Local intratumoral treatment of glioblastoma with retrograde microdialysis of Cisplatin – pilot experiment

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Introduction

One factor limiting chemotherapy of brain tumours is the blood/brain barrier hampering drugs to enter the tumour/brain. Interstitial delivery of drugs may increase the therapeutic efficacy and reduce systemic side effects. In this study we have utilised the technique of microdialysis for delivering Cisplatin to glioblastoma tissue. We also intended to simultaneously monitor the metabolic effect induced by the treatment.

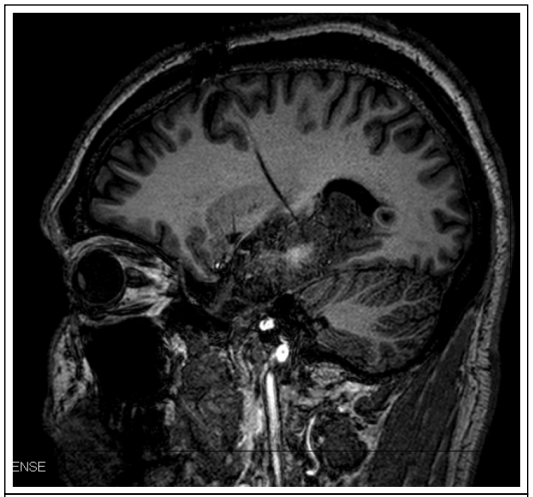
Methods

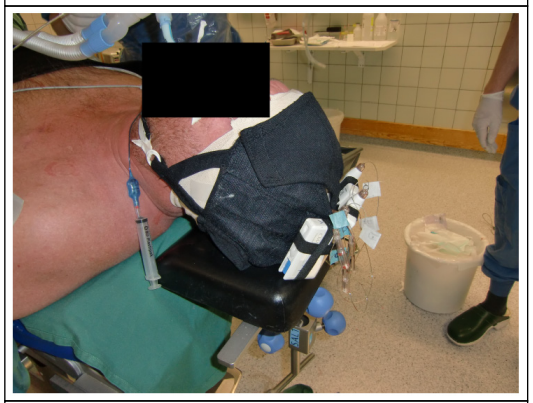
In vitro

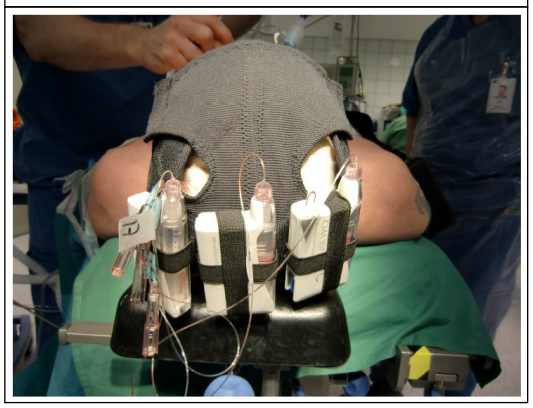
Microdialysis catheters (100 kDa cut-off) were applied within a buffer solution resembling the extra cellular fluid in the brain. The system was thereafter run with a perfusate containing Cisplatin at different concentrations and with different flow-rates. The buffer solution was analysed to evaluate amount of Cisplatin entering it. The results were used for calculating the doses and flow -rates in the clinical situation.

In vivo

Three patients with recurrent gliobastoma not suitable for further conventional treatment participated in the study. Two to three microdialysis catheters were implanted to tumour tissue by stereotactic technique. Our aim was to administer a dose of 1 mg/day Cisplatin for a period of 12 days.







Results

In vitro

Cisplatin can be delivered through the catheters at doses of 0.03 – 3 mg/day. The administrated dose can be controlled using different Cisplatin concentrations and flow-rates.

In vivo

The patients could be mobilised the day after surgery. During the first days of treatment the patients were observed at a high dependency ward. Later they could be transfered to a general neurosurgical ward.

Toxicity in terms of edema was observed within 6–8 days of treatment probably due to mainly ultrafiltration. This effect was reversible by steroid treatment. However, the planned treatment of 12 days could not be archived. No significant regression of tumour mass could be observed radiologically. The treatment did not influence the glucose matabolism, however, in all patients the treatment induced an elevation of glutamate indicating a cytotoxic reaction induced by the treatment.

Conclusions

1 mg/day of Cisplatin can be administered to glioblastoma tissue using retrograde microdialysis. The technique seems feasable and, apart from the edema induced, the patients tolerated the procedure well. The clinical effect of the treatment was difficult to evaluate due to toxicity and few patients. The study will continue using catheters with lower cut-off.

Learning Objectives

By taking part of the study, the reader will learn about the technique of retrograde microdialysis and its use in a pilot study administrating cisplatin to glioblastoma tissue.