

# TREATMENT OF ESTABLISHED SEVERE ANEURYSMAL SUBARACHNOID HAEMORRHAGE WITH INTRAVENOUS NIMODIPINE

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## INTRODUCTION

Severe aneurysmal subarachnoid haemorrhage is associated with a poor prognosis. In this small study poor grade patients with an established clinical deterioration were treated with intravenous Nimodipine, a calcium antagonist with claimed cerebrovascular selectivity.<sup>1-23</sup>

## METHOD AND MATERIALS

Five patients with aneurysmal subarachnoid haemorrhage were selected for treatment; two of these patients were treated in the immediate post haemorrhage phase and the other three had developed classical 'vasospasm'. All patients were clinically observed for at least six hours (see Table) prior to administration of intravenous Nimodipine and found to be in an established clinical deterioration. C.T. scan was repeated in the patients suffering from vasospasm to rule out rebleeding and treatment commenced immediately.

The patients were treated with intravenous Nimodipine via an infusion pump starting with 0.5 mg per hour working up to 2 mgs per hour after one to two hours. In all cases a degree of titration of Nimodipine dosage against systemic systolic blood pressure was required, and in one case it was not possible to achieve maximum dosage. A degree of hypotension was noted in all patients and arbitrary parameters allowing no more than a drop of 15mms Hg in the normotensive patient, and 25 mms Hg in the hypertensive patient were used in dose titration. Nimodipine caused hypotension in all our patients, but this was controlled by alternative day volume expansion with 'Haemaccel'. All patients received concomittant steroid administration. Intravenous therapy continued for seven days followed by a further two weeks of oral therapy up to a total daily dose of 360 mgm Nimodipine. Blood pressure measurements using an automatic sphygmomanometer were recorded every fifteen minutes at the commencement of treatment reducing to two hourly measurements depending on the blood pressure stability. It was not found necessary to use direct arterial blood pressure measurement. Urea and electrolyte measurements were performed on all patients at forty eight hourly intervals for the first week.

## RESULTS

The results are summarised in the table. Two patients began treatment within twenty-four hours of an acute subarachnoid haemorrhage and were later found to have intracranial aneurysms. Both these patients appeared to improve within two to four hours of administration of

Nimodipine. The other three patients developed classical vasospasm between seven and ten days after the initial ictus. These three patients had intracranial aneurysms and appeared to improve within two to six hours after administration of Nimodipine. In Case 3 an immediate pretreatment C.T. scan showed a well demarcated left middle cerebral infarct and it was therefore not surprising that although the patient's conscious level had rapidly improved, she still had a marked left sided weakness with some dysphasia. For this reason in this case it was decided that operation on her terminal basilar artery aneurysm was unwarranted and she died of a rehaemorrhage three weeks later. The other four patients went on to have successful aneurysm surgery between seven and twenty-one days after the commencement of treatment with Nimodipine. Nimodipine in either intravenous or oral form was continued throughout the perioperative period in these patients.

## DISCUSSION

There is increasing evidence that Nimodipine may be the first clinically available drug to improve the prognosis in aneurysmal subarachnoid haemorrhage.<sup>18-22</sup> The emphasis has been on the prophylaxis of cerebral 'vasospasm' in these studies and length of clinical observation on very poor grade patients is not recorded. Patients with subarachnoid haemorrhage have a notoriously fluctuating clinical course and it is not uncommon that a patient with a coma producing subarachnoid haemorrhage may be observed to be Grade V<sup>24</sup> on hospital admission, but will have improved within a matter of hours. Our patients were selected from the worst end of the subarachnoid haemorrhage spectrum and we believe that they all, possibly with the exception of Case 5, had a hopeless prognosis (see table). The survival of such patients as ours, with such established neurological deficit, is very rare, although of course, five patients can hardly be regarded as carrying statistical significance. After treating these five patients however, we felt it was no longer ethical to continue observing deteriorating patients without treatment, and since that time, all patients with Grade III or worse have been treated with intravenous Nimodipine immediately.

Petruk et al<sup>22</sup> treated fourteen Grade V patients with Nimodipine of which thirteen died and one remained moderately disabled at three months; however only oral Nimodipine (90 mgm four hourly) was used in this study. Auer<sup>18</sup> operated acutely on patients with ruptured cerebral aneurysms using Nimodipine; seven Grade V patients did badly. It is our policy to delay surgery until patients have

been established at at least Grade III. Koos et al<sup>20</sup> have used intravenous Nimodipine on twenty nine patients of Grade IV and six patients of Grade V with gratifying results (50% recorded as favourable); however the length of established poor grade is not noted.

Nimodipine is an expensive drug (approximately £500 per week per patient given intravenously). The accumulated evidence, in our opinion, would appear to suggest that in its intravenous form Nimodipine may well come to be regarded as useful not only in the prophylaxis of cerebral vasospasm following subarachnoid haemorrhage, but also in the acute

ictus. It may well be that further confirmatory evidence of Nimodipine's efficacy will lead to a policy of immediate treatment of patients with subarachnoid haemorrhage prior to neurosurgical unit referral.

With the increasing evidence of Nimodipine efficacy, however, it is difficult to see how further trials of this drug can be ethically mounted.

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Age	Sex	Post Haemorrhage Time	Length of Observed Deterioration	Aneurysm Site	Grade & Signs Prior to Treatment	Improvement Time and Signs	Surgery	Outcome Six Months
53	M	20 hours	18 hours	Terminal Basilar	V No response Pinpoint pupils Poor response	Fully conscious at 2 hours Dysarthric	Yes	Independent Ataxia and dysarthria due to brain stem haematoma
56	M	18 hours	18 hours	Posterior Inferior Cerebellar	V No response Ventilated Unreactive pupils	Fully conscious at 4 hours	Yes	Complete recovery
69	F	10 days	6 hours (Left middle cerebral infarct on C.T. scan)	Terminal Basilar	V No response Pupils sluggish reaction	Fully conscious at 8 hours (R) Hemiparesis Dysphasia	No	Died rebleed at 3 weeks
43	F	9 days	6 hours	Right Middle Cerebral	V Decerebrate BP 220/140	Fully conscious at 2 hours. Mild (L) Hemiparesis	Yes	Complete recovery
62	M	7 days	6 hours	Right Middle Cerebral	IV (L) Hemiplegia Responds to deep pain only, pupils reacting. Deteriorating	Alert at 6 hours Mild (L) Hemiparesis resolved 24 hours	Yes	Complete recovery

Table 1 – Nimodipine Treatment of Aneurysmal Subarachnoid Haemorrhage

\*A list of references can be obtained from the authors.

### Answer to quiz on page 124

Scabies. A scabies mite, *Acarus scabiei*, is present within its burrow in the horny layer of the epidermis. The head of the mite faces the blind end of the burrow and the mite has a liquid diet of inflammatory exudate.