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IMPORTANCE OF FORCED EXPIRATORY CURVE DEVIATION FROM THE EXPONENTIAL TYPE

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KEY WORDS: forced expiration curves; obstruction of the respiratory passages; restriction of the lungs; small respiratory passages; large respiratory passages; time constant.

The forced expiration (FE) curve for the healthy subject is close to the exponential type. It is suggested in this paper that deviation of the FE curve from exponential be used to determine the time course of changes in patency of the respiratory passages during FE, to determine whether an obstruction is in the small or the large respiratory passages, and to establish the site of action of broncholytic agents.

Preliminary communications on the suggested method were published previously in thesis form [4, 5].

EXPERIMENTAL METHOD

The original source of information on the state of the human bronchopulmonary system is the ordinary FE spirogram. For healthy subjects, as was shown previously [3, 4], the FE curve represents volume as an exponential function of time. The volume V_t which the subject can still breathe out at time t depends on time in the following manner: $V_t = V_0 e^{-t/\tau}$, where V_0 is the initial volume, namely the forced vital capacity (FVC), e is the base of natural logarithms, and τ the time constant, characterizing the velocity of the exponential process. It can be considered that τ is the product of the resistance of the respiratory passages and the compliance of the lungs, at least for healthy persons [3-6]. However, during FE the conditions under which this is applicable are disturbed, i.e., the flow in many parts of the tracheobronchial tree becomes turbulent, and FE itself cannot be considered to be free emptying of the lungs. That is why τ is not the product of compliance of the lungs and resistance of the respiratory passages [7], although for healthy persons it is perhaps close to it in magnitude and essence [6]. Nevertheless, because FE is exponential in character, τ can be considered to characterize the ability of the lungs to empty quickly. The higher its value, the greater the obstructive changes in the respiratory passages.

In the present investigation informative changes in the FE curve were sought in its deviation from an exponential curve. In the course of FE the time course of the parameter τ was monitored, by splitting up the FE curve into separate segments (Fig. 1), where it was approximated by the corresponding exponential functon, similar to that given above. For the i-th segment, for instance, this relationship assumed the following form:

$$V_{t_i} = V_{t_{i-1}} e^{-\Delta t_i/\tau_i},\ \Delta t_i = t_i - t_{i-1},\ i = 1, \ldots, m.$$

Hence: $\tau_i = \Delta t_i / (\ln Vt_{i-1} - \ln Vt_i)$.

Here V_t is the volume to be expired at time t_i, Δt_i is the time interval defining the i-th segment of the subdivided curve, τ_i the time constant characterizing the velocity of the exponential process in the i-th segment, and m the number of segments of the subdivided curve. Dependence of τ on volume in the course of FE was determined and plotted graphically by computer, using the equations given above. The corresponding program was effected at the Information-Computer Center of the Fourth Main Board, Ministry of Health of the RSFSR, and also at

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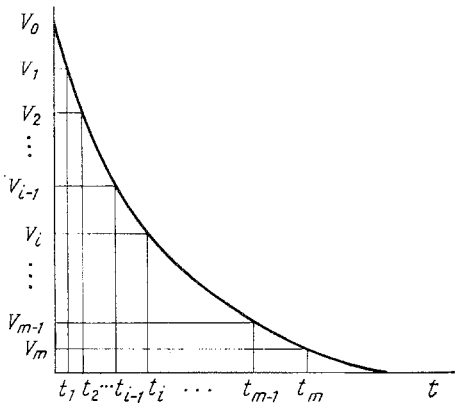

Fig. 1. Pointwise subdivision of forced expiratory spirogram into m segments to determine the value of τ for each of them.

the Moscow Tuberculosis Research Institute on the "Élektronika DZ-28" microcomputer. The FE curve was subdivided manually in a relatively arbitrary fashion into 10 segments. This number of subdivision segments gives sufficiently complete information on the time course of τ. Although increasing the number of segments of subdivision would give the dependence of τ on volume rather more accurately, it would increase the manual part of analysis of the curve. If it is possible to lead the FE curve directly into the computer, this subdivision of the curve, as well as subsequent calculations and plotting of the graph, may be done by computer.

The reproducibility of the method differs in different segments of the curve. If an FE curve of good quality is obtained it is under 10% over the whole range of volumes except the initial part, where it is about 1/5 of FVC, depending on the patient's effort, and it is therefore of no diagnostic value, and the final part of the curve, where it is about 1/4 of FVC, and is of great interest in the diagnosis of the state of the small respiratory passages [3, 8, 9], where reproducibility is about 20% of the measured value.

EXPERIMENTAL RESULTS

Practically identical values of τ were obtained throughout FE in normal subjects (15 persons), as reported previously [4, 5]. The norm for the parameter τ is considered to be 0.5 sec [3] and 0.6 sec [2]. The authors cited determined τ in this case for the whole FE curve. Values of τ obtained for clinically healthy subjects by this method were always under 0.5 sec in the first part of the FE curve, and in some of them the value of this parameter increased from 0.5 to 1 sec toward the end of expiration. This last fact was associated with the great sensitivity of the method for the detection of early pathology of the small respiratory passages. In patients with bronchopulmonary pathology an increase in the parameter τ was observed in the course of FE; in the region of the small respiratory passages in some patients it reached 5-7 sec. The increase in τ was connected with an increase in resistance of the respiratory passages in the course of FE [4, 5]. Graphs for a healthy individual [3], for an apparently healthy individual found to have pathology of the small respiratory passages [2], and for patients with known bronchopulmonary pathology [1, 4] are given in Fig. 2.

The following series of experiments was then carried out. Healthy subjects (five persons) and patients with bronchopulmonary pathology (seven persons) performed FE with different levels of air-filling of the lungs. Expiration in healthy subjects was characterized as before by an exponential dependence of volume on time and had the same values of τ. The character of the curves for the patients remained similar in shape; values of τ also were unchanged within limits of reproducibility for the same relative volumes, expressed as percentages of FVC. Hence the opposite conclusion was drawn: If in the course of treatment the value of FVC increased but the values of τ remained the same for the same volumes, expressed as percentages of FVC, this is evidence of a decrease in restriction accompanied by preservation of the same obstructive changes. If the values of τ decrease or increase, obstruction is reduced or increased. The method can thus differentiate clearly between obstructive and restrictive changes in the lungs.

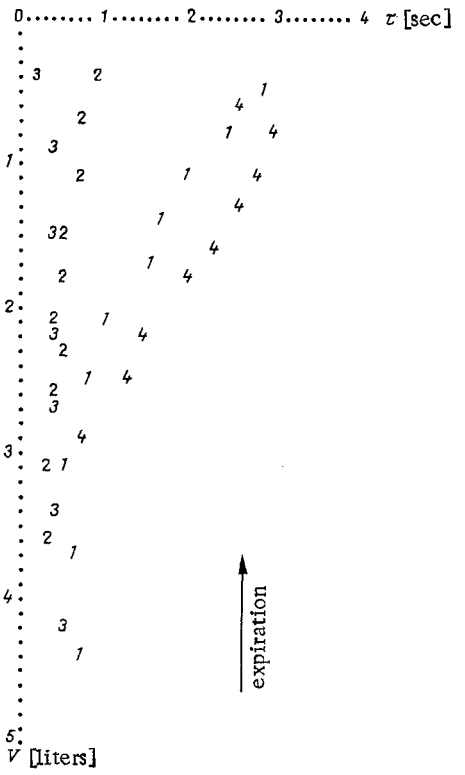

Fig. 2. Graphs showing changes in parameter τ during FE, plotted by computer. 1, 4) Patients with bronchopulmonary pathology; 2, 3) healthy subjects.

It is considered that the large respiratory passages, if the seat of pathology, make a contribution to the course of the middle part of the FE curve, whereas the small respiratory passages make their contribution to its last part [3, 8, 9]. Allowing for this, the graph thus obtained showing changes in τ in the course of FE can reveal pathology of both the small and the large respiratory passages.

When the effect of a broncholytic agent is being evaluated, the site of its action can also be estimated. If an improvement (a decrease in τ) takes place in the middle part of FE, this indicates an improvement of patency of the large respiratory passages, over 2 mm in diameter. If improvement is observed in the last third of FE, patency of the small respiratory passages under 2 mm in diameter is improved. By the use of a similar method, side effects of a preparation chosen for treatment or inhalation can be detected.

Recording FE from flow–volume coordinates is widely used nowadays as a method of investigating respiration [1, 2]. Although it has many advantages, this method also has disadvantages and, in particular, variability of the readings obtained for the same subject. Even the ratio between values obtained for $\dot{V}_{75}$, $\dot{V}_{50}$, and $\dot{V}_{25}$ (FE rates at volumes of 75, 50, and 25% of FVC respectively) to FVC do not completely eliminate this variability. It arises because the values of $\dot{V}_{75}$, $\dot{V}_{50}$, and $\dot{V}_{25}$ depend on high quality of recording the first part of FE, which depends on the effort exerted [2, 3], whereas this segment is also included in the value of FVC by which the flows are divided. The most stable part of the flow–volume curve is the slope of the curve after the maximal rate of expiration, and its changes in the last part of expiration. This part of the curve is essentially close to the τ-curve obtained by the suggested method, for slope is the reciprocal of τ. Besides greater stability of its results, the suggested method also has greater sensitivity to obstructive changes, especially in the small respiratory passages.

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ACCUMULATION OF GASEOUS LIPID PEROXIDATION PRODUCTS IN THE EXPIRED AIR IN CHILDREN DURING HYPERBARIC OXYGENATION

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Hyperbaric oxygenation (HBO) has recently found successful application in clinical practice [2, 3, 5]. However, the widespread use of this method is prevented by the possibility of development of toxic effects of oxygen, which are based on damage to membranous structures of the cells of different tissues [1, 4, 6]. The key mechanism of this harmful action of HBO is activation of endogenous lipid peroxidation (LPO) [6]. Consequently, a problem of practical importance is the development and use of quantitative methods of estimating concentrations of LPO products in the human body. The most promising method in this respect is that of recording gaseous products of endogeneous LPO in the expired air, for their content, as experiments on animals have shown [8], adequately reflects the intensity of LPO in the body. The method consists essentially of recording volatile hydrocarbons (methane, ethylene, ethane, propane, pentane, etc.) that are formed in vivo during LPO as a result of successive decomposition of lipid hydroperoxides [7, 10]. An important advantage of this method compared with all other methods of analysis of LPO products is that it requires no intervention on the subject or procedures of isolation of cellular or lipid fractions, which are inevitably associated with the appearance of artefacts.

The aim of the investigation described below was to study the possibility, in principle, of using a noninvasive method of recording gaseous products of endogenous LPO in man during HBO.

EXPERIMENTAL METHOD

Concentrations of gaseous LPO products in the expired air were determined immediately before HBO and also at different times (10 min, 1 and 2 h) after sessions of HBO conducted on seven children aged from 5 to 14 years with tumors in various situatons. HBO was carried out in a type OKA-MT single-person therapeutic pressure chamber in pure oxygen at 1 atm. The saturation time was 60 min. Quantitative analysis of hydrocarbons in the expired air was based on the assumption that the chief substrates of LPO are ω-6-polyunsaturated fatty-acid residues of phospholipids and, correspondingly, that the principal gaseous product of LPO quantitatively is pentane [9]. Accordingly, to ensure maximal sensitivity of the method the pentane concentration in the expired air was determined. The expired air was collected in polyethylene bags with a capacity of 2 liters, previously ventilated with pure nitrogen. Or-

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