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EDITORIAL

Cardiovascular risk factors in growth hormone deficiency: is vitamin D a new kid on the block?

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It is now close to 30 years since two pioneering studies on GH treatment of adult patients with GH deficiency (GHD) were published [1, 2]. Both groups reported beneficial effects of GH on cardiac function and body composition. Since then cardiovascular function, morbidity, and risk factors have remained in focus of numerous publications in the field.

Some of the classical cardiovascular risk factors that are associated with GHD in adults include insulin resistance, unfavourable shifts in serum lipid pattern including increased serum low density lipoprotein (LDL)-cholesterol concentration, impaired fibrinolysis, and increased sympathetic nervous activity (for review see [3]). More recently reported cardiovascular risk factors include homocysteine and C-reactive protein (for review see [4]) and pregnancy associated plasma protein-A (PAPP-A) which has been observed to be elevated in GHD patients [5]. Furthermore, PAPP-A is considered to be both a cardiovascular risk factor and modulator of IGF-I bioavailability [5]. In addition, body composition often deteriorates in hypopituitary adults with increased body fat and decreased body cell mass.

During the last years, vitamin D deficiency has emerged as a potentially important cardiovascular risk factor in general, although cut-off levels for deficiency and definition of normal levels remain controversial. Its role in GHD has now been explored by Savanelli et al. [6]. Although some evidence exists to suggest a reciprocal regulation of the GH/IGF-I system and vitamin D, this is the first study to systematically evaluate vitamin D status in adult patients with GHD compared to controls. Interestingly, in this study, GHD patients had significantly lower levels of vitamin D than controls and also higher frequency of vitamin D deficiency and insufficiency. Low levels of vitamin D were quite strongly associated with dyslipidaemia, hypertension, and the metabolic syndrome but not with diabetes mellitus. Although this study has many limitations, including a comparatively small study population of which some patients have had previous radiotherapy and possibly not receiving optimal replacement therapy with other hormones, it is none the less interesting and warrants further studies on this topic. Results obviously need to be confirmed in other and larger study populations and also challenged to see if they are associated with endpoints such as cardiovascular morbidity and mortality. It will also be interesting to see if vitamin D is linked to GHD per se and will be improved by GH substitution treatment and/or vitamin D supplementation is important to optimise positive effects of GH therapy. GH replacement therapy normalises most of the cardiovascular risk factors observed in hypopituitary patients (for review see [3]). Body composition is rapidly normalised by GH replacement therapy and appear to be at least partly sustained after 15 years of therapy. Unfavourable changes in serum lipid concentrations and fibrinolysis are also improved by GH replacement therapy. A modest improvement of sympathetic nerve activity was found after 1 year of GH replacement. The effects by GH replacement on insulin sensitivity are still controversial, although in one study, a 7-year GH replacement provided protection from the age related decline in insulin sensitivity. Whether GH

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replacement therapy will improve vitamin D status and as a consequence also decrease cardiovascular morbidity in GHD patients remains to be determined.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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