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THE USE OF VENOUS ALLOGRAFTS IN VASCULAR SURGERY

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The availability of adequate vascular prostheses remains an urgent problem in emergency reconstructive vascular surgery. The main reason is that the severity of the patient's state in an emergency situation calls for the shortest possible duration of surgical intervention. Synthetic prostheses can be used successfully to repair the aorta or arteries of large diameter [2, 10], whereas reconstruction of arteries of average and small caliber can best be achieved by replacement with an autologous vein [4, 8]. However, in 15-30% of cases it has a dispersed type of structure, a small diameter, or changes resulting from previous thrombophlebitis, and it is therefore unsuitable for use as a prosthesis [5, 9, 11].

The use of venous allografts is therefore interesting for such purposes. By now, the use of "fresh" allografts has achieved popularity, when used within 1-2 h after preparation [1, 7].

The aim of this investigation was to develop a simpler method of conserving venous allografts based on a study of changes in their biomechanical properties, morphology, and tissue metabolism.

EXPERIMENTAL METHOD

A 2% solution of neutral formalin and an isotonic buffered salt solution (Hanks' solution) were used for conservation.

Venous grafts were taken from 54 patients undergoing operations for varicose veins of the lower limbs without any trophic disturbances. The patients' ages were from 23 to 60 years and the duration of the disease from 1 to 20 years. After removal, the samples of the grafts were kept in the above-mentioned solutions at 4°C and their biomechanical, biochemical, and morphological properties were studied on the 1st, 2nd, 3rd, 4th, 5th, 6th, and 7th days of conservation.

Changes in the mechanical properties of the grafts were studied by the method of uniaxial stretching of flat specimens. Specimens measuring 20 × 5 mm were prepared in the longitudinal direction and their properties tested on the "Instron-1122" universal testing machine. Tests were carried out on 187 specimens.

The following characteristics of the material were determined:

a) the tensile strength σ = p/f mPa, where p denotes the load required for complete rupture of the test specimen, and f the area of cross section of the specimen;

b) the deformation $\varepsilon = (l - l_0)/l_0$, where l and l_0 denote initial and deformed length of the specimen;

c) the tangential modulus of elasticity (E, in mPa) was determined as the tangent of the angle of slope to the abscissa, the tangent and the deformation curve, and calculated for several values of stretching tensions.

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To assess changes in tissue metabolism of the venous grafts in the course of conservation, an "Impact-400" automatic biochemical analyzer ("Ciba-Corning," England) and radioimmunoassay kits from "Amersham," England) were used. Activity of some cytoplasmic enzymes, namely lactate dehydrogenase (LDH), hydroxybutyrate dehydrogenase (HBD), and creatine phosphokinase (CPK), the principal substrates of carbohydrate metabolism (glucose, lactate), and a universal intracellular mediator, 3,5-cyclic nucleotide (cAMP) were studied in homogenates of the vessel wall. All these parameters were determined in parallel tests and in appropriate conserving medium.

Morphological changes in the venous grafts were studied by electron microscopy in 33 preparations.

EXPERIMENTAL RESULTS

Studies of biomechanics showed that during conservation of varicose veins their tensile strength increased: in Hanks' solution from 1.750 ± 0.048 mPa on the 1st day to 2.051 ± 0.042 mPa on the 7th day ($p < 0.05$), in formaldehyde from 1.813 ± 0.075 to 2.492 ± 0.134 mPa ($p < 0.05$). Deformation of the veins after conservation in Hanks' solution showed virtually no change: 0.953 ± 0.017 on the 1st day and 1.011 ± 0.019 on the 7th day ($p < 0.05$), whereas in formaldehyde solution the deforming properties decreased from 0.932 ± 0.011 to 0.820 ± 0.028 ($p < 0.05$).

The dynamics of the change in rigidity of the specimens of the veins was studied as a change in the tangential modulus of elasticity at various values of tension. Comparison of these values with minimal and maximal loads on the 1st and on the 7th days showed an increase in rigidity of the specimens of varicose veins: in Hanks' solution at $p = 0.05$ kg by 34% ($p < 0.01$) and at $p = 9$ kg by 15% ($p < 0.01$), but in formaldehyde by 76% ($p < 0.01$) and 50% ($p < 0.01$) respectively.

Comparison of the time course of the biochemical parameters determined in varicose veins in Hanks' medium and in 2% formalin solution showed higher activity of the cytoplasmic enzymes (LDH, HBD, CPK) in veins preserved in Hanks' solution at all stages of the investigation.

Incidentally, when conservation in formaldehyde was used, escape of the enzymes from the tissue into the conservation medium was substantially less than with conservation in Hanks' medium (by 5-10 times on average), evidently due to the tanning properties of the formalin, which are exhibited in particular during long-term conservation.

Considering that the cAMP concentration in the cell is linked through an equilibrium reaction with ATP, and since the ATP level in the cell is more than 50 times greater than the AMP concentration, even a small decrease in ATP will cause a considerable increase in cAMP [3]. The fact that significantly higher cAMP concentrations (by five times on the 1st day and by 60 times on the 7th day) are found in tissues conserved in formalin than in a vein preserved in Hanks' medium is indirect evidence of the great loss of ATP-basic substrate, which performs the role of universal method of energy transmission in the living system. In other words, preserving the venous graft in formaldehyde leads to a more marked disturbance of energy metabolism in tissues of the venous wall.

Comparing the data for levels of glucose and lactate and LDH activity in the veins tested, it must be emphasized that no significant changes in this set of parameters characterizing carbohydrate metabolism were observed in grafts preserved in Hanks' medium for up to 7 days. In homogenates of veins conserved in formaldehyde, after only 2 days the glucose concentration was reduced by more than half ($p < 0.01$), with a simultaneous 10.3-fold increase in the lactate concentration ($p < 0.01$). Under these circumstances the effectiveness of LDH was reduced by 1.5 times ($p < 0.01$). The changes discovered are evidence of enhancement of anaerobic glycolysis with an increase in the degree of cellular acidosis, leading ultimately to a disturbance of the functional systems of the cell that are structurally interconnected.

During the study of the morphology of the venous grafts it was noted that in the 1st day the structure of the cells and of the intercellular matrix was maintained whether they were conserved in Hanks' medium or in formaldehyde. After 2 days of keeping in the preservatives, fragmentation of the structures of the intercellular matrix began to take place, with the appearance of foci of translucency. If the grafts were kept in formaldehyde, besides changes observed in the intercellular substance, signs of injury to smooth-muscle cells were found during this period. The initial changes in cellular structures and in the intercellular matrix in tissues preserved in both media correlate with features of reversible tissue damage. Long-term keeping in formaldehyde leads to changes in the cell nucleus: fragmentation and vesiculation of the cytoplasm of the smooth-muscle cells were more marked than in veins kept in Hanks' medium.

These biomechanical, biochemical, and morphological studies of varicose veins showed that if they are preserved in Hanks' solution, activity of the enzymes maintaining the basic processes of energy formation in the cell is preserved, evidence that the tissue of the vessel remains viable. In the case of conservation in formaldehyde, enzyme activity lasts only 2 days. Later, destruction of the tissue structures takes place, leading to a stable decrease in enzyme activity, an increase in acidosis and, as a result, loss of viability of the tissues. The mechanical properties of the veins, however, remain at quite a high level.

It can thus be concluded on the basis of the above facts that in the absence of autologous venous material for prosthetic operations on the main lower limb arteries, venous allografts conserved in Hanks' solution and in a 2 solution of neutral formalin can be used. In this case the optimal keeping time is 1 day. Grafts conserved in Hanks' solution also remain viable, as shown by their biomechanical, biomorphological, and biochemical parameters, for up to 7 days whereas conservation in a 2% solution of neutral formalin permits their use for not longer than 2 days.

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CHANGES IN THE SYMPATHOADRENAL SYSTEM DURING STRESS IN RATS WITH HIGH AND LOW RESISTANCE TO ACUTE HYPOXIA

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A leading role in the development of stress, which has many pathogenetic links in common with hypoxia [3], is played by changes in activity of the sympathoadrenal system (SAS) [4], and the possibility therefore cannot be ruled out that the initial level of activity of SAS, which may perhaps be genetically determined, can influence the resistance of animals to hypoxia, and also determine differences in their response to stress. Consequently, in animals differing in their sensitivity to acute hypoxia (AH) differences may be observed in the time course of changes in the sympathetic and adrenal components of the SAS during stress. Meanwhile no morphological investigations of SAS during stress in animals differing in their resistance to AH have been undertaken.

The aim of this investigation was to study the SAS of adult rats with low (LRH) and high (HRH) resistance to AH associated with catecholamine-induced stress.

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