PREDICTION OF CRITICAL TIME IN ANOXIC MYCARDIUM OR BRAIN BY AUTOMATICALLY EVALUATED OXYGEN CHRONOPOTENTIOMETRY

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ABSTRACT:

A technique has been developed to make estimates of the safe duration of anoxic heart arrest during open heart surgery. It can be applied for monitoring of critical states in other organs. Its principle is the determination of tissue resistance and the polarization of a platinum electrode, using current chronopotentiometry,automatic evaluation of the critical time for the duration of hypoxia or anoxia. The chronopotentiometry of oxygen and hydrogen ions using a blank platinum semi-microelectrode and controlled current offers some advantages over classical controlled voltage polarography. In open heart surgery the method has enabled us to achieve complete resuscitation and recovery in 90% of experimental animals if the critical time was not surpassed. Each time the anoxic period was longer than the critical time, resuscitation was not possible. The evaluation of critical time is done by computational methods. Possibilities of automatic evaluation by purpose-built hardware are envisaged.

INTRODUCTION:

The use of electrodes in studies of tissue metabolism is a well-established procedure in many experimental situations. In clinical applications their use has been limited mainly to biological fluids whereas the use of electrodes in tissue leaves still very much methodological improvement to be done. The reasons for this are twofold: 1) The theory of electrode processes in tissue is not yet sufficiently developed. In blood or serum we may reasonably assume certain well-defined physical-chemical conditions but the same cannot be said for tissue. 2) We do not quite know how far we have to go in interpreting a pathological state of an organism, organ or tissue. Is it desirable to trace the eventual irreversible damage of the heart or brain to changes in cell boundaries, sodium-potassium ion equilibrium, protein hydration, extracellular pH, oxido-reduction potential, oxygen availability, oxidative phosphorylation, disturbances in hydrogen bonds or electron transport? All these apparently influence the electrode processes in tissue; they are all more or less implicated in a case of hypoxic tissue damage. They all should be prevented or treated in case of severe stress to the heart or brain during surgery. The surgeon needs an efficient monitoring procedure that will react, if possible, to all the above aspects of hypoxic tissue damage. In terms of present concepts, the requirements would be for the monitoring in tissue of available oxygen, hydrogen ions, oxido-reduction potential, extracellular and intracellular ion and water distribution, conductivity, or semi-conductive properties, etc. Provided all these phenomena would be monitored we would be able to predict the extent of irreversible damage introduced e.g. during cardiac arrest. Since some of these methods do not detect any significant changes while others do, we may attribute more prognostic significance to the positive results and discard the negative ones. With these requirements in mind we have developed a new approach to tissue electrochemistry; its aim is to detect the earliest possible changes in the state of the tissue by a complex of methods using polarographic reactions.

METHOD:

We are measuring essentially processes on a polarized platinum electrode occurring during equilibrium, a positive and a negative polarization as well as the potential drop in the vicinity of the electrode. We measure the transient voltage response using currents of 1 microamp., both positive and negative with respect to the reference. The polarization is of sufficient duration to allow not only the transient response to be observed but also a reasonable estimation of the steady state value. The voltage course is measured with a voltmeter having a high input impedance and the output is recorded. The probe consists of two electrodes, one being a polarizable platinum-iridium electrode of 2.83 mm^2 polarization area, the other a stainless-steel auxiliary point-electrode in 1 mm distance from the polarized one. Two voltage curves are recorded: the polarization curve of the Pt-electrode at equilibrium, positive and negative polarization respectively (chronopotentiogram); and the voltage on the auxiliary electrode - the latter being measured with the help of an A/C-coupled preamplifier with an input impedance of 100 megohm/30 picofarad. As a reference electrode for polarization measurements we use a saturated calomel electrode; another stainless-steel electrode is used for impedance measurements. The theory of chronopotentiometry in biological applications was published by MILGRAM (1970). For practical prognostic purposes we use the following working hypothesis: the Pt-electrode is polarized both by a positive and negative pulse in sequence. The current has to be kept very low for physiological reasons and, therefore, the electroreduction voltage for oxygen (-0.8 volt) is not always reached. However, the duration of the rise of the transient (transition time) is

related to the amount of depolarizers in the vicinity of the electrode and so is the value of polarization resistance attained during the passage of current. The depolarization of the electrode will depend mainly on diffusion and will be determined by mechanical factors and by the diffusion coefficient of the tissue. Evaluation should be made of the following values: the equilibrium potential, the time and amplitude characteristics of both the polarization and depolarization curves; and the tissue impedance.

EVALUATION OF EXPERIMENTAL RESULTS:

From "eye-ball" evaluations of experimental results we know that rather sudden changes occuring in curves during anoxia are manifested in several points of a curve, e.g. elevation of the negative equilibrium potential higher rising rate of the up-slope (polarization); lower rate of the down-slope (depolarization) together with a wider angle at the start of the down-slope. The tissue impedance during anoxia increases. A computer program (for an IBM 1800 computer) was written to analyse these values together with the integral of the curve from its start over a time period of about 15 seconds. At present the curves are digitized by a suitable device from strip-chart recordings; in further experiments automatic on-line conversion will be used. Several outstanding points thus obtained during the first period of anoxia are used together with a so far empirically established factor to calculate the critical time for the anoxic heart arrest. Further relationships which could possibly influence the factors involved are being studied. So far values obtained by calculating the area under the curve together with the angle of the down-slope seem to be the most promising as they are least influenced by the over-all shape of the curve which varies depending on the current density, electrode site and other factors. After the first estimate a more precise value for the predicted critical time can be obtained by evaluating the rate of change of relevant values in consecutive curves.

RESULTS:

The experimental results obtained in 33 dogs enabled us to use the method clinically and measurements done in 15 patients undergoing cardiac surgery have proven the usefulness of the method in the determination of a safe period for anoxic heart arrest. Only the equilibrium potential and cathodic polarization were evaluated in these experiments. After clamping the aorta, the equilibrium potential shifts to more negative values; the rise-time of the polarization curve shortens so that higher values of polarization resistance are attained; the depolarization slows down. The velocity of development of these changes differs according to clinical or physiological conditions. With higher velocity the estimated critical time for safe heart arrest becomes shorter. The detailed experimental and clinical results will be presented elsewhere (KRAJICEK, KRYSPIN, METHNI, TRIMBLE 1970).

DISCUSSION:

There are two conditions that should be met during polarographic measurements; unfortunately this cannot be done for uncovered electrodes in tissues: the polarographic current is not determined by diffusion only and the effects of convection (particularly due to mechanical movement of tissue) cannot be excluded (CLARK AND SACHS 1969). For these reasons the theory of electrode processes in tissues is rather involved. Presently we are developing a semi-empirical theoretical description of tissue electrode processes. We feel that the advantages of direct measurements in tissues justify the semi-empirical approach, particularly in monitoring tissue changes in hypoxia. We hope that based on the evaluations obtained by computer it will be finally possible to design a single-purpose device for the automatic prediction of the critical time for anoxic tissues during surgery.

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