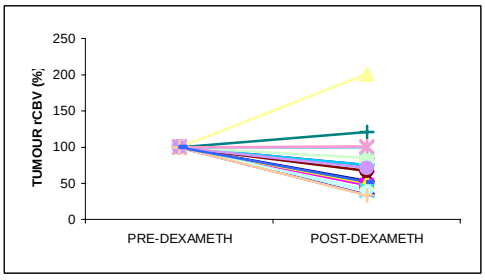
MR perfusion and blood-tumour barrier kinetics: effects of steroid therapy

I. D. Wilkinson[1], D. A. Jellinek[1], D. Levy[1], F. L. Giesel[1], B. A. Miller[1], P. D. Griffiths[1]
[1]Academic Radiology, University of Sheffield, Sheffield, South Yorkshire, United Kingdom

Introduction: The glucocorticoid-analogue dexamethasone is often administered to patients with intracranial tumours, its purpose being to alleviate some of the symptoms traditionally associated with raised intracranial pressure (ICP). Therapy usually begins shortly after the demonstration of a space-occupying lesion on cross-sectional imaging. The underlying neurophysiological mechanisms that gives rise to often dramatic clinical improvement remain unclear, despite the steroid's widespread use. Suggested modes of action include alterations to cerebral blood volume (CBV) or the degree of reactive oedema leading to reduced ICP. This study sought to investigate localised microvascular perfusion plus brain-tumour barrier and blood-brain barrier (BTB / BBB) integrity before and after administration of dexamethasone in patients with enhancing cerebral mass lesions. The aims of the study were to: (i) establish whether MR perfusion or BTB / BBB integrity alters following therapy; (ii) increase our knowledge surrounding the brain's physiological response to dexamethasone and (iii) determine whether steroids should be controlled for in MR studies involving intracranial neoplasms.

Methods: The study group consisted 17 patients (12 men and 5 women, mean age 50yrs, range 29-94yrs) who presented with known intracranial enhancing mass lesions on CT and were dexamethasone-naive. Following this study, histopathological classification (biopsy or surgical resection) classified the lesions as: 11 astrocytomas (grade IV); 2 anaplastic oligodendrogliomas; 1 sarcoma; I meningioma; I demyelinating plaque and 1 of uncertain pathology. All patients underwent MRI at 1.5T (Eclipse, Philips Medical Systems, Cleveland, Ohio) before and 3 days after initiation of high-dose dexamethasone (4g taken 4 x per day). Two exogenous-contrast based methods were used. Contrast 'T1-uptake' time-curves were calculated using a dynamic, T1-weighted, RF-spoiled FAST (TE=4ms; TR=37ms; acq matrix=128x256 over a 230mm FOV; three 5mm thick axial anatomical slices) technique. Fifty time-frames were collected over 162sec and a 10ml bolus of Gadovist (Schering AG, Germany) was administered on the 10th time-point. T1-uptake was defined as maximum signal change relative to baseline from normal appearing contralateral white matter. Regional CBV and first-moment mean Transit Time (TT_{FM}) were assessed via a dynamic, T2*-weighted single-shot EPI sequence (TE=60ms; TR=1400ms; acq matrix=192x188 over a 250mm FOV; twelve 5mm thick anatomical slices). The perfusion technique collected 70 time-frames over 98sec, again, a 10ml bolus of Gadovist was administered on the 10th time-point. Perfusion analysis methodology was similar to that published previously (1). Results were compared using paired t-tests.

Results: Following initiation of steroid treatment: tumour rCBV was reduced by 27% ($p<0.005$; fig 1a); contralateral normal appearing white matter rCBV was reduced by 16% ($p<0.05$); contralateral TT_{FM} increased by 6% ($p<0.05$; fig 1b) and maximum uptake of tumour contrast was found to have decreased by 28% ($p<0.005$).



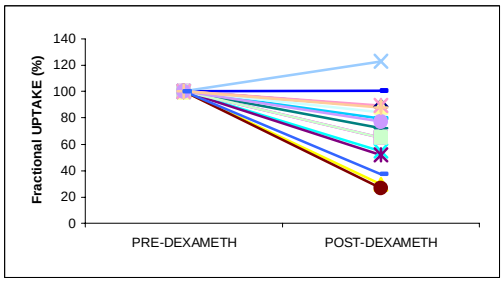


Figure 1. Percentage changes in tumour (a) rCBV and (b) T1-uptake following 3 days of steroid therapy. Both differences between the means were significant ($p<0.005$). The only lesions not to show decreased T1-uptake were the meningioma (extra-axial) and the sarcoma.

Discussion: Suggested mechanisms underlying symptom resolution following dexamethasone therapy include a decrease in vasogenic oedema following tightening of the BTB or changes in rCBV with subsequent lowering of ICP. Our results are supportive of both of these possible mechanisms. In addition to changes localised to tumour, we found that rCBF within normal appearing white matter is also lowered following drug initiation. This work highlights the need to control for steroid therapy in MR studies involving cerebral neoplasms, particularly in those which assess or may be influenced by cerebral perfusion, BTB or BBB integrity.

Reference:

1) Wilkinson ID *et al*. AJNR 2003; 24(8):1501-1507.