TITLE : CURATIVE TREATMENT WITH INTRAVENOUS NIMODIPINE FOR CEREBRAL VASOSPASM AFTER SUBARACHNOID HAEMORRHAGE DUE TO ANEURISM RUPTURE

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INTRODUCTION :

Cerebral vasospasm is considered to be the most frequent complication in patients suffering from subarachnoid haemorrhage due to aneurism rupture (S.A.H.). Cerebral vasospasm is also the main cause of death and disability in this population. Two recent studies have demonstrated the efficacy of Nimodipine in cerebral ischaemia due to vasospasm when used early and preventively (1,2). However, in case of pre- and postoperative fixed vasospasm, no treatment has proved effective to date. The purpose of this multicentric prospective, double blind, randomized placebo controlled trial was to study whether intravenous Nimodipine could reduce the severity of ischaemic neurological deficits (N.D.) due to fixed cerebral vasospasm.

METHODS :

The protocol was approved by the Institutional Ethical Comittee and informed consent was obtained from all patients. During an 18 month enrollment period patients suffering from vasospasm within 15 days after S.A.H. were selected ; patients were included either within 24 hours of onset of an ischaemic N.D. due to the vasospasm (confirmed by angiography and/or CT. Scan.) or within 24 hours of a preoperative angiography film demonstrating a severe (> 50% narrowing) or diffuse (> = 2 vessels) vasospasm. Treatment started with each patient receiving a continuous peripheral intravenous infusion of 0.02% Nimodipine (N) or its Placebo (P) at a rate of 0.15ml.kg-1.h-1 for a minimum 7 days and a maximum 14 days. To assess clinical efficacy (mortality and/or severe morbidity) at the end of the intravenous treatment the Glasgow Outcome Scale (G.O.S.) was used. "Severe morbidity" included all patients in vegetative state or with severe N.D. Case reports were checked by an independant review comittee before the randomization codes were broken. Student's "t" test for unpaired data and "meta-analysis" test were used for statistical analysis.

RESULTS :

One hundred and eighty eight patients were included in the study (N = 102, P = 86), 127 patients met the entry criteria (valid cases : N = 73, P = 54). The 2 groups were comparable with respect to age, sex, delay between bleeding and treatment, duration of treatment, etc. as to whether they were entered on clinical (N = 40, P = 33) or angiographic grounds (N = 33, P = 21). At the end of the intravenous treatment, rate of mortality + severe morbidity for valid cases was N = 39%, P = 57% (p = 0.05). The risk of disability for the treated group (N) was decreased by 50% (p = 0.05) as compared to P. Regarding neurological ischaemic deficits due to vasospasm alone : the severe morbidity rate was : N = 13%, P = 20% (p = 0.30) ; mortality rate was N = 2.7%, P = 16.7% (p = 0.01) ; and mortality + severe morbidity rate was N = 16%, P = 37% (p = 0.01). The risk of disability for the treated group was decreased by 66% (p = 0.01) and 82% (p = 0.01) respectively, as compared to P. For the sub-group of valid cases with a "clinical" inclusion, mortality + severe morbidity rate due to vasospasm alone at the end of intravenous treatment was N = 20%, P = 45% (p = 0.02). Mortality was N = 2.5%, P = 15% (p = 0.05). For the sub-group of valid cases with "angiographic" inclusion, mortality + severe morbidity rate due to vasospasm alone at the end of the intravenous treatment was N = 12%, P = 24% (p = 0.27). Mortality was N = 3%, P = 19% (p = 0.15). No deleterious cardiovascular effects or abnormal laboratory parameters due to treatment were observed.

DISCUSSION :

Results demonstrate efficacy of intravenous Nimodipine for the treatment of cerebral vasospasm after S.A.H. : there was a significant decrease in the number of deaths and severe ND. (when patients were treated with Nimodipine after an ischaemic neurological deterioration due to vasospasm alone). To our knowledge it is the first time that in a double blind, curative study a therapy was proven to be effective for the treatment of vasospasm after S.A.H.

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