Brazilian Viper and BP Control

JV Pai-Dhungat*, Falguni Parikh**

Pathologist Goldblatt’s experiments on renal arteries (1934) had resulted in the first animal model of chronic hypertension. In 1954, Leonard Skeggs first described existence of renin and two forms of peptide "hypertensins" and a converting enzyme and in the serum of the horse blood. By 1958, hypertensin and angiotenin were uniformly designated angiotensins. During the 60s, numerous group of researchers accurately delineated renin-angiotensin-aldosterone system (RAAS).

John Vane along with Bakhle and other colleagues in London, demonstrated that the conversion of angiotensin converting enzyme (ACE) I to II occurred on luminal surface of small blood vessels, predominantly in the lung (1968). In 1971, SH Ferreira and colleagues from Sao Paulo Brazil published a landmark paper in the Lancet. They recognised that the venom of the South American pit viper Bothrops jararaca lowered blood pressure through what they called bradikin in-potentiating enzyme and also recognised that this kininase was identical to ACE. They suggested the use of this enzyme to detect over-activity of RAAS in hypertensive subjects. John Vane suggested that ACE inhibitors might help control high blood pressure (Vane won Nobel Prize in medicine in 1982 for his work on Aspirin).

Ferreira and colleagues also isolated a bradykinin potentiating peptide, which blocked the conversion of ACE-I to active hypertensive peptide in rats. The snake compound was too unstable for clinical use and did not prove suitable. However, for the researchers, this served as a model for drug design. With the use of the X-ray crystallography technique, it became clear that important part of the active site of ACE was zinc. Further research led to the discovery of first ACE inhibitor captopril by Bristol-Myer Squibb, released in the late 70s, which is still being prescribed.

The next two decades has seen veritable explosion of clinical research with these agents and in turn ACE II receptors and agents blocking them. It has also seen their use being extented from hypertension to heart failure treatment, MI and finally to vascular protection, in high risk people including diabetes. There is no better recent example in therapeutics of effective linkage between basic and clinical research endeavours to improve the understanding of disease mechanisms and clinical outcome.

---

*Professor of Medicine, T.N. Medical College (Retd.), Hon. Physician, Bhatia Hospital, Mumbai; **Consultant Internal Medicine and Infectious Diseases, Kokilaben Dhirubhai Ambani Hospital, Andheri (West), Mumbai

Stamps issued on Kidneys and hypertension - Uganda, 1978; John R Vane - Micronesia 2001 and Bothrops Jararaca Viper - Brazil, 2001