CHOICE OF BLOOD-COAGULATION PARAMETERS FOR AUTOMATIC DIGITAL RECORDING

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The possibility of producing a thromboelastometer, automatically recording the four most commonly used parameters of the state of the blood-coagulation system (BCS) in clinical practice in digital form was described previously [1].

Confirmation of the urgent need for such a digital thromboelastometer was given by investigation [2] aimed at choosing the most informative of some of the parameters used at the present time. As a result, the parameter r characterizing the latent response of the blood clotting process was chosen for digital recording and a new parameter S, an integral parameter of the blood clotting (BC) process and consisting essentially of the area beneath the blood-coagulation curve bounded by the maximal amplitude $a_m$, was suggested (Fig. 1). However, the conclusion that these two parameters are adequate for digital recording cannot be accepted for the following reasons. First, omission of the parameter r from the number of those recorded leads to loss of the velocity characteristic of the comparatively fast phase of the BC process (prothrombin → thrombin). Second, on changing from an instrument with graphic recording to a digital instrument the question of reproducibility of the BC curve from the digital results must be taken into account. This is because of the need to compare and standardize the results obtained by the different instruments and also the possibility of preserving as much as possible of the clinical data already obtained for the further study of the BCS. Difficulties facing medical staff in the perception of digital information must also be mentioned, at least in the early stages of the use of the digital thromboelastometer.

The method of decoding the coagulogram, like the thromboelastogram reflecting BC as a function of time, has been suggested as a characteristic of the BCS in [3], but the coagulogram was obtained by means of a detector constructed on a different physical basis. The parameters of the coagulogram recommended, as can easily be seen, are the geometric analogs of the parameters adopted in thromboelastography and, for that reason, they add nothing new to the examination of the problem examined in this paper.

Reproducibility of the picture of BC and, consequently, the fullest information can be obtained from a table compiled from values (numbers) characterizing the amplitude of BC after equal (or changing in accordance with a certain law) time intervals. A large number of memory and indication (or recording) elements is necessary for its construction. Such a cumbersome table is difficult to take in and requires further processing, like the thromboelastogram, although unlike the latter it is free from subjective errors. Consequently, the information obtained from the output of the "BC amplitude - numerical-pulse code" must be subjected to processing in the digital instrument in order to reduce the number of outputs of the instrument.

In order to obtain an integral of the highly informative parameters, enabling the BC curve to be reproduced from a minimal number of them with sufficient accuracy for practical use, methods of investigation of mathematical functions must be used and they must be chosen from the list of characteristic parameters of BC as a function of time. Characteristic points on the BC curve (Fig. 1) are O and A - points denoting the beginning and end of the latent reaction; B - the point at which the process reaches a maximum;...
C - the point of the maximum of the first derivative of the BC function; D and E - extreme points of the second derivative. The available range of modern technical devices includes instruments for the digital processing of information by means of which the coordinates of the above-mentioned points and the angular characteristics of the BC curve at these points can be obtained. However, digital differentiating instruments for calculating angular and linear coordinates of the points D and E are very complicated. When a digital instrument is constructed, in the writer's opinion, it is sufficient to confine attention to parameters characterizing the BC curve at points O, A, B, and C, if it is remembered when so doing that the BC curve is always convex downward in the region of point D and convex upward in the region of point E. The physical and biological significance of these parameters is as follows. The segment OA characterizes the time of the latent coagulation reaction \( r \); the point B characterizes the ordinate \( a_m \), of the BC process. At point C the coagulation process has its highest velocity \( V_m \), the value of which is determined by the angle \( \alpha \) of inclination of the tangent to the curve at that point. Since two systems of factors participate in the process under examination - clotting and anticoagulation - and the BC curve is the resultant of their interaction under the conditions of the experiment, it is evident that at the point of inflection C the intensities of the biochemical reactions due to the factors of these systems become equal. In some papers [3] this moment is described as the end of clot formation. Growth of the function beyond the point C indicates continued action of the clotting factor; for that reason the interpretation of the point of inflection as the moment of final formation of the clot is incorrect [5].

By comparing these parameters with those suggested by Hartert [3, 5] both complexes are found to be similar in composition, but differences are found in the nature of the velocity parameters \( k \) and \( V_m \). The inadequacy of the results based on the parameter \( k \), confirmed by many investigations, occurred because the identical value of the amplitude, namely the mean of those measured at the point of inflection of the BC curve of a clinically healthy subject, was adopted for all cases but is not characteristic of possible pathological states of the BCS, and in certain cases of hypocoagulation it cannot be measured. (However, this drawback is not a result of the fact that "...constant values cannot be compared with variable..." [5], for the method of measuring the time of reaching a constant, preassigned value of a parameter that varies with time does not infringe the laws of metrology.)

The combination of recommended parameters \( r, a_m, \) and \( V_m \) does not contradict the integral assessment \( S \) that has already been used and does not rule out the possibility of its use in the future. Addition of the parameter \( S \) to this combination in order to broaden the informativeness of the thromboelastographic method, taking into account the usefulness of the integral assessment demonstrated earlier [2], requires a more detailed examination of the accuracy of its calculation.

Analysis of a series of thromboelastograms shows that the time taken for the BC process to reach its maximum differs from one measurement to another, and in some cases it differs considerably from the mean value chosen by some workers [2] as the integration time. During integration, a component of error \( \Delta S \), depending on the difference \( \Delta t \) between the actual time \( t_m \) taken to reach the maximal ordinate and the integration time \( t_i \), arises during integration in the digital thromboelastometer: \( t_i = t_m + \Delta t \). Since in the region of the point B, i.e., over an interval 2\( \Delta t \), the values of the function are close to \( a_m \), it can be taken that \( \Delta S = \pm \Delta t \cdot a_m \). The actual value of the integral assessment based on the results of analysis of thromboelastograms is given by \( S = (0.55-0.7) \cdot t_m \cdot a_m \).

Hence, the relative error \( \delta S \) of calculation, which depends on the relative error of assignment of the integration time \( \delta t \), is given by

\[
\delta S = \frac{\Delta S}{S} = \frac{\pm \Delta t \cdot a_m}{(0.55-0.7) \cdot t_m \cdot a_m} = \pm (1.8-1.4) \delta t.
\]

This technical error cannot be excluded, but it can be considerably reduced. If a device disconnecting the integrator when the amplitude \( a_m \) is reached is introduced into the circuit of the digital thromboelastometer, the error \( \delta S \) will be reduced to a value determined by the degree of quantization of the amplitude and by the time interval between adjacent measurements, so that the diagnostic value of the parameter \( S \) is increased.

To construct a digital thromboelastometer it is accordingly suggested that the following four parameters, taken together, constitute a sufficient basis: \( r, a_m, V_m, S \). However, it must be borne in mind that not all of them can be expressed unambiguously. At the points B and C the function of BC is characterized by both amplitudinal and temporal indices, and at the point C, by the angle \( \alpha \) also. Consequently, the fullest assessment of the state of BC is given by the following indices measured experimentally and inscribed on the diagram: \( t_r \) the latent response time; \( a_m \) the maximal ordinate; \( t_m \) the time taken to reach \( a_m \); \( \alpha \) a