



Antihypertensive Vaccines

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In JNC-7 report the stress was on individualized treatment (1). The prevention of hypertension is a major public health challenges. A population approach that decreases the BP level in the general population by even modest amounts has the potential to substantially reduce morbidity and mortality or at least delay the onset of hypertension.

Immunization against components of the renin-angiotensin system offers a potential novel alternative as a population approach to daily medication in patients with hypertension or heart failure. The ray of hope in such a strategy is mass treatment of hypertension and heart failure. Over many decades, several attempts have been made to treat hypertension using a vaccination strategy to inhibit the renin-angiotensin system. Renin vaccination successfully inhibited renin activity and reduced blood pressure in animal models, but caused autoimmune disease of the kidney. Similarly, most previous studies of angiotensin vaccination failed to reduce blood pressure in animal models, despite producing high titers of antibodies that prevented the pressor response to exogenous angiotensins (2). However, recently clinical trials (3,4) have provided some ray of hope. Vaccines directed at small peptides including angiotensin I and II and a segment of the AT(1) receptor produce antibodies of sufficient titer and affinity to reduce blood pressure in patients with hypertension without causing autoimmune disease.

Although, in humans, angiotensin I vaccination did not reduce BP. However, more promising is the AngQb vaccine, which uses an immunization technology involving conjugation of angiotensin II to virus-like particles. In a phase 2 trial, hypertensive patients vaccinated with 300 microg showed a difference of 9.0/4.0 mm Hg from baseline in mean daytime ambulatory BP after 14 weeks ($P = 0.015$ for systolic BP, $P = 0.064$ for diastolic BP), and a marked reduction in early morning BP. No serious adverse events were attributed to vaccine administration (3). In another randomized clinical trial patients with essential hypertension responsive to an ACEI or ARB's were randomly assigned to receive three or four injections

of the Ang I vaccine PMD3117 or aluminium hydroxide over a 6 week period. Antibody titre was measured prior to each injection and every 30 days until disappearance. Indices of renin blockade were changes in renin and aldosterone (blood and urine) and a within-patient comparison of the pre- and post-vaccination rise in 24 h ambulatory blood pressure after 2 weeks of withdrawal of ACEi or ARB. The anti-(Ang I) antibody titre rose from the second injection in both regimes and peaked on day 64. Median half-life was 85 days. Vaccination did not influence blood pressure, but significantly blunted the fall in plasma renin following withdrawal of ACEi or ARB. At 42 days after the first injection, aldosterone excretion was decreased by PMD3117. In patients with essential hypertension, PMD3117 generated a prolonged antibody response to Ang I. Biochemical measurements show evidence of blockade of the renin system, but higher titres will be required to achieve a decrease in blood pressure (4).

In spite of the hope generated in these preliminary trials which suggested RAAS immunization to be an innovative and promising approach for the treatment of hypertension, many questions remain unanswered regarding its efficacy, safety, appropriate dose selection to achieve higher titer to achieve adequate BP lowering response, timing of administration and duration of response and regarding its booster dose requirement. Thus, these hurdles remain to be addressed before this strategy can compete with current oral medications for hypertension.

References

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