Medical treatment of macroprolactinomas. Escalation and de-escalation of dopamine agonist dose.

Anne-Cécile Paepegaey, Sylvie Salenave, Peter Kamenicky, Jacques Young, Philippe Chanson

Assistance Publique Hôpitaux de Paris, Hôpital de Bicêtre, Service d'Endocrinologie et des maladies de la Reproduction, Le Kremlin-Bicêtre, France

Background: Cabergoline (CAB) is the most effective dopamine agonist (DA) used for the treatment of macroprolactinoma. Few data on the dose of CAB necessary for achieving and maintaining normal prolactin (PRL) levels are available. We aimed to study these parameters in a large series of patients with macroprolactinomas.

Patients and methods: We analyzed characteristics of 260 patients (135 men and 125 women). At diagnosis, the median [min; max] age, PRL level and maximal tumor diameter was 32.7 [10.6; 83.1] years, 680 [6; 38000] ng/ml and 20 [10; 110] mm, respectively. Then CAB was initiated at mean dose of 0.97 ± 0.65 mg per week. When PRL levels were normalized dose of CAB was maintained in a subgroup of patients or was tapered in another subgroup of patients, according to physician preference.

Results: PRL levels were normalized in 153 patients (70%) under CAB treatment.
CAB dose de-escalation was tried in 84 (54.9%) out of the 153 patients normalized. This dose de-escalation was successful in 77 out of 84 patients (91.7%). CAB dose was decreased from mean dose of 1.52 ± 1.17 mg per week at time of normalization to mean dose of 0.56 ± 0.44 mg per week at last visit, $p < 1.10^{-4}$.
CAB dose was maintained in 69 patients (45.1%) with mean dose of 1.05 ± 0.74 mg per week at time of normalization and mean dose of 0.99 ± 0.73 mg per week at last visit, NS. Figure 1.

Figure 1. CAB dose at treatment initiation, necessary for normalizing PRL and maintaining normal PRL (blue : dose de-escalation, red : no dose de-escalation)

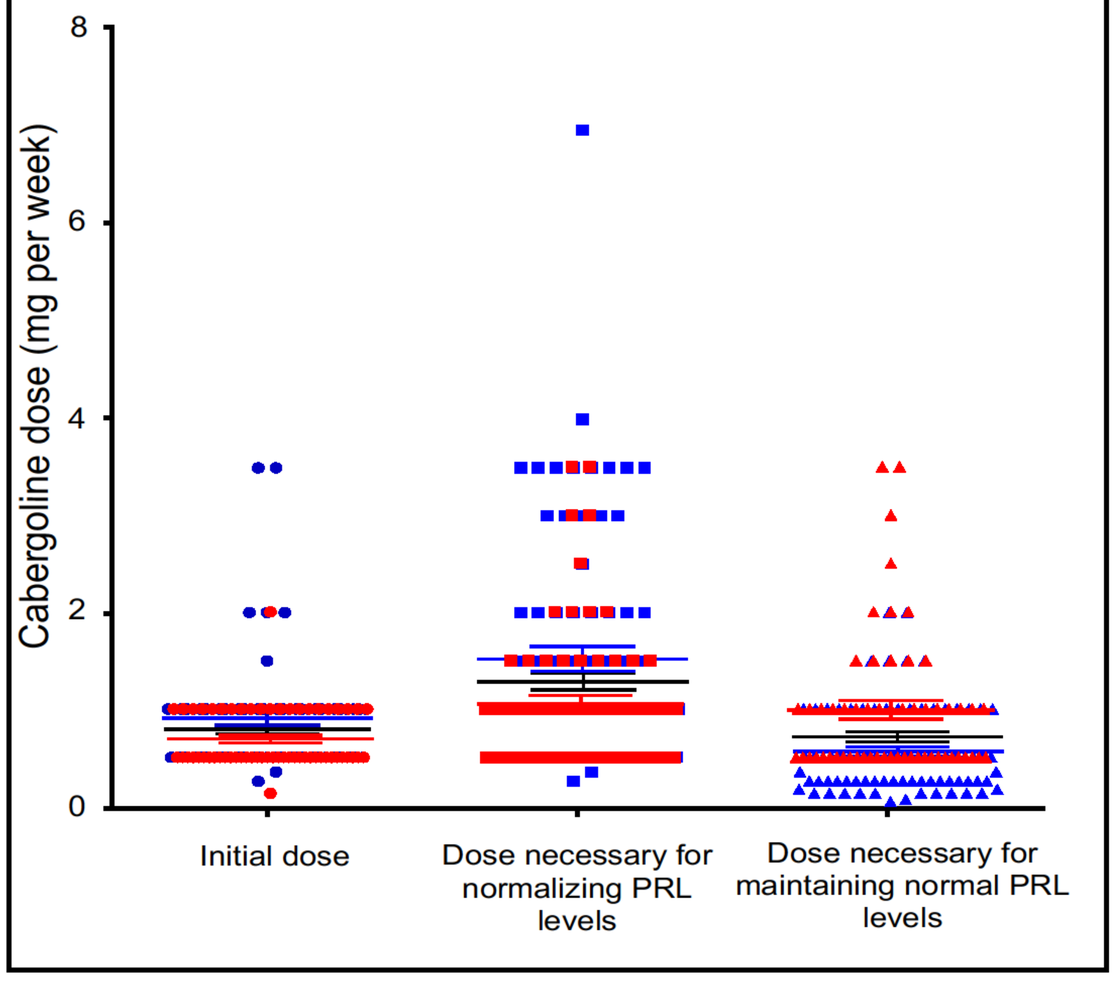
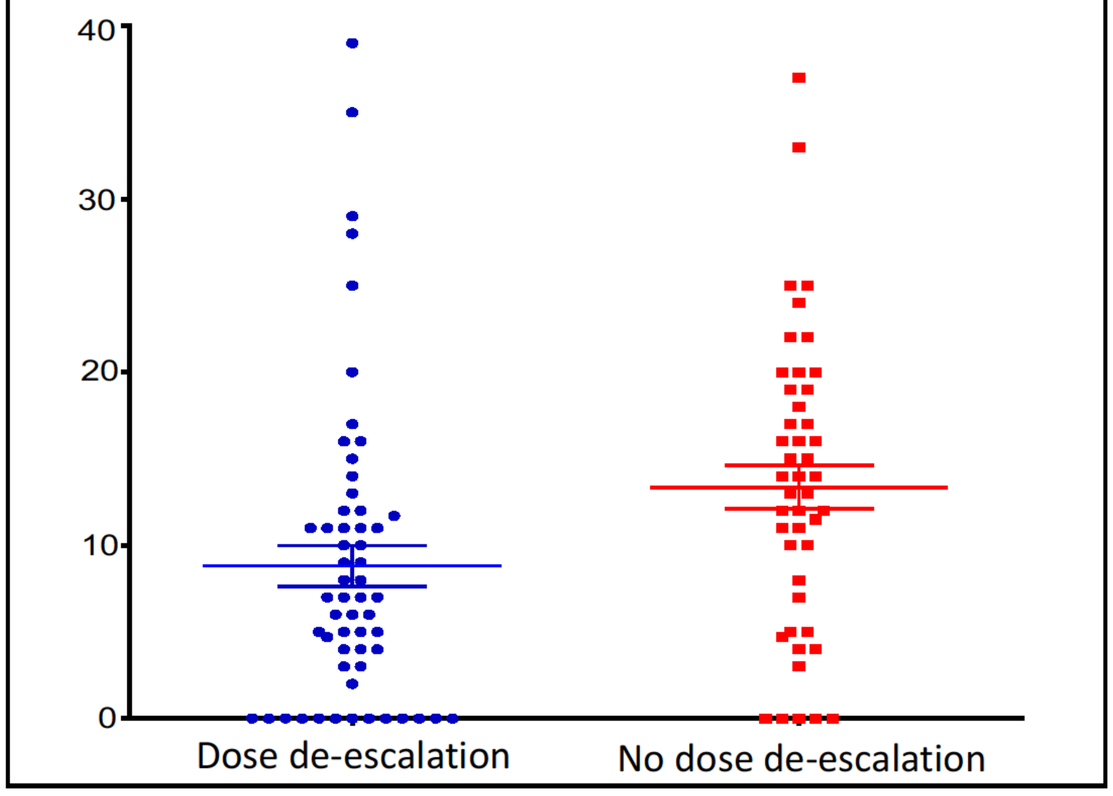


Figure 2. Tumor volume at last visit (blue : dose de-escalation, red : no dose de-escalation)



CAB dose de-escalation had no effect on long term tumor reduction : 8.8 ± 8.8 *versus* 13.4 ± 8.5 mg per week, $p < 0.01$. Figure 2.

An example of patient with dose de-escalation successful is represented on figure 3. A macroprolactinoma of 26 mm, with 1 200 ng/ml of PRL level, was diagnosed at the age of 52. CAB treatment was initiated at 0.5 mg per week . This dose was gradually increased up to 3.5 mg per week to achieve a normalization of prolactin levels and a significant tumor reduction. Then doses were gradually decreased to 0.25 mg per week without being observed new increase prolactin levels or tumor volume.

Conclusion: The dose of CAB necessary for maintaining normal PRL level on long term is lower than the dose necessary for normalizing PRL levels. Dose de-escalation after normalization of PRL levels is possible and potentially useful when considering the potential side effects of the drug which depends on its cumulative dose. Moreover this dose de-escalation strategy has no impact on tumor volume.

Figure 3. An example of patient with success of dose de-escalation