MATHEMATICAL MODEL OF VASORENAL HYPERTENSION

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The use of mathematical models is a most promising method of analysis of diseases with a complex pathogenesis [2, 3, 5]. Attempts have been made to use mathematical methods to predict the results of surgical treatment of patients with vasorenal hypertension [1].

The authors have analyzed the character of development of vasorenal hypertension by establishing equations and a mathematical model of this disease.

To construct the mathematical model, a logic of basic equations, suggested by Marchuk [2] for the creation of mathematical models in immunology, was used. Temporary changes in interconnected characteristic values were examined in the equations of the mathematical model and differentiation of functions was carried out with respect to time. Changes in the basic characteristics of the disease were evaluated according to the degree of their deviation from the norm. For this purpose, an equation was first deduced for a relative criterion defining the degree of deviation of the parameters from normal: an equation of vasorenal hypertension. Differentiation was carried out with respect to this relative criterion.

To construct the equation of the disease, in the first stage of the work the basic function and morphometric parameters, the degree of deviation of which could be used to judge the presence and stage of development of the pathological process, were determined. A necessary condition was the obtaining of sufficiently complete variance series to allow variability of the features of the disease to be estimated reliably. The second step in construction of the equation was determination of the index of the influence of the feature (by analogy with the index of severity of the disease suggested in [2]). The value of the index was found to depend directly on the strength of correlations between features of the disease, whereas the character of its change was determined by the rate of development of pathological changes in the kidney. Dependence of the pathological changes in the kidney, the severity of which depends on the duration of vasorenal hypertension, on the degree of reduction of the renal blood flow was defined as the function f_i. In that case $F_i = \partial f_i/\partial\tau$ is a function reflecting the dynamic capacity of the system (the response to a change in the intrarenal blood flow), whereas $\Phi_i = \partial F_i/\partial\tau$ is a function of the rate of change of the dynamic capacity of the system. The greater the degree of loss of the dynamic capacity of the system, the more severe the pathological changes in the kidney will be; consequently, the function $k_i = -\xi_i \cdot \Phi_i = -\xi_i \cdot \partial F_i/\partial\tau = -\xi_i \cdot \partial^2 f_i/\partial\tau^2$ is an index determining dependence of the severity of the pathological changes in the kidney on the pathogenetic mechanisms determining the rates of development of the disease. ξ_i is a coefficient whose value corresponds to the characteristic region of changes in f_i (Fig. 1). Thus, if the blood flow through the kidney on the side of the lesion falls to 100 ml/min, the index of influence k_i will be 2.

To construct the equation of vasorenal hypertension the condition was stipulated that it reflected the degree of influence of each feature, it was dimensionless, and it had a minimum (0) under normal conditions and a maximum corresponding to complete shrinking of the kidney. In that case the equation has the following form:

$$P = \sum_{i=1}^{n} k_i \left| \frac{f_{iN} - f_{i\tau}}{f_{iN}} \right|,$$

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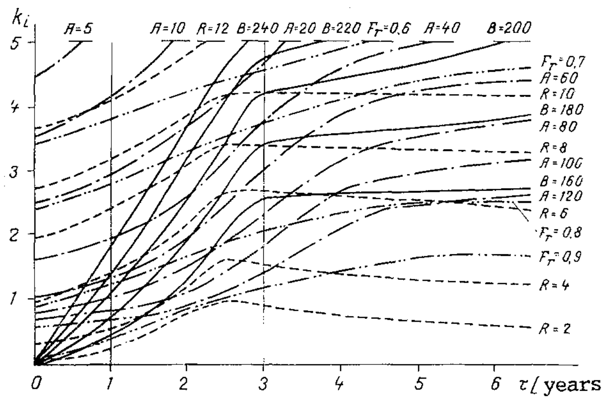

Fig. 1. Nomograms showing coefficient k_i (index of influence of the feature) as a function of duration of the disease. A) Renal blood flow, ml/min; B) arterial pressure (systolic), mm Hg; R) plasma renin level, ng A/ml/h; F_r) form parameter.

where f_{iN} is the value of the i-th functional parameter under normal conditions, and $f_{i\tau}$ is the value of the i-th functional parameter at the time of investigation τ. $|f_{iN} - f_{i\tau}/f_{iN}|$ reflects the relative change in the functional parameter compared with normal. In the region of values of the parameter of pathology P from P_0 to P_{max} characteristic stages of development of the pathological process can be distinguished: the initial stage of development of vasorenal hypertension with an approximate duration of up to 1 year, the stage of established clinical picture of the disease, from 1 to 3 years, and the terminal period, lasting more than 3 years (Fig. 2).

Having determined the value of the functional (renal blood flow, plasma renin activity, arterial pressure [1]) and morphometric (area of the juxtaglomerular apparatus, the juxtaglomerular index, form parameter, relative volume of the endoplasmic reticulum and of different kinds of granules in the epithelioid cells of the juxtaglomerular apparatus [4]) parameters, and correlating them with the corresponding region of pathology, conclusions can be drawn regarding prognosis and the tactics of treatment can be chosen. Moreover, if it is impossible to determine all the parameters reflecting the state of the kidney, but if the values of most of them are known, by means of a graph it is possible to calculate the hypothetical value of these parameters.

It was considered important to construct a mathematical model which would take account of correlations and the mutual influence of functional and objective morphological parameters. If the development of the pathological process in time is not always uniform in value, dependence of functional characteristics on the severity of the pathological changes is always determined. The coefficients k_i, reflecting the development of pathology at time τ, is included in the definition of the parameter P, which reflects the time course of development of the disease. We thus consider that the correct course is to plot the dependence of changes of all parameters on the state of development of vasorenal hypertension, which reflects P. Having determined all the functions of $f_i(P)$, for each concrete patient with functional parameters f_i, duration of the disease τ, and parameter of pathology P, determined by the function $k_i(P)$, we can concretely suggest the character of various pathological changes, on the basis of which the prognosis of the disease can be assessed and the tactics of treatment chosen. For example, in vasorenal hypertension a fall in the velocity of the renal blood flow (A) causes hyperplasia of the juxtaglomerular apparatus — of the endoplasmic reticulum in epithelioid cells (E) and a change in the character of granule formation — with predominance of rhomboid protogranules (F_r — the form parameter), and plasma renin activity (R) and arterial pressure (B) rise. The system of equations of the model has the form:

$$\frac{\partial A}{\partial P} = -\alpha E + \beta F_r$$

$$\frac{\partial \varepsilon}{\partial P} = \gamma R - \varepsilon F_r$$

$$\frac{\partial B}{\partial P} = \delta R + \lambda \varepsilon - \theta A - \chi F_r.$$

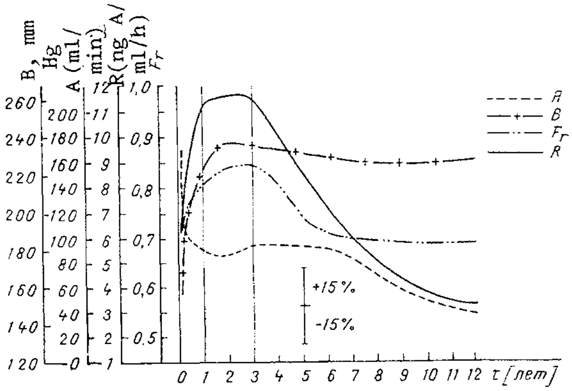

Fig. 2. Mean statistical (± 15%) character of changes in certain parameters determining presence and development of pathological processes in vasorenal hypertension depending on duration of disease.

The most difficult step in solution of the system of equations is determination of the coefficients of proportionality (α, β, γ, ε, δ, λ, θ, χ, and so on), showing the character of changes in some features relative to others. The performance of numerical experiments, which the situation demands, and also data processing necessitate expenditure of much computer time. Solution of the system of differential equations and the practical use of analysis of the mathematical models of vasorenal hypertension will be future topics for the authors' research.

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