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Review Article

The Kidney as the Endless Responsible for Hypertension

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Abstract

Hypertension is one of the most important and growing problems listed as a major risk factor for cardiovascular disease (CVD) and premature death. An advanced study around centuries gives us the idea that the kidney and its physiological adaptive response governs the regulation of blood pressure. These link between kidney and blood pressure remains controversial in understanding completely the pathogenesis of it. Moreover, the precise cause of hypertension is not apparent in the vast majority of patients. This review focuses on the pathophysiological mechanisms of hypertension, defining the kidney as the culprit or victim for hypertension and understands our limitations and obstacles to apply individualized approaches for prevention, treatment and identifying new specific therapies.

INTRODUCTION

Hypertension is one of the main risk factors for chronic kidney disease (CKD), cardiovascular and cerebrovascular diseases, affecting more than 1 billion people worldwide, not leaving Mexico behind where 31.5% of adult population is affected [1-4]. In just six years between 2000 and 2006, the prevalence of HT increased 19.7%, affecting 1 of 3 adults in Mexican population (31.6 %). In Mexico its high prevalence acquires more importance if we consider in 2006, 47.8 % of adults with hypertension where not yet been diagnosed, and only 39.0% of those where already been diagnosed and receiving specific treatment [5]. Hypertension surveillance in Latin America is still problematic due to significant methodological limitations in published studies along with scarce and poor quality of data [6]. Most recent publications on hypertension surveys from 35 countries in Latin America and the Caribbean did not meet the basic methodological criteria to be considered useful for surveillance purposes [7]. Conversely, several reviews summarized accumulated evidence in support of a hypertension as a sensible public health measure [8,9].

Renewed interest in the pathogenesis of hypertension makes us focus these review on the role of sodium, the distinction of pressure natriuresis concepts and so no mew concepts of the relationships between salt intake and blood pressure with require of the immunological, metabolic and neuro hormonal response of the kidneys [10,11].

The connection or dysfunctional relationship between kidney and BP

Over the years the kidney plays an important role in hypertension [12]. Dr. Bright proposed initially that urine abnormalities altered blood in such a way that increases vascular resistance, leading to high blood pressure and increased cardiac mass [13]. Starling, in the early 1900s, clarified the concept that volume homeostasis and blood pressure regulation are closely linked and emphasized the importance of renal fluid retention in maintaining arterial pressure in particular circumstances, especially those associated with circulatory depression, such as heart failure [14].

As noted by Guyton and colleagues the concept of pressure natriuresis mechanism, exposes hypothetical mechanisms which suggests the effect of arterial pressure on the renal excretion of sodium/water [15]. Limiting this statement in the capacity for the kidney to excrete sodium, where its permissive modification response is required to perpetuate a chronic elevation disequilibrium end point [16].

The pressure natriuresis theory of chronic end point would appear to follow from what Guyton and Coleman called “the three laws of long-term arterial pressure regulation”. These classical model of hypertension shows different factors that alter the renal function curve (and thereby to alter the long-term level at which the arterial pressure is regulated) divided into 1) intrinsic changes that occur within the kidneys and 2) extrinsic changes that occur outside the kidneys but that either directly or indirectly affect the kidneys’ ability to excrete sodium. This does not imply that hypertension is a renal disease, but indicates that a renal functional abnormality is a sine qua non condition for the development of any type of hypertension [17]. This last perception confirmed by studies from past century by Bianchi et

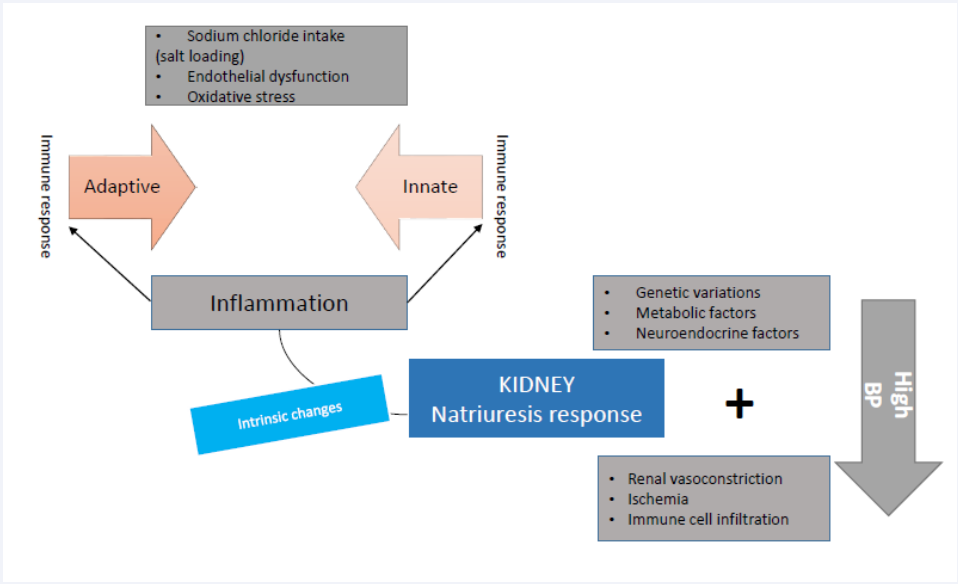

Figure 1 Factors involve in hypertension [29].

al., [18] and more definite well controlled experimental studies from Rettig et al., [19,20] stating that "blood pressure goes with the kidney."

Some authors state that "in all forms of hypertension including essential hypertension, pressure natriuresis is abnormal" [21]. It is further contended that hypertension "cannot be sustained if pressure natriuresis is unaltered" [22] and that "in all forms of hypertension that have been studied, there is a shift of renal-pressure natriuresis that sustains the hypertension." This central role of renal excretory function remained highly controversial, primarily because not all forms shows obvious renal defects or disturbances in sodium excretion that could clearly prove that arterial pressure had a long-term effect on sodium excretion. The fact that a normal rate of sodium excretion (equal to sodium intake) is maintained despite higher blood pressure indicates that pressure natriuresis is reset in chronic hypertension [23-25]. Recently, Crowley and Coffman have reviewed "evidence supporting the premise that an impaired capacity of the kidney to excrete sodium in response to elevated blood pressure is a major contributor to hypertension, irrespective of the initiating cause" [12,26,27]. Few investigators question the idea that chronic hypertension is sustained by abnormal pressure natriuresis regardless of the initial cause of the hypertension. The evolution of this concepts have embraced our nephrology community, but it remains still a controversial circle whether this is just compensatory a pathway or if it's an independent state.

Classical models suggest that sodium plays an important pathophysiological role in blood pressure values and in the development of hypertension. Studies performed more than a quarter of a century ago showed blood pressure response to changing salt intake and several methods were used to determine salt sensitivity [28]. Despite differences in the techniques and criteria used for the definition of salt sensitivity and resistance by different investigators, congruence and reproducibility of the responses have been demonstrated in the majority of carefully performed studies. The most accepted method was introduced by Weinberger, who recognized the not only heterogeneity of the blood response to salt and developed the concept of salt sensitivity. Demonstrating on follow up studies the increased risk of salt sensitivity in non hypertensive individuals and how mechanisms may contribute to mortality [29-31].

Controlled studies strongly support that during acute or chronic increases in salt intake, normal salt resistant subjects undergo substantial salt retention and do not excrete salt more rapidly, retain less sodium, or undergo lesser blood volume expansion than do salt-sensitive subjects.

These observations: directly conflict with the widely held view that renal excretion of sodium accounts for resistance to salt-induced hypertension, and have implications for contemporary understanding of how various genetic, immunologic, and other factors determine acute and chronic blood pressure responses to high salt diets [32]. So far these suggest kidney function can remain and provides a new novel platform for studying non kidney based theories of hypertension. Even Franz Volhard postulated: "I doubt very much whether hypertension has any useful purpose. We are confronted with a vicious circle which is responsible for progression of hypertensive renal disease and the final outcome of renal insufficiency" [33,34].

Hypertension also includes important role of metabolic and neuro-hormonal factors in the determination of blood pressure in addition to the effect of genetic variations. Regulation of sodium, water reabsorption and, thus, volume homeostasis involves the renin-angiotensin-aldosterone system, the sympathetic nervous system, the system of natriuretic peptides, insulin, leptin and various endothelial effectors with endocrine and/or paracrine activity [29].

Including a large body of good quality evidence in its favor as a determinant of hypertension, and in those salt sensitivity individuals, in addition to the effect of a genetic variation.

Unfortunately, there is little or no evidence on truly effective manoeuvres that could impact the long-term response to salt intake reduction in real life conditions. In fact, drastic and abrupt short-term sodium restriction produces strongly dependent blood pressure immune and neuro-endocrine adjustments [29]. Not every person reacts to changes in dietary salt intake with alterations in blood pressure, dividing people in salt sensitive and insensitive groups. It is estimated that about 50-60 % of hypertensives are salt sensitive. In addition to genetic polymorphisms, salt sensitivity is increased in aging, in black people, and in persons with metabolic syndrome or obesity. However, although mechanisms of salt-dependent hypertensive effects are increasingly known, more research on measurement, storage and kinetics of sodium, on physiological properties, and genetic determinants of salt sensitivity are necessary to harden the basis for salt reduction recommendations [35].

Other mechanisms involve on the adaptive immunity response in hypertension, including antigen presentation, lymphocyte activation, and antibody production. This has become a critical area of study in the pathogenesis of hypertension because there is no still jet specific responsible due by the immune response in essential hypertension. Specific therapeutic strategies of potential clinical use may result from the insights gained in studies on the role of immunity in hypertension [36].

After all hypertension is part of the burden of chronic diseases, increasingly worldwide, due to population growth, increasing longevity, and changing risk factors [37]. Literature through these centuries describes somehow sodium excretion; kidney and blood pressure are directly related. There is no doubt that, in general, early detection and pharmacological treatment and non-pharmacological has important benefits on morbidity and mortality rates.

CONCLUSION

Reviewing past and present investigations, provides substantial insights into the pathogenesis of hypertension. Refreshing concepts such as basic mechanisms that link renal excretion of sodium and water with blood regulation, experimental evidence abnormalities of pressure natriuresis as causal of hypertension and the important role of metabolic, neuro-hormonal and the adaptive immunity response.

Being part of an undeveloped country and part of a group of nephrologists, makes us review, learn and understand the importance of kidney and blood pressure. Its emerging prevalence affecting primarily disadvantaged populations in whom the detection and control also tends to be poor. Knowing by now that epidemiologic predisposition is as important as knowing the relationship of this association, its control methods, and essentially target blood pressure in each individual. Current evidence is not exact; lack of knowledge on genetic or other intrinsic modulators in Hispanic population is still key and our goal, until scientific breakthroughs help us definitively understand this interesting pathogenesis of our marvelous kidney.

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