Western Blotting Profile of IGF I Binding Proteins (IGFBPs) in Patients on Total Parenteral Nutrition Treated with Recombinant Human Growth Hormone (rhGH)

V. JUSTOVÁ, J. MAREK, Z. LACINOVÁ, V MELENOVSKÝ, J. KÁBRT

LEM, 3rd Medical Department, 1 LF UK, Prague, Czech Republic

INTRODUCTION

The anabolic effect of rhGH in patients with growth hormone deficiency has been confirmed in a lot of clinical trials since the preparation of rhGH (1). Treatment of patients with rhGH is also an extensive project at our clinic. Recently, our interest has been focused on the effect of rhGH administration to malnourished patients totally dependent on parenteral nutrition (TPN) (2), where the effect of rhGH was studied by means of the RIA's analysis of endogenous GH, IGF I and IGFBP-3.

The goal of this paper is to continue in our previous study (2) by monitoring the changes of IGF I binding to its low and high molecular weight IGFBPs and their fragments during the rhGH treatment of GHD patients on TPN to contribute to the elucidation of the mechanism of the bioavailability of IGF I in the above mentioned diagnosis. Spectrum of IGFBPs, their low and high molecular weight analogues were measured by the techniques of Western ligand blotting and Western immunoblotting (WLB, WIB).

RESULTS

There were mainly IGFBP-3 and IGFBP-2, just a little quantity of IGFBP-4 and practically unidentified amount of a sum of IGFBP 1, 3 and 5 in the whole WLB spectrum of IGFBPs so thats why 100 % area of all IGFBPs, measured by densitometry, is roughly a sum of IGFBP-3 and IGFBP-2.

The IGFBPs levels in WLB and or WIB profile showed a dramatic changes after rhGH administration in all patients with basal values differing in a great

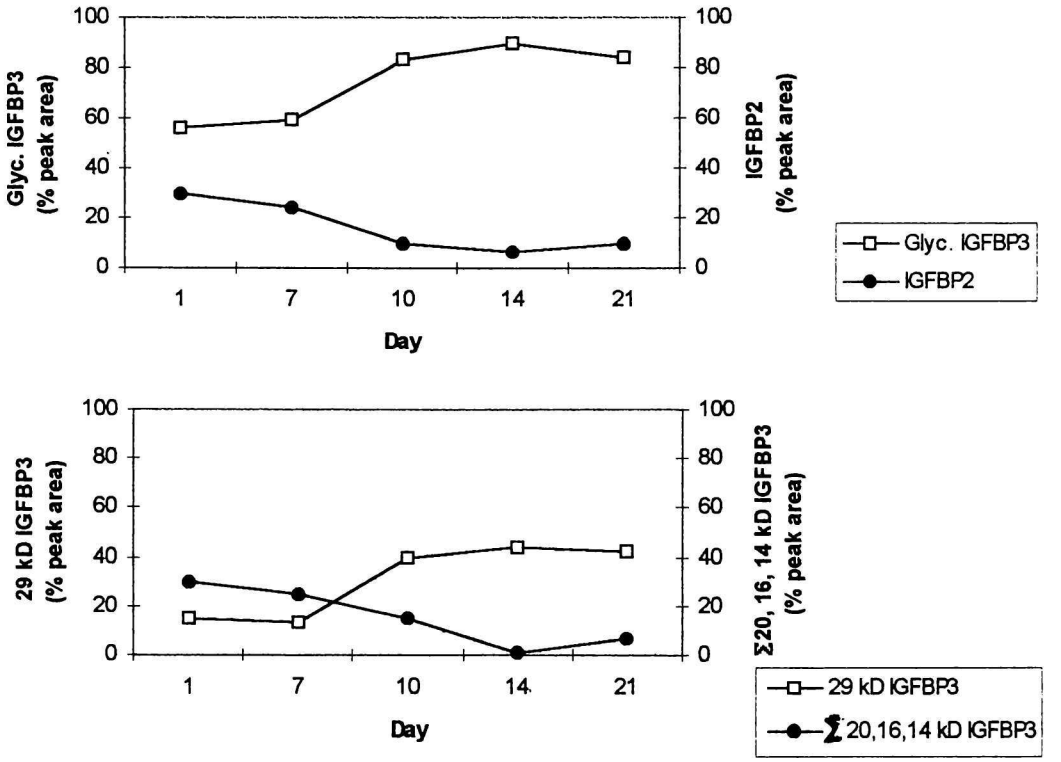

Fig. 1a,b. Representative WLB and WIB of IGFBPs in patient L.L

deal from those of normals (Fig. 1a, b). The patients with normal basal values did not much change their characteristics of IGFBPs during the rhGH treatment.

CONCLUSION

Our results confirmed the anabolic effect of rhGH including the IGFBPs feedback regulators. There were very great interindividual variations in responses of IGFBPs.

Suppressed IGFBP-3 on behalf of IGFBP-2 (WLB) during TPN predicted shortening of the half life of IGF I, i.e. releasing IGF I for biological activity. Concerning IGFBP-3 spectrum from WIB: At the beginning of the rhGH therapy there was a tendency to form low M. w. IGFBP-3 fragments i.e. by this way to facilitate the IGF I bioavailability. During rhGH therapy with higher IGF I levels IGFBP-2 diminished (WLB), low M. w. fragments (WIB) disappeared and concentrations of glycosylated IGFBP-3 and/or 29 kD derivatives increased.

Futher work has to be done to elucidate the mechanism of IGF I bioavailability.

Acknowledgements. This work was supported by grant IGA MZ ČR 3661-3.

REFERENCES

1. Johannsson G., Jorgensen J. O. L., Russell-Jones D. L. (ed.): Treatment of GH deficiency in adults. OCC Ltd., Oxford 1998.
2. Justová V., Marek J., Lacinová Z., Melenovský V Kábrt J.: Effect of GH administration to the patients on parenteral nutrition. Correlation of GH axis on vitamin D metabolites. Tenth workshop of vitamin D, Strasbourg 1997, Proceedings of X. Workshop on vitamin D, ed. A. W. Norman, R. Bouillon, M. Thomasset, 1997, pp. 725–726.