Growth hormone: cardiovascular events in young adults

The results of a Swedish cohort study, published in 2021, have shown a link between treatment with growth hormone (*somatropine*) in childhood and the occurrence of cardiovascular events in early adulthood (1).

This cohort included 3408 patients who had been exposed to growth hormone in childhood, between 1985 and 2010. They were compared to 50 036 unexposed controls, matched for age, gender and region. About 70% were men, and the average age at the start of growth hormone exposure was 9.3 years. *Somatotropin* had been administered for treatment of isolated growth hormone deficiency, growth retardation in children born small for gestational age, or idiopathic short stature (1).

Patients and controls were followed up for a median of 15 years, reaching a mean age of 25 years at the end of the study. During this period, 1809 first cardiovascular events were recorded in these patients, i.e. a mean annual incidence of 25.6 events per 10 000 exposed patients, versus 22.6 events per 10 000 unexposed controls. After adjustment for a range of factors, the risk of a cardiovascular event was around 1.7-fold greater in patients exposed to growth hormone (95% confidence interval [95CI]: 1.3 to 2.2). The excess risk of cardiovascular events did not appear to depend on the reason for growth hormone treatment, but appeared to increase with the duration of exposure and the total cumulative dose received (1).

An increase in mortality had already been shown in 2010 in a French cohort of young adults exposed to growth hormone in childhood, including an excess of cerebrovascular events (2).

In practice These adverse effects in adulthood should be taken into account when deciding whether or not to use *somatropin*, all the more so because in the case of idiopathic growth hormone deficiency, there is only a modest gain in adult height, estimated in one French cohort as 1.3 cm per year of treatment (3).

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Thiazide diuretics: choroidal effusion and acute myopia

In 2020, the European Medicines Agency (EMA) decided to include choroidal effusion as an adverse effect in the summaries of product characteristics (SPCs) for medicines containing thiazide and thiazide-like diuretics, such as *hydrochlorothiazide*, *chlortalidone* and *indapamide* (1). Choroidal effusion is an accumulation of fluid in the vascular layer of the eye, behind the retina. These effusions are usually bilateral. They sometimes lead to vision disorders and visual field defects (1).

Myopia and acute angle-closure glaucoma are known adverse effects of thiazide diuretics, and regress when the diuretic is withdrawn (1-3). Choroidal and ciliochoroidal effusions due to thiazide diuretics cause bilateral myopia of rapid onset (within a few hours), through forward displacement of the iris and lens, increasing focal length. These changes reduce the depth of the anterior chamber of the eye and reduce the iridocorneal angle, leading to a risk of acute angle-closure glaucoma (3).

All of these disorders typically regress within a few days after stopping the thiazide or thiazide-like diuretic. However, acute angle-closure glaucoma can leave sequelae, such as visual field defects or blindness (1,3-5).

The postulated mechanism is immune-mediated hypersensitivity. Ocular adverse effects of this type are also observed with sulfonamides and the antiepileptic drug *topiramate*, which are structurally related to thiazide diuretics (1,2).

In practice If visual disorders develop rapidly in a patient taking a thiazide or thiazide-like diuretic, an ophthalmological examination should be arranged without delay, in particular to observe the retina and measure intraocular pressure. Stopping the diuretic responsible is often followed by regression of the disorders and prevents the visual sequelae of acute angle-closure glaucoma.

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