ABSTRACT OF PhD DISSERTATION

Microdialysis for the investigation of gentamicin in bone tissue

An experimental study

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ABSTRACT

Pharmacokinetic investigations of antibiotics in peripheral tissue are important for appropriate and effective treatment of infections and for prophylactic use. Bone tissue is difficult to harvest, handle and analyse. The aim of this PhD dissertation was to apply microdialysis to bone tissue for the investigation of gentamicin in bone tissue.

Microdialysis probes consist of thin semi-permeable membranes. They can be inserted into nearly any tissue and dialysates are harvested. The advantages of microdialysis are, 1) it can easily be applied to any tissue inducing only a minor trauma, 2) it allows continuous measurements of the free, unbound and active part of a drug. First an in vitro study was performed to investigate different calibration techniques for the microdialysis. Then in two in vivo studies we evaluated the technique of microdialysis for the investigation of gentamicin in cortical and cancellous bone tissue and compared it to values obtained from bone specimens. When we compared the pharmacokinetic parameters, no differences were found between microdialysates and bone specimens in both studies. Reproducibility of the measurements from the microdialysates was evaluated from the ratio of the two microdialysis catheters implanted into the same bone. The mean value was 1.12 in the cortical bone study and 1.02 in the cancellous bone study. In a third in vivo study nine animals were randomized to either wet or dry application of a Gentacoll sponge to bone. Two catheters were inserted one and two centimetres apart from the implant. The results showed that neither way of application nor distance of the catheter to the sponge had significant impact on the pharmacokinetics of Gentacoll in bone tissue.

The results showed that microdialysis is a suitable, relatively non-invasive and reproducible technique for dynamic and quantitative measurements of gentamicin in bone tissue, either applied intravenously or as local implant.