The potential of MRI and MRA in the evaluation of cerebral vasospasm in a rat model of subarachnoid hemorrhage

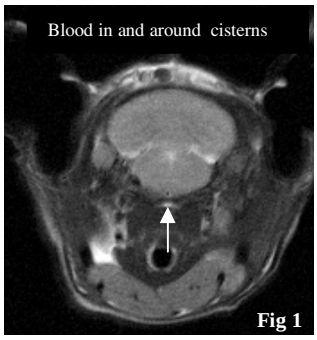
S. R. Ramdurg[1], A. Suri[1], D. Gupta[1], S. K. Mewar[2], U. Sharma[2], N. R. Jagannathan[2], and B. S. Sharma[1]

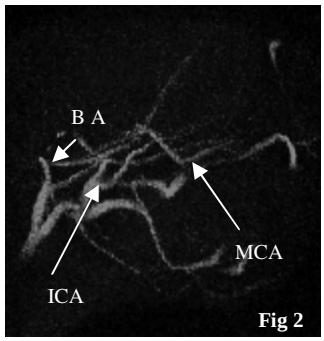
[1]Department of Neurosurgery, All India Institute of Medcial Sciences, New Delhi, Delhi, India, [2]Department of NMR and MRI Facility, All India Institute of Medcial Sciences, New Delhi, Delhi, India

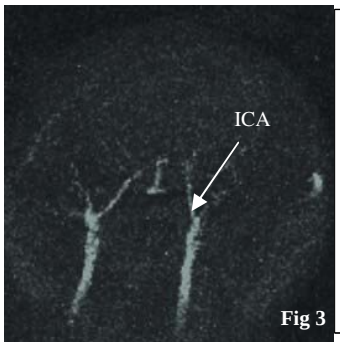
INTRODUCTION: Incidence of subarachnoid hemorrhage (SAH) is estimated to be around 6- 8% lakh per year. One quarter of them die within the first 24 hours. Mortality is estimated to be around 45% at 30 days. Histopathological studies of brains of patients who died shortly after subarachnoid show global ischemic change, the cause of which is unclear. Cerebral vasospasm is a major cause of morbidity and mortality after subarachnoid hemorrhage. This usually occurs in about 3 to 9 days after the aneurismal subarachnoid hemorrhage. Some form of ischemic deficits develops in 27-38% of patients due to cerebral vasospasm [1-3]. MRI and MR angiography (MRA) is an effective modality in the study of subarachnoid hemorrhage in humans. However there are only few studies to demonstrate the effect in rats [4]. Though various techniques are used for the development of effective model of SAH [6], in this study we used direct injection of blood in cisterna magna, as it provides controlled and quantifiable data to study the of pathophysiological changes due to subarachnoid hemorrhage induced vasospasm. The objective was to evaluate the potential of MRI and MRA to study the pathophysiology of vasospasm after subarachnoid hemorrhage.

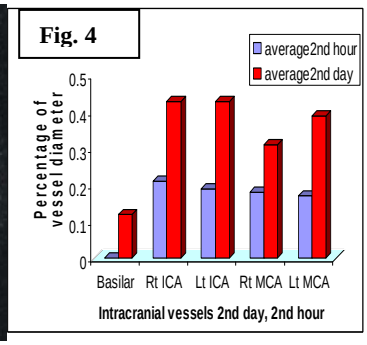
METHODS: Ten Wistar albino rats weighing 150-200 gm were used. Five rats served as controls for demonstration of normal vascular anatomy, while five were used to demonstrate the effects of subarachnoid hemorrhage induced vasospasm. Rats were anaesthetized using intra peritoneal chloral hydrate. MRI and MRA were performed using a 4.7 T (Bruker, Germany). TOF MRA was performed using a 3D gradient echo sequence with TR/TE =15/2.8ms; flip angle 20 degrees; FOV = 4x4x2 cm^3; matrix =256x256x128. T_2 - weighted images were acquired using a multislice multiecho CPMG sequence: TR=3000ms, TE=56 ms; 14 echoes; FOV=4x4 cm^2; slice thickness =2mm; interslice distance=2mm; matrix size =256x256. Five rats underwent the surgical procedure subarachnoid hemorrhage. A midline posterior skin incision was made and muscles were separated. Space between occiput and C1 vertebra was defined. Cisterna magna was defined. 0.1ml of rat tail blood was then injected into the cisterna magna to reach the sub arachnoid space. Sequential MRI and MRA were carried out on these rats prior to SAH, after 2hrs and after 2 days. The effect of SAH was evaluated in those rats. Two rats died following the induction of subarachnoid hemorrhage. The study was approved by the Institute Animal Ethics Committee.

RESULTS: The injected blood in the brain was well seen on the T1-weighted image (see arrow in Fig. 1). Fig. 2 shows the MRA of normal rat brain showing various vessels (BA- basilar artery, ICA- internal carotid artery, MCA- middle cerebral artery). The average vessel diameters in normal rats varied from 0.35 to 0.50 mm. However in the MRA acquired after 2 hrs i.e. post vasospasm, most of the major vessels were not clearly visible (Fig. 3). Increase in vessel diameter was observed in the MRA aquired after two days, however, still remained smaller than the pre subarachmoid phase. The maximum vasospasm was observed in the basilar artery where the concentration of injected blood was high. The effect on the other major vessels is lesser. The percentage increase of vessel diameter of various vessels calculated after 2nd hr and after 2nd day is shown in Figure 4.









DISCUSSION:

Our results demonstrate that rats can be used as an effective model for SAH induced vasospasm as the pattern resembles the human subarachnoid hemorrhage. The noncraniotomy model used in our study is simple and effective for the creation of SAH. Vasospasm induced by subarachnoid hemorrhage is maximal at second hour and tends to persist till second day albeit, at lower levels (see Figure 4). This observation needs further study on large number of rats. However, our preliminary study on such a model system help in correlating with human vasospasm using various treatment modalities. Our study showed that the animal model used here provides comparison of diameters of the vascular anatomy of normal rats as well as SAH induced rats. In SAH induced rats, there was partial improvement of the diameters of major vessels on second day. This would possibly provide the time period, during which effective drug treatment can be instituted.

REFERENCES: (1) Asano T, Sano K . *J Neurosurg* 1968: 46: 254- 466; (2) Cook DA. *Pharmcol Therapeutics* 1995: 66: 259- 284; (3) Borel CO, McKee A, Parra A, Haglund MM, Solan A, Prabhakar V et al. *Stroke* 2003: 34: 427- 433; (4) Kim Y., Dai G. , Bogdanov A., Rosen B., J. *Magn. Reson Med.* 2005: 13. 304; (5) Kim, Y.R., Savellano, M.D., Savellano, D. H., Weissleder, R & Bogdanov, A. *J. Magn. Reson* 2004: 52, 485- 94; (6) Busch E; Beaulieu C, de Crespiyny A, Moseley M. E. *Stroke* 1998; 29: 2155-2161.