolactin levels returned to normal in 15(78.9%) and symptoms improved in 12(63.1%) by bromocriptine therapy.

The total number of patients treated with bromocriptine was 48 (35 women, 13 mean). Of these patients, bromocriptine were given to 13 as the a sole therapy, to 26 after surgery; to 8 after surgery + radiotherapy and to 1 after radiotherapy without surgery. Twenty-six patients had microadenoma and 22 had macroadenoma. Two patients with microprolactinoma were lost during follow-up. Of the remaining 24 patients, serum prolactin levels returned to normal in 21(87.5%) and symptoms improved in 19(79.1%). Of the macroprolactinoma patients, two were lost during follow-up; of remaining 20 patients, serum prolactin levels returned to normal in 16(80.0%) and symptoms improved in 12(60.0%) (Table 4).

DISCUSSION

The exact prevalence of prolactinomas is not known yet. In autopsy studies, microadenomas were shown to be present in 23-27% of cases, of which 40%, based upon immunocytochemistry, were prolactinomas (2,3). The sex distribution shows that the overall female/male ratio is about two in patients with pituitary tumors (4). This ratio is higher in prolactinomas (5). In our study, female/male ratio is 3.16. The reason for more frequent occurence of prolactinoma in women may be growth stimulatory effects of estrogen (1).

In our study the main symptoms in women were amenorrhea (94.7%), galactorrhea (78.9%) and headache (59.6%). It has been reported that amenorrhea is the most frequent symptom in women with prolactinoma and galactorrhea incidence changes between 30-80% (5). These Figure 1 are consistent with ours. Although non-specific, headache is a common symptom and it has been reported to be found in 50% of the patients with pituitary microadenomas while to be present in 27% of normal population (6).

In our study, the main symptoms and signs in men were visual field defects (77.7%), headache (66.6%) and sexual dysfunction (55.5%). In the literature, sexual dysfunction has been reported between 83-91% and visual field defects as 41% (7). Visual problems were the most frequent findings in our study.

Table 3. Evaluation of surgical results

	Improvement (%)	
Symptom/finding	Microadenomas	Macradenomas
visual defects	(-) before surgery	44.4
other symptoms	26.0	11.7
serum prolactin	26.0	11.7

Table **4.** Evaluation of bromocriptine treatment

		Improvement	
		Microadenomas	Macroadenomas
•Group 1: (n-11)	Prolactin	11/11 (%100)	—
	Symptoms	10/11 (%90.9)	
"Group 2: (n-33)	Prolactin	10/13 (%76.9)	16/20 (%80.0)
	symptoms	9/13 (%69.2)	12/20 (%60.0)
Total: (n=44)	Prolactin	21/24 (%87.5)	16/20 (%80.0)
	symptoms	19/24 (%79.1)	12/20 (%60.0)

* Patients treated with bromocriptine alone

** Patients treated with bromocriptine after surgery and/or radiotherapy

This event may be to result from referring to a doctor is generally delayed in our country. This may result from delayed refferal in our country until visual field impairment, serious symptom occurs. Generally patients do not seek medical attention. It must be expected that the patients at this stage have sexual dysfunction as well. This symptom which is unacceptable to some patients for socio-cultural reasons may be hidden from the doctor.

A summary of surgical results from 31 published series has showed that surgical success rates were quite variable, ranging from 38% to 91% (mean: 71.22%) for microadenomas and from 11% to 80% (mean: 31.8%) for macroadenomas (8). The surgical success rates are highly dependent on the experience and skill of the surgeon as well as the size of the tumor. Recurrence rates have been reported as 17.4% for microadenoma and 18.6% for macroadenomas (8). But on the long term follow-up, the recurrence rate rises to 50 % (9). In our study, surgical success rate is lower (26.0% for microadenomas and 11.7% for macroadenomas).

In the studies designed to evaluate the efficacy of bromocriptin therapy in hyperprolactinemia, it has been reported that serum prolactin levels were lowered to normal in 64-100% and symptoms were improved in 57-100 of patients (10). It is generally accepted that normoprolactinemia occurs in 80% to 90% of patients with prolactinoma treated with bromocriptine (8,11). It is also known that clinically évaluable shrinkage can be obtained in 65% to 90% of these patients, even with large macroadenomas (8,11,12). Moreover, it has been reported that visual field improvent occurs with bromocriptine therapy in 80% to 90% of patients with significant visual field abnormalities (8). In our study, normalisation of serum prolactin levels has been achieved in 100% of patients treated only with bromocriptine were evaluated, normoprolactinemia has been occured in 87.5% of patients with microadenoma and in 80% of patients with macroadenoma. As for the patients treated with bromocriptine after surgical failure, the ratio of normalization of serum prolactin levels has been found as 76.9% for micro and 78.9% for macroadenomas, these figures are higher than the frequency 57.5% reported for microadenomas in another study (13). Generally, the results of bromocriptine therapy in our study are consistent with the literature and are much better than the results of surgical therapy. However, it is known that recurrence rate is high following discontinuation of dopamine agonist therapy and life-long administration of the drug has been recommended (11). Surgery is restricted to patients whose tumours do not shrink or whose in circulating prolactin levels do not return to normal despite therapy adequate doses of dopamine agonist or in patient who show a genuine intolerence to these drugs (14). It has been claimed that the patients prolactinoma may have an underlying hypothalamic defect in the dopaminergic control of pitutitary lactotrophs which predisposes to the development of prolactinomas (15). In this context, it seems that drug therapy is a much better choice than surgery for these patients.

In our study, the efficacy of radiotherapy can not be determined for the number of the patients treated with radiotherapy was not enough. But it is known that radiotherapy can seldom normalize serum prolactin levels and only in a long time, this is reason it is recommended only as an adjuvant therapy for the cases who do not respond drug therapy or surgery (9, 15).

Proiactinomalı 75 hastanın değerlendirilmesi: ilaç tedavisi ile cerrahi tedaviden daha iyi sonuçlar

Bu çalışmada, kliniğimizde izlenen prolaktinoma hastalarının klinik özelliklerini incelemeyi, cerrahi ve medikal tedavilerin etkinliğini belirlemeyi amaçladık. 1986-1993 yılları arasında izlenmiş olan 75 prolaktinoma hastası retrospektif olarak değerlendirildi. Hastaların 57'sikadın (%76), 18'ierkekti (%24). Ortalama yaş kadınlarda 29.2±7.9, erkeklerde 34.7±11.3 idi. Serum prolaktin düzeyinin 150 ng/L'nin üzerinde olması ve pituiter kitle saptanması prolaktinoma tanısı için yeterli kriterler olarak kabul edildi. Semptomlar, fizik bulgular, CT ve/veya MRI bulguları, tedaviye cevaplar kaydedildi. Tedavinin başarısı serum prolaktin düzeylerinin normale dönmesiyle gösterildi. Cerrahi başarı oranı mikroadenomlar için %26, makroadenomlar için %11.7 idi. Dopamin agonisti tedavisinin başarısı ise çok daha yüksekti (Mikroadenomlar için %87.5, makroadenomlar için %80). Prolaktinoma hastalarında ilaç tedavisinin cerrahi tedaviye göre çok daha etkili olduğu sonucuna varıldı. [Turk J Med Res 1994; 12(5): 210-213]

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