THE NEW ARMENIAN MEDICAL JOURNAL
Vol.7 (2013), No 2, p. 87-88

THE LETTER TO EDITORIAL OFFICE

TARGETING ARTERIAL HYPERTENSION: IN SEARCH OF THE RIGHT DRUG FOR THE RIGHT PATIENT

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Received 4/08/2013; accepted in final form 5/15/2013

Arterial hypertension remains one of the main cardiovascular problems, with more than 950 million people affected worldwide [Kearney P. et al., 2005]. Arterial hypertension is one of the most preventable causes of early hospitalization and mortality, as a major risk factor for stroke, myocardial infarction and heart failure, chronic kidney disease and peripheral vascular disease. It is well-known that most hypertensive patients are not aware of their condition, but it is also evident that blood pressure regulation is not easily achieved and many treated patients are often far away from optimal control [Kearney P. et al., 2005; Hajjar I., Kotchen T., 2003]. Blood pressure level is regulated by complex physiological interactions: there are disorders in the specific points of these mechanisms (secondary arterial hypertension) in some cases, but in the majority of patients you can not find such disorders in the mechanisms of regulation (essential hypertension). Essential hypertension is often the combined result of many factors affecting catecholamine and sodium homeostasis [Mendlowitz M. et al., 1964], involving a large number of elements (enzymes, channels, receptors, etc.).

Most physicians are familiar with the problem of optimal blood pressure control, which is often the result of individual unpredictable response of patients to pharmacological treatment. The aim of research was to identify some of the factors in patients that could predict blood pressure changes prior to drug administration [Weder A., Julius S., 1994]. For instance, age [Kaplan N., 1989; Robertson J., 1990], sex [Hayes S., Taler S., 1998], pretreatment blood pressure indexes [Gill J. et al., 1985; Sumner D. et al., 1988], plasma renin activiy [Blumenfeld J., Laragh J. 1998; Preston R. et al., 1998] have been unsuccessfully studied to create the optimal methods for the choice of antihypertensive drugs [Chobanian A. et al., 2003]. Due to above mentioned difficulties, an interest in pharmacogenetics of hypertension of dissolving issues of how genetic differences influence on the variability of the effects of antihypertensive drugs has increased in recent years [Turner S. et al., 2001], and how, at last, to avoid the long and disappointed treatment. Primary hypertension has the multifactorial pathophysiological basis and it has been estimated that approximately 50% of the variation in blood pressure is explained by genetic factors [Arnett D. et al., 2006]. Additionally, it is also evident that the individual response to drugs has a genetic component [Motulsky A., 1957].

In this context, there are many factors regarding interactions of genetic polymorphisms and antihypertensive treatments. Recently, Sydorchuk and Amosova published the results of the pilot study in "The New Armenian Medical Journal" [Sydorchuk L., Amosova K., 2011], aimed at evaluating daily blood pressure changes in hypertensive patients treated with different drugs according to genes polymorphisms of angiotensin-converting enzyme (ACE), angiotensin II receptor, endothelial No-synthase, peroxisome proliferators-activated receptor-g2 and b1-adrenergic receptor. Data from 249 patients with various degrees of hypertension and 50 patients from control group were analyzed and the main finding was that in the carriers of the I-allele of ACE gene the combination of hydrochlorothiazide (HCTZ) and angiotensin II receptor blocker (ARB II) was more effective than HCTZ and β1-blocker (β1-AB) or HCTZ and ACE-inhibitors (ACEI). The data also showed that for the persons of DD-genotype of the same gene combinations of calcium channel blockers (CCB) and ARB II and CCB and β1-AB were more effective than CCB and ACEI.

Undoubtedly, this interesting study may be useful as the additional knowledge to better comprehension of the mechanisms of the clinically observed heterogeneity of hypertension and antihypertensive drug responses. On the other hand, the readers will pay attention to the genetic predictors. It is obvious that with the advancement in pharmogenetics the great opportunities for the treatment of an individual based on its characteristics will be found, but it is also evidently that we are still far from practical application of this idea [Arnett D. et al., 2009]. First of all, it should be underlined that the published studies, discussed by Sydorchuk and Amosova are very contradictive. Some of the possible causes are differences in study designs, heterogeneous phenotypes (e.g. response variables), small sample sizes and short duration of follow-up periods. Furthermore, individual genes, which showed variability in blood pressure in the population have not been identified. In addition to these considerations, future researches will also try to develop pharmacogenetics screening tests in order to standardize patients' polymorphisms [Arnett D. et al., 2006]. Moreover, physicians should have

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all the necessary information for the correct interpretation of genetic analysis and its application to the appropriate clinical choice [Arnett D., Claas S., 2009].

Further studies in the field of pharmacogenomics will be in great demand. Meanwhile, clinicians should find the best drug in certain clinical situations "by themselves". It can be difficult not only because of individual variability in response to treatment, but also due to the fact that the physicians make the choice of drugs within the guidelines of official reports, meanwhile, not forgetting about the pathophysiological features of this case and comorbidities [Fragasso G. et al., 2012]. In fact, it should be clear that, apart from lowering blood pressure, a main target when treating arterial hypertension should be to counteract all the possible pathophysiological mechanisms involved in hypertension and in existing/potential comorbidities. Furthermore, all the ancillary positive and negative effects of the administered drugs should be taken into consideration [Fragasso G. et al., 2009]. One must take into consideration all positive and negative effects of prescribed drugs. In patients with arterial hypertension the disorders of tolerance to glucose, diabetes, dyslipidemia, or developing atherosclerosis are frequently found.

In conclusion we can say that the studies of pharmacogenetic hypertension, similar to Sydorchuk and Amosova, will show better knowledge of the molecular basis of hypertension, aimed at efficient choices of drugs for an individual. By that time the physicians should make the simple clinical choice based on pathophysiological mechanisms and comorbidities finding out the appropriate drug for a particular case.

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