

## Implementation of intracerebral microdialysis in NEURO INTENSIVE CARE

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### Introduction

We have tested a system for microdialysis monitoring of the brain for two years in the Dept of Neurosurgery in Lund consisting of a flexible microdialysis catheter, a microdialysis pump and a bedside chemical analyser. The system has subsequently been introduced for various purposes in all six Neurosurgery clinics in Sweden.

The inclusion criteria for microdialysis monitoring in Lund is severe brain trauma or subarachnoid hemorrhage. We usually implant three microdialysis catheters in a trauma patient: 1) One catheter is placed in

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the cortex in front of the ICP measuring catheter through a separate burr hole. 2) Another catheter is placed in the penumbra of the contusion or bleeding. The position is decided from inspection of the CT and the brain during surgery. 3) A third, reference catheter, is placed subcutaneously in the abdomen. The idea is to capture the metabolism in the "best" and the "worst" parts of the parenchyma as well as obtaining a systemic reference value from the subcutaneous catheter.

The catheters are perfused by battery driven microdialysis pumps (CMA106) using disposable precision syringes. The flow

rate of the Ringer solution is low (0.3 µl/min) in order to reach high concentrations of analytes in the dialysate. The 10 mm dialysis membrane of the CMA70 brain catheter gives approximately 80% of the concentration in the extracellular fluid. The 30 mm dialysis membrane of the CMA60 subcutaneous catheter makes it possible to reach close to 100% recovery. The dialysate is collected in microvials designed for low evaporation and minute volumes. The samples are analysed in the bedside CMA600 Microdialysis analyser every hour.

### Chemical Analysis

We are monitoring glucose, lactate, pyruvate, glutamate and glycerol:

**Glucose** is the energy source of the brain. The level of glucose is essential and hypoglycemia, as well as hyperglycemia is considered harmful to the brain after trauma.

**Lactate** and the **lactate/pyruvate ratio** relate to the extent of glycolysis and anaerobic metabolism. A high level of lactate can be due to hypoxia or ischemia but also to increased glycolysis. By looking at the lactate/pyruvate ratio it is possible to distinguish between these conditions. Pyruvate production falls during ischemia, which causes a decrease in the lactate/pyruvate ratio.

Increased release of the excitotoxic amino acid **glutamate** is considered to be an important cause of brain damage after ischemia. Several drugs blocking glutamate receptors or decreasing glutamate release are now in clinical trials for the treatment of stroke and trauma.

**Glycerol** has emerged as an interesting compound signaling cellular damage. Glycerol is an integral part of the hydrophilic portion of the bilayer of glycerophosphate and fatty acids which constitute most cell membranes. We have seen massive increases

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in extracellular glycerol during ischemia, hypoxia and infections in human as well as animal brain. It seems conceivable that the influx of calcium, caused by energy failure, activates phospholipids which start the decomposition of cell membranes.

### Participation of nurses

In order to achieve reliable and continuous bedside monitoring in the ICU it is necessary to involve the regular nurses. We have trained a "microdialysis nurse" who is responsible for managing the equipment, storing data for later analysis in various research projects and training two nurses in each "eight hour team".

We have made a point of not changing the normal routines around the patient by avoiding special microdialysis protocols. Instead, the nurses record the information we consider important in their normal protocols. The nurses and the resident anaesthe-

siologist/neurosurgeon follow the intracerebral chemistry on the CMA600 monitor observing absolute levels as well as shifts in chemical trends.

In order for the nursing staff to accept microdialysis the benefit for the patient must

be obvious. It is well understood that the physiological and pharmacological tools we use in the treatment of the patient are aimed at normalising brain chemistry. The fact that the microdialysis analyser displays chemical trends on a bedside monitor makes it easy for

the staff to understand the relationship between microdialysis and the treatment of the patient.

### *Clinical routines*

- 1. The microdialysis nurse on duty in the ICU** is notified when the patient arrives in surgery. The nurse starts up the CMA600 by mixing reagents and starting the calibration. She labels the microvials and places them in vial racks. The racks serve the dual purpose of keeping samples in order and closing them to avoid evaporation during storage.
- 2. In surgery the assistant scrub nurse brings in the tray** with the microdialysis instruments which are stored in the same place as the ICP equipment. The nurse fills the syringes with Perfusion Fluid, puts batteries into the pumps and hands the sterile nurse the catheters, the tunnelator and the special forceps.
- 3. The brain catheters are tunneled under the scalp.** The meninges are opened by a small incision and the catheter is placed obliquely in the cortex. The inlet and outlet tubing are fixed to the scalp by suturing around the cuff which surrounds the tubings. This fixation prevents the displacement of the catheters due to accidental pulling of the tubing during handling of the patient.
- 4. The surgeon holds the female luer connector and docks it with the syringe** held by the assistant scrub nurse. The nurse places the syringe in the CMA106 Microdialysis pump and closes the lid of the pump which starts the flush cycle filling up the tubings and removing all air. The surgeon places the sterile microvial, included with the catheter set, in the vial holder. By removing and examining it he can determine when the system is filled up and functioning.
- 5. Before wrapping the head of the patient** the inlet tubing connected to the pump and the outlet tubing connected to the vialholder are labeled in order to know which pump and vial holder that belongs to a particular catheter. During transportation to the ICU the pumps are usually taped to the chest of the patient.
- 6. At the end of the operation the assistant nurse** makes a brave attempt to catch the surgeon before he leaves the operating room asking him to mark the localisation of the catheters on a drawing of the brain. He is also asked to determine which CT scans that best describe the extent of the lesion so they can be scanned into the computer for permanent storage together with the microdialysis data..
- 7. Once the patient arrives in the ICU the microdialysis nurse** on duty implants the subcutaneous catheter, usually in the periumbilical region of the abdomen. The CMA600 instrument is placed bedside and the sampling starts by changing samples every hour.
- 8. The vial racks are kept in an insulation box** together with a cool clamp. As soon as all 12 vials in a rack are analysed the racks are moved to the freezer and the cool clamp in the insulation box is exchanged for a new one. The samples may be used for later HPLC analysis of amino acids, ions, purines, various neurotransmitters etc.
- 9. The microdialysis catheters are pulled** at the same time as the ICP catheter. The microdialysis data in the CMA600 are copied to a disk and transferred to the computer which is used for storing microdialysis data.

### *A clinical database*

Our patient data are stored in a computer at the Dept of Pharmacology at the Karolinska institute, with the aim of creating a microdialysis database connected to a webserver. The data will be made available

to other users of intracerebral microdialysis over the internet. It is our hope that all clinics using a similar approach to intracerebral microdialysis will contribute patients in order to create a reference database for use in

evaluating various clinical conditions. We are presently examining data from more than 50 patients which will form our initial reference database. According to our plans the database will also be available on CD.

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