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Construction and Validation of a Microprocessor Controlled Extracorporal Circuit in Rats for the Optimization of Isolated Limb Perfusion

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Abstract:

Although a few experimental approaches to isolated limb perfusion (ILP) are described in the literature, none of these animal models mimics the clinical perfusion techniques adequately to improve the technique of ILP on the basis of valid preclinical date. Therefore, we developed an ILP setup in rats allowing online monitoring of essential perfusion parameters such as temperature (in perfusate, various tissues, and rectum), pH (perfusate), perfusion pressure, and O_2 concentration (in perfusate, tissue), by a tailor-made data acquisition system. This setup permits close supervision of vital parameters during ILP. Various interdependencies, concerning the flow rate and the pressure of perfusate as well as tissue oxygenation were registered. For the measurement of PO_2 values in the perfusate and in different regions of the perfused hind limb, a novel type of microoptode based on quenching of a fluorescent dye was devised. Stable normothermic (37°C) perfusion conditions were maintained at a constant perfusion pressure in the range of 40-60 mm Hg by administration of the spasmolytic moxaverine (0.5mg/mL of perfusate as initial dose) at a perfusate flow rate of 0.5 mL/min for 60 min. At the end of an ILP, there were no signs of tissue damage, neither concerning laboratory data (K^+, myoglobin, creatine kinase, lactic dehydrogenase) nor histopathological criteria. The reported ILP model is not only well suited to investigate the effects of hyperthermia but also to assess the efficacy of new antineoplastic approaches, when nude rats, bearing human tumours in the hind limbs, are used.

Key-words: Limb perfusion, rat, online monitoring, oxygen-microoptodes, perfusion pressure