Macroprolactinomas: dopamine agonists for how long?

Mª Joana Santos[1], Rui Almeida[2,3], Olinda Marques[1,3]
1. Department of Endocrinology; 2. Department of Neurosurgery; 3. Pituitary Tumours Group, Hospital de Braga, Portugal

Background and Aims

Dopamine agonists (DA) effectively normalize prolactin (PRL) secretion and reduce tumour size in most patients with macroprolactinomas. However, some patients have partial or discordant responses to treatment, while others are considered resistant. Although treatment adjustments are usually made according to prolactin secretion, the importance of tumor shrinkage in this decision and when the therapeutic response should be expected must be clarified. It would also be important to establish what is a trully resistant macroprolactinoma, the ideal duration of medical treatment and the role of surgery as an adjuvant therapy in the non responders. The aim of this study was to assess the response of macroprolactinomas to DA based on prolactin secretion and tumour size in a cohort of patients treated in our hospital.

Materials and Methods

- Observational, analytical and retrospective study
- Inclusion criteria: DA as first line treatment for ≥ 12 months; good adherence
- After 24 months of treatment, patients were classified as "Sensitive", "Partially Resistant" (PR) or "Resistant" according to Table 1
- Analysis of response to treatment after 1 year, 2 years and at follow-up
- Statistical analysis with SPSS v20.0 using the following tests: Friedman, Mann-Whitney, McNemar, Chi-square, Wilcoxon, ANOVA repeated measures, Independent-Samples T Test and Paired-Samples T Test; p<0,005.

Tumoural diameter reduction	Normal Prolactin	↑ Prolactin
<10%	PR	Resistant
10-50%	PR	PR
> 50%	Sensitive	PR

Table I – Classification at 2 years

Results

Patients caractheristics

- **N=52**
- **Male:** 51,9%; **Female** 48,1%
- **Age at diagnosis:** 40,3±16,3 years
- **Follow-up:** 6,8±4,1 years
- **DA**: Bromocriptine 90%, Cabergoline 10% (cabergoline dose: 0,25-2,0mg/week)

Classification at 2 years

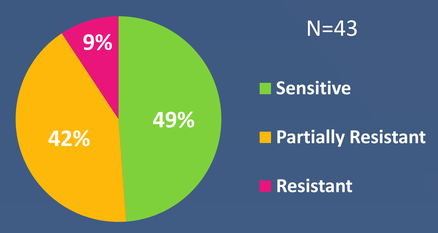


Fig. 1 – Classification at 2 years

Prolactin Secretion

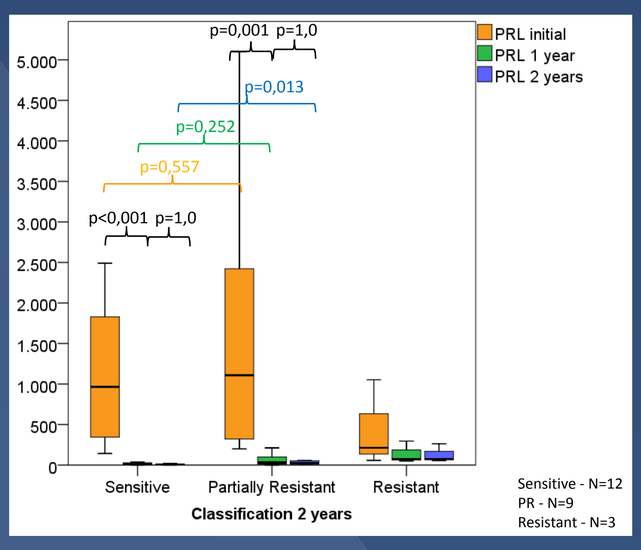


Fig. 3 – Prolactin secretion in the first 2 years

Prolactin Normalization

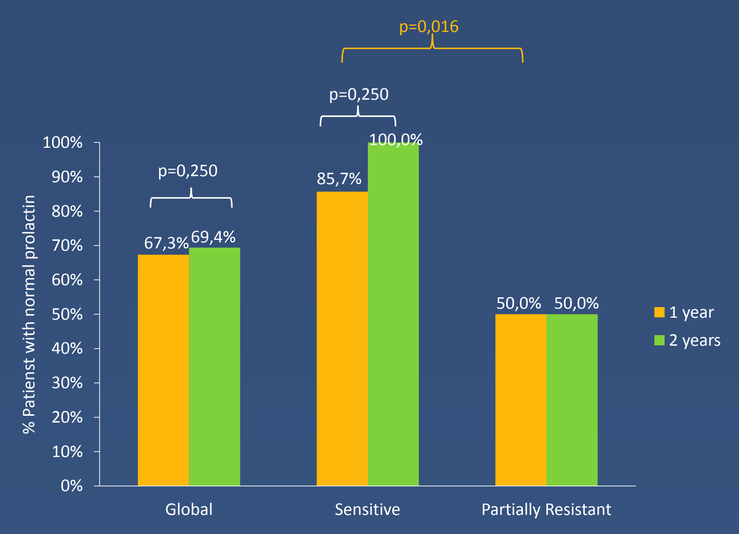
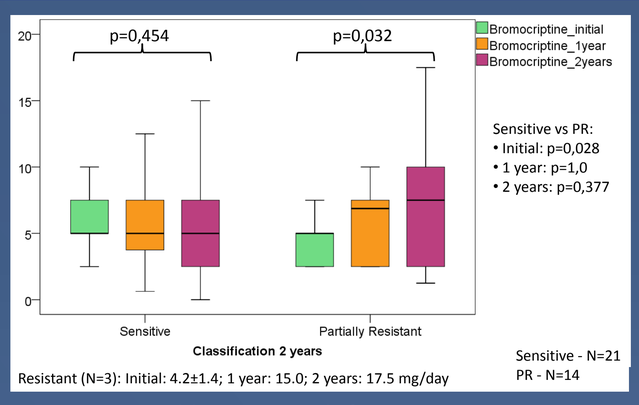


Fig. 4 – Prolactin normalization in the first 2 years

Treatment with Bromocriptine



Resistant (N=3): Initial: 4.2±1.4; 1 year: 15.0; 2 years: 17.5 mg/day

Fig. 2 – Treatment with bromocriptine in the first 2 years

Maximal tumour diameter

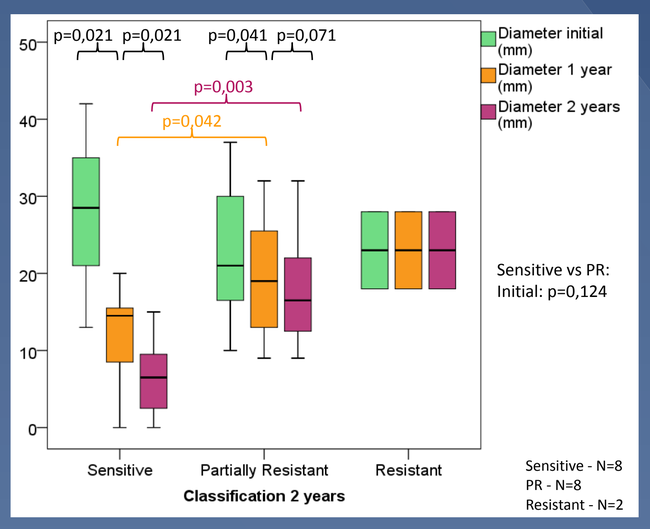
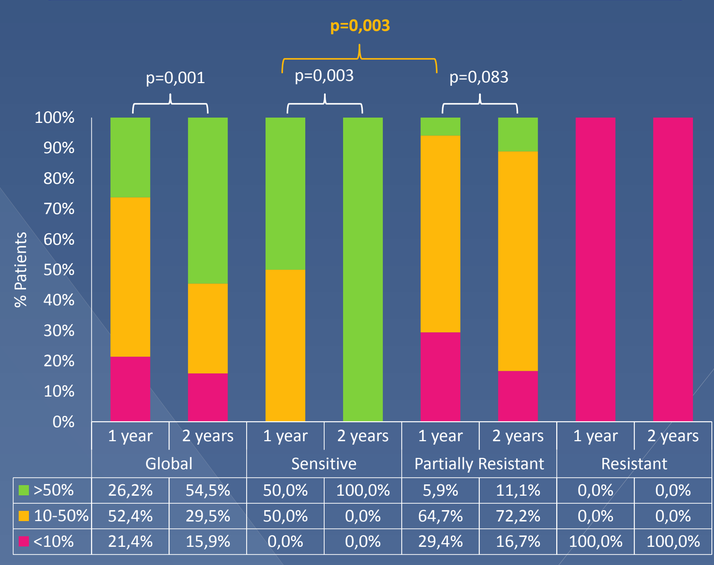


Fig. 5 – Maximal tumour diameter in the first 2 years

Maximal tumour diameter reduction



	Global		Sensitive		Partially Resistant		Resistant	
	1 year	2 years	1 year	2 years	1 year	2 years	1 year	2 years
>50%	26,2%	54,5%	50,0%	100,0%	5,9%	11,1%	0,0%	0,0%
10-50%	52,4%	29,5%	50,0%	0,0%	64,7%	72,2%	0,0%	0,0%
<10%	21,4%	15,9%	0,0%	0,0%	29,4%	16,7%	100,0%	100,0%

Fig. 6 – Maximal tumour diameter reduction in the first 2 years

Follow-up >2 years (N=37)

Partially Resistant	2 years	Follow-up	
Prolactin (Md (IQR))	25,2 (38,3)	13,1 (10,6)	p=0,033
PRL Normalization	6 (40,0%)	13 (86,7%)	p=0,016
Max. tumour diameter	16,8±8,6	12,3±10,8	p=0,028
Max. tumour diameter reduction			
<10%	2 (13,3%)	1 (6,7%)	p=0,008
10-50%	11 (73,3%)	6 (40,0%)	
>50%	2 (13,3%)	8 (53,3%)	

Table II – Evolution of "PR" from 2 years to follow-up

Current Status	DA treatment	Surgery	DA suspension	Recurrence after DA suspension
Sensitive	14	0	4	0
PR	15	1	0	0
Resistant	2	3	2	0

Table III – Status at follow-up

Conclusion

As expected, in our cohort of patients DA were effective. After 1 year significant differences between "Sensitive" and "PR" groups were detected. In the majority of "Sensitive" patients PRL normalization had already occurred and the second year was important for tumour reduction. "PR" patients needed more time of treatment to achieve therapeutic goals and globally the DA dose titration was slow. The early identification of these individuals might be important to increase the dose or change the therapy. In the small group of "Resistant" patients, despite prolonged treatment, there was no clinical improvement. However, surgery was successful and recurrence did not occur. DA suspension was only possible in 4 "Sensitive" postmenopausal women and in 2 "Resistant" operated patients.

Bibliography

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