High prolactin serum level predicts low inflammatory damage during INF-beta treatment in patients with MS

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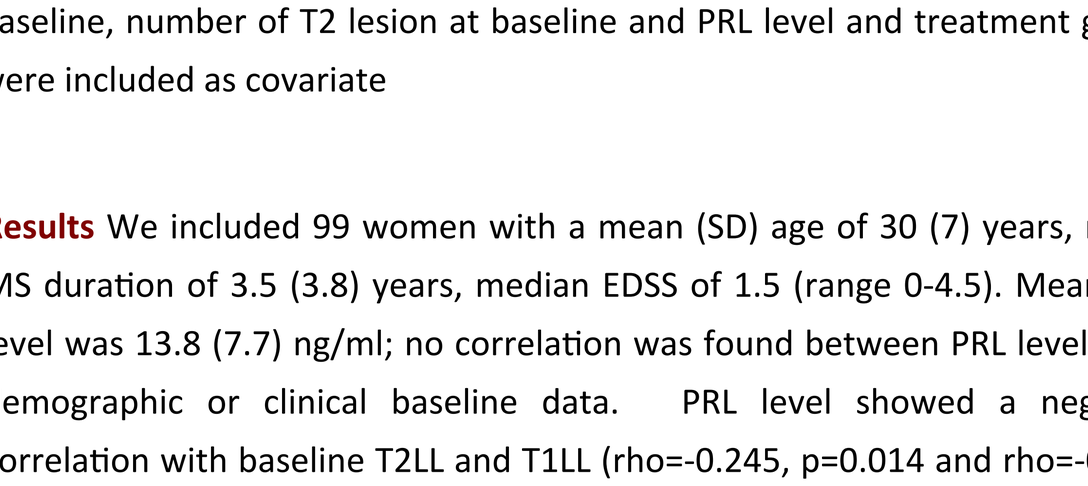
Background: The relationship between prolactin (PRL) serum levels and white matter volume in patients with multiple sclerosis (MS) supports a role of PRL in promoting myelin repair. [1] In experimental models, PRL shows beneficial effects on clinical signs of disease when administered in combination with Interferon beta (IFN beta) [2].

Objective: to test whether PRL serum levels predict the development of inflammatory damage during treatment with IFN beta

Methods We recruited relapsing-remitting MS (RRMS) from the trial registered in ClinicalTrials.gov with number NCT00151801 [3]. Blood samples for the assessment of PRL plasma level were obtained before randomisation. Patients were randomly assigned in a 1:1:1 ratio to receive subcutaneous IFN-beta-1a only or in combination with two different dosages of oestro-progestins. They underwent 1.5 Tesla MRI and clinical evaluation at baseline and after 1 and 2 years. We quantified hyperintense lesion volumes on T2-weighted images (T2LL) and hypointense lesion volumes on T1-weighted pre and post-contrast images (T1LL and Gd+LL) with a semi-automated method; we calculated the number of combined unique active (CUA) lesions, defined as new T2 lesion or gadolinium enhancing (Gd+) lesions without double counting. Predictor of CUA number were assessed with a Poisson regression model: age, disease duration, EDSS baseline, presence of Gd+ lesions at baseline, number of T2 lesion at baseline and PRL level and treatment group were included as covariate

Results We included 99 women with a mean (SD) age of 30 (7) years, mean MS duration of 3.5 (3.8) years, median EDSS of 1.5 (range 0-4.5). Mean PRL level was 13.8 (7.7) ng/ml; no correlation was found between PRL levels and demographic or clinical baseline data. PRL level showed a negative correlation with baseline T2LL and T1LL (rho=-0.245, p=0.014 and rho=-0.236 p=0.018 respectively) (**figure 1)** but not with Gd+LL. Mean number of CUA was 1.9 (2.6) at year 1 and 1.4 (3.17) at year 2; we found a negative correlation between CUA number at 2 year and baseline PRL level (rho=-0.221, p=0.02) (**figure 2**).

Figure 1: correlation between PRL level and lesion load in T2 (a) and in T1 (b).



An higher number of CUA number in the second year were predicted by a lower EDSS score, lower PRL levels, absence of Gd+ lesions, allocation to treatment with IFN-beta-1a only (**table 1).**

Figure 2: correlation between PRL level and number of CUA in the second year.

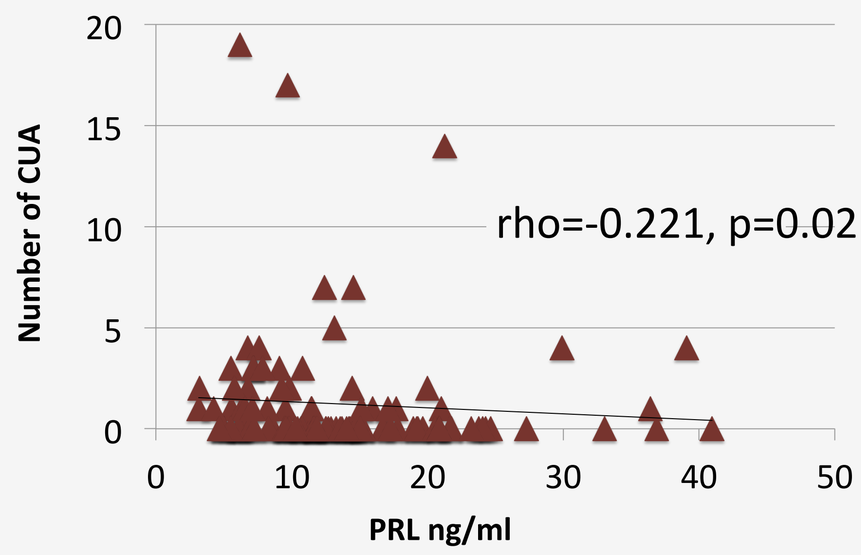


Table 1: predictors of CUA number in the second year of treatment

predictor	HR	95% CI	p
Presence of Gd+ lesions at baseline	3.734	2.146-6.498	<0.001
PRL level	0.559	0.401-0.779	0.001
EDSS	0.384	0.269-0.54	<0.001
IFN-beta-1a + high dose oestro-progestins	0.390	0.257-0.592	<0.001
IFN-beta-1a + low dose oestro-progestins	0.354	0.216-0.582	<0.001
Number of T2 lesions	1.008	1.006-1.011	<0.001

Conclusions

The association between higher baseline levels of PRL and lower inflammatory damage at follow-up suggests that PRL is an independent predictor of tissue damage development during treatment with IFN beta .

Bibliography

1. Relationship between Prolactin Plasma Levels and White Matter Volume in Women with Multiple Sclerosis. De Giglio L, Marinelli F, Prosperini L, et al. Mediators Inflamm. 2015;2015:732539.
2. Prolactin in combination with interferon-β reduces disease severity in an animal model of multiple sclerosis. Zhornitsky S, Johnson TA, Metz LM, Weiss S, Yong VW. J Neuroinflammation. 2015 Mar 19;12:55.
3. Oral contraceptives combined with interferon β in multiple sclerosis. Pozzilli C, De Giglio L, Barletta VT, et al. Neurol Neuroimmunol Neuroinflamm. 2015 Jun 18;2(4):e120.

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