Clinical Nephrology

Evidence-based medicine vs inferential reasoning: the case of hypertension associated with renal disease

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Introduction

Under the name of evidence-based medicine, the physician’s experiential learning and inferential reasoning of traditional medicine has been replaced by impersonal knowledge of a probability of a given result. This modern approach to clinical problem solving has expanded into a real movement, and almost inevitably, has become a subject of debate [1]. Proponents of evidence-based medicine claim that it is invaluable, as it improves the clinicians’ understanding of research methods and makes them critical in using data, it improves confidence in management decisions, and is the only way for doctors to keep up with the latest research [2]. Opponents state, however, that it is hopelessly out of touch with reality, as it disregards the many uncertain ‘grey zones’ of clinical practice and that doctors must defend clinical reasoning against the effects of epidemiology and outcome research [3].

Hypertension-related renal disease is a characteristic example of the apparent discrepancy between personal experience and impersonal knowledge. Forty years ago, when no specific antihypertensive therapy was available, renal insufficiency was the most common complication of hypertension, with an incidence of 18%, compared with an incidence of 16% for coronary heart disease and of 12% for cerebrovascular accidents [4]. In recent years, clinicians very rarely see a hypertensive patient who progresses to renal insufficiency; and even then, they cannot be certain whether this particular patient has hypertension-related glomerulosclerosis, or atheromatous disease of the renal artery, or even some other co-existing renal disease, such as chronic glomerulonephritis. Yet, hypertension-related renal disease features prominently in statistics as a cause of end-stage renal disease. For example, the incidence of hypertension as cause of end-stage renal disease has doubled in the ERA–EDTA Registry in the past two decades, and is reported to be as high as 28.5% in the US [5]. It is, therefore, evident that the question ‘Can essential hypertension cause progressive renal disease’ cannot be answered solely on the basis of personal experience. On the other hand, by using inferential reasoning based on research focused exclusively on the biology of the disease, the answer to this question would tend to be positive. In fact, clear experimental evidence exists that systemic hypertension induces or accelerates the progression of renal disease, presumably through accumulation of mesangial extracellular matrix and increased transcapillary protein traffic [6].

Evidence-based medicine

An alternative approach to the problem would be the use of evidence-based medicine. The first step in the process of evidence-based medicine is to formulate a clear clinical question relating to diagnosis, prognosis, treatment, iatrogenic harm, quality of care, or health economics. The question ‘Can essential hypertension cause progressive renal disease’ is, therefore, proper to initiate evidence-based medicine, as it relates to prognosis. The second step is to search the literature for relevant clinical articles. The most appropriate publication type to answer this sort of question is epidemiological studies. Search of the literature reveals four cohort, and two case-control studies. The results from two of the four cohort studies are negative: no significant change in renal function was found in treated hypertensives followed for more than 5 years in one of them, and no relationship was present between blood pressure and increase in serum creatinine within 1 year or more, in the other. The other two cohort studies give positive results: a correlation between mean blood pressure and rate of renal function decline, or between serum creatinine and blood
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pressure measured more than 12 years before, was found in each of them. On the other hand, both case-control studies report a greater rate of decline in renal function in hypertensive patients.

The third step in evidence-based medicine is to critically appraise the evidence for its validity and usefulness. Unfortunately, those of the above studies that gave positive results lack methodological rigor to be reliable enough for answering positively to the initial question: either the sample size was too small or, the possibility that some of the patients studied had clinically undetected renal disease at entry could not be ruled out; or the population studied comprised a great proportion of black people, who as a group differ in many respects from white hypertensives; or the increase in rate of renal function decline in hypertensives was too small to predict evolution to end-stage renal disease. Thus, epidemiological data concerning the renal consequences of essential hypertension can be regarded as more or less confirmatory of the doctor’s experience with individual patients. As far as the difference between the results of epidemiological studies and the end-stage renal disease registry data is concerned, the seeming discrepancy may be because of a misclassification, a common trap in statistical research. In fact, the registry-based incidence may be overestimated because the diagnosis is usually made by exclusion, and because other types of renal disease, such as atherosclerosis of the renal artery and cholesterol crystal microembolization can mimic hypertensive nephrosclerosis [7,8].

The fourth step in evidence-based medicine is to implement useful findings from the relevant literature to clinical practice. Of course, the question ‘Can essential hypertension cause progressive renal disease’ is quite relevant to the problems that a hypertensive patient faces. Nevertheless, it is not the kind of question that directly concerns clinical-management decisions. Depending on the specific characteristics of the patient, the questions directly related to the choice of an appropriate approach would be: ‘Can antihypertensive treatment prevent or delay progressive deterioration of renal function in a hypertensive patient without renal disease?’ or ‘in a hypertensive patient with renal disease?’ or ‘in a normotensive patient with renal disease?’, ‘Does the potential renal protective effect depends on the class of antihypertensive drugs used to lower blood pressure?’, and ‘What target blood pressure is necessary to preserve renal function?’. Obviously, no individual clinician can give the right answer to any of these questions solely on the basis of his personal experience or through inferential reasoning on the ground of theoretical knowledge. In order to be successful in his intervention, the clinician needs information regarding the best effective treatment rather than the mechanisms by which hypertension affects the kidney.

Evidence addressing this type of question derives from randomized controlled trials, systematic reviews (meta-analyses), observational studies, and practice guidelines. Among them, large randomized trials and systematic reviews are proposed as the types of publications which offer the strongest level of evidence, although the results of well-designed observational studies, with either a cohort or a case-control design, do not systematically overestimate the magnitude of the effects of treatment as compared to those in randomized controlled trials on the same topic [9,10]. Search of the relevant literature reveals many randomized trials, a few systematic reviews, and several guidelines. After appraising evidence from the literature, the following conclusions can be drawn: (i) in patients with essential hypertension or primary renal disease, antihypertensive treatment, irrespective of the agent used, exerts beneficial effect on proteinuria and renal function, proportional to the degree of blood pressure reduction. (ii) In addition, ACEI and possibly, non-dihydropyridine calcium antagonists might have further effect on proteinuria, independent of blood pressure reduction. (iii) Blood pressure levels lower than 130/85 mmHg should be targeted in hypertensive patients with renal disease [11]. Consequently, in order to give their patients the full benefit of antihypertensive treatment, clinicians must implement the above guidelines in their routine practice.

In conclusion, evidence-based medicine has emerged in response to the need to improve the quality of advice given to clinicians. Although modern biology has enormous implications for medicine, a deeper understanding of the biology of the disease does not necessarily help individual physicians to make decisions in every day practice [12]. In order that advances in scientific understanding will be converted to advances in treatment, clinical decisions should be based on the best available evidence, and best available evidence can only be identified by using epidemiological and biostatistical ways of thinking [13].

References