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Vaccination against hypertension—first clinical experiences

Treatment for hypertension is based on lifestyle intervention and drug treatment, both of which require patient adherence. Poor compliance is common for both approaches, and this might be the main cause of inadequate hypertension control. The idea of vaccination against hypertension is therefore attractive.

The effect of immunization against angiotensin II with CYT006-AngQb on ambulatory blood pressure was studied in patients with mild-to-moderate hypertension, in a multicenter, double-blind, randomized, parallel-group (two doses of CYT006-AngQb), placebo-controlled phase IIa trial.¹ Seventy-two patients with mild-to-moderate hypertension (men and surgically sterilized or postmenopausal women, age 18 to 65 years) were randomly assigned with a computer-generated randomization list to receive subcutaneous injections of either 100 µg CYT006-AngQb (24 patients), 300 µg CYT006-AngQb (n=24 patients), or placebo (24 patients), at weeks 0, 4, and 12. Twenty-four hour ambulatory blood pressure was measured before treatment and at week 14. The primary outcomes were safety and tolerability. The secondary aim of the study was to evaluate the effect of vaccination on blood pressure.

Most side effects were transient and mild.¹ There were 253 adverse events in the 100 µg group, 234 in the 300 µg group, and 135 in the placebo group. The higher frequency of adverse events with active treatment was due to the higher occurrence of local reactions. Symptoms compatible with a systemic reaction to the vaccine—flu-like symptoms, rigors, raised body temperature or pyrexia—presented within hours of dosing in 21% participants on active treatment (three in the 100 µg group, seven in the 300 µg group). One patient had an episode of syncope 10 min after receiving his first injection and did not receive any further injection.

By week 14, a decrease in the mean ambulatory daytime systolic blood pressure by 9.0 mm Hg was observed in those treated with the 300 µg injection compared with placebo ($P=0.015$).

Maximal decrease in blood pressure compared with placebo was found in the early morning hours (between 0500 h, and 0800 h) in the 300-µg group after baseline corrections with a change at 0800 h of -25 mm Hg in systolic blood pressure ($P<0.0001$) and -13 mm Hg in diastolic blood pressure ($P=0.0035$).¹ However, there was a significant increase in mean renin from baseline to week 14 in the 300 µg group (from 5.1 to 6.3 pg/mL, $P=0.02$), which was coincident with blood pressure reduction.

This study is the first to show that vaccination against angiotensin II can reduce blood pressure in man.

The induced antibody against angiotensin II response was reversible, with a half-life of about 4 months after the third injection. This is much longer than the effect of any drug which inhibits the renin-angiotensin-aldosterone system (RAAS).

The study raises some questions. We do not know yet whether it will be safe to inhibit the actions of circulating angiotensin II for several months without the ability to quickly reverse inhibition, which is easily done for drugs by withdrawal of treatment.² The RAAS plays a fundamental role in electrolyte and volume homeostasis. In situations of salt or volume depletion, such as severe dehydration, trauma, and clinical shock, rapid activation of the RAAS is crucial.² Whether this safety concern can be solved by doses of the vaccine that result in only partial inhibition of the activity of angiotensin II is unknown.

Another safety issue is whether repeated stimulation of the immune system by booster doses of an endogenous peptide linked to a virus-like particle can cause autoimmune disease.²

At present, vaccination against angiotensin II is still at the exploratory stage.

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