Treatment of Vasospasm Secondary to Subarachnoid Hemorrhage Using Intra-Arterial Nimodipine in Low Dosage

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Key words: vasospasm, angioplasty, subarachnoid haemorrhage, Nimodipine

Summary

There are currently no consensus criteria to define the dosage of intra-arterial Nimodipine to be used to obtain permanent remission of vasospasm secondary to subarachnoid haemorrhage.

The purpose of this paper is to establish a mathematical relation between the number of vessels affected by this kind of vasospasm and the Nimodipine dose that must be used for intra-arterial angioplasty to obtain permanent remission of the vasospasm.

Introduction

There are no articles or reviews in the international literature on which to assess the percentage of cases in a series of patients diagnosed with vasospasm secondary to spontaneous subarachnoid haemorrhage that should be treated by each kind of endovascular angioplasty technique (mechanical or chemical) and which dose of anti-vasospasm drugs should be used for this purpose.

The objective of this paper is to establish a mathematical relation between the number of vessels affected by vasospasm and the Nimodipine dose that should be used for chemical angioplasty of vasospasm secondary to subarachnoid hemorrhage to obtain permanent remission of the vasospasm.

Materials

To evaluate the patients admitted for spontaneous subarachnoid hemorrhage (s-SAH) we used a monoplane fluoroscopy system [GE® Advantix/IDF®]. For all diagnostic procedures, the chosen materials were Medikit Super Sheath Set® (5F or 6F) and Terumo® Radiofocus® Glidecath® catheters types Simmons or Angled Taper (5F or 4F). To perform therapeutic procedures, we used Medikit Super Sheath Set® (6F) and Cordis® Envoy® (6F) guide catheters. For the chemical and mechanical angioplasty procedures, we used Cordis® microcatheters and balloon systems.

Methods

At admission, we performed digital subtraction angiography (DSA) for all patients under local anaesthesia by femoral artery puncture according to the Seldinger technique. The same procedure was applied for re-evaluation of patients with clinical/doppler signs of intracranial vasospasm. At admission, for re-evaluation (in case of an inconclusive result of the admission angiography) and for evaluation of residual aneurysm neck post coiling/post aneurysm neck clipping (anc), we performed DSA with selective catheterization of four vessels [both internal carotid arteries (ICA) and both vertebral arteries (VA)].

For all patients and procedures we applied the following criteria:

Spontaneous Subarachnoid Hemorrhage

- all SAH cases diagnosed on patients with no history of cranial trauma and/or no non enhanced computed tomography signs of intracranial posttraumatic lesions;

Extent of SAH

- all circumscribed SAH (degree 1 of the Fischer score) were classified as focal¹;
- all uncircumscribed SAH cases (degrees ≤ 2 of the Fischer score) were classified as diffuse¹;

Vasospasm

- reduction of calibre of ≤ 1 segments of medium calibre intra-cranial vessel(s) and/or slow blood flow within the affected vessel(s) (observation of simultaneous arterial and venous contrast filling within the vascular territories during DSA);

Normal

- the DSA with no identifiable signs of vasospasm and no aneurysms, dural fistulas, arteriovenous malformations or other signs of arterial wall pathology that could, by any means, be considered the cause of SAH;

Re-evaluation criterion

- in all cases, the control DSA were requested by the ward physician based on emerging symptoms or signs of vasospasm, namely transcranial doppler signs²;

Type of angioplasty procedure applied

- intra-arterial angioplasty procedures were decided, case by case, based on the result of the admission/re-evaluation DSA and were performed following selective catheterization of the affected medium calibre vessels;
- chemical angioplasty was performed during selective catheterization of the segment of the affected vessel proximal to the spastic segment or, if this was not possible, in the most distal segment of the artery proximal to the affected one.

Results

From the 1st January 2002 to 19th June 2005, 1800 DSA were performed. From these, 482

(26,78%) were admitted for s-SAHA (see definition in *Methods*) and 150 (8,33%) for re-evaluation. The admitted patients' ages ranged from 15 to 94 years, with an average of 59 years. The data below refer to the percentage of DAS admitted for s-SAHA (N=482).

From the s-SAHA cases (Graph 1), 119 (24,69%) were classified as focal and 361 (74,90%) as diffuse. In two cases (0,41%) the diagnostic procedures were requested because the spinal taps previously performed on the patients revealed xanthochromic CSF (both patients had NECT negative for SAHA signs).

Along with CT signs of SAHA, 118 patients (24,43%) had signs of intraventricular hemorrhage (IVH). Of these IVH cases, five (4,24%) were associated with focal SAHA and 113 (95,76%) were associated with diffuse SAHA (Table 1).

Our department performed 44 post embolization control DSA and 58 post cca DSA. The gap between admission and control DSAs varied from 0 to 16 days (average 5.25 days) (Graph 2).

Control DSAs were requested for every patient whose neurological status was worsening (lowering of the GCS ≤ 3) or whose Glasgow Coma Score (GCS)³ became persistently ≤ 10 after endovascular therapy/surgery.

Graphic 1: localization of the spontaneous SAH.

SAH+IVH	
N=118	
focal SAH + IVH	diffuse SAH + IVH
N=5	N=113
%=4,24	%=95,76

Table 1: percentage of types of SAH associated with IVH.

Graphic 2: post coiling/cca control angiographies.

Graphic 3: percentage of vasospasm.

One hundred and eighty-five patients (38.38% of the admitted s-SAH) had to repeat the DSA for inconclusive results at admission.

The absolute number of vasospasm cases (Graph 3) was 92 (77.31% of all s-SAH), of these 45 (48.91%) had occurred previously in patients submitted to cca and 47 (51.09%) in patients submitted to coiling.

We registered signs of vasospasm of one arterial stream bed in 50 cases (54.35% of the cases of vasospasm). These corresponded to spasm of the proximal segment of the affected medium calibre intracranial artery (MCIA) (namely A1 or M1) in 48 patients (96% of the cases of vasospasm affecting one MCIA) and to slowing of blood flow, without irregularity of the vascular diameter in two cases (4%) (Graph 4).

We registered signs of vasospasm of two arterial beds in 30 cases had been observed (32.61% ibidem), all of these (100%) corresponded to spasm of the proximal segments of the affected MCIA (namely, A1/A2 and M1/M2).

We registered signs of vasospasm of six arteries [cavernous segments of both internal carotid arteries (ICA), of both anterior cerebral arteries (ACA) and of both medial cerebral arteries (MCA)] in one patient (1.09% idem), which corresponded in one (100%) to diffuse stenosis of the ACA, MCA and the named ICA segment. Our series counts five cases (5.43% ibidem) of diffuse vasospasm. These corresponded in five patients (100% ibidem) to spasm of all ACA and MCA segments, of the ACoA, of both ACoP and slowing of blood flow in the basilar artery and both posterior cerebral arteries.

Graphic 4: arterial beds affected by vasospasm.

Graphic 5: analysis of different angioplasty methods.

The angioplasty methods applied to reverse the identified vasospasm were (Graph 5):

- in seven cases (7.61% of the patients submitted to angioplasty) intra-arterial balloon angioplasty;
- in 34 cases (35.87% ibidem) chemical angioplasty (intra-arterial infusion of anti-vasospasm drugs: Nimodipine and Papaverine);

– in five cases (5.43% *ibidem*) both mechanical and chemical procedures were applied.

In the 31 patients (33.70% of all patients submitted to angioplasty) for whom we used only Nimodipine during the angioplasty procedure (not associated with other drugs or mechanical methods), the following were obtained:

– total reversal of vasospasm in 24 cases (77.42% of the patients where only intra-arterial Nimodipine was used as the angioplasty method);

– subtotal reversion in four cases (12.90%) with normalization of the speed of blood flow with attainment of calibre 90% of the normal vessel diameter);

– partial reversion, neither of the above in three cases (9.68%);

– all patients (100%) submitted to mechanical angioplasty had subtotal reversion of vasospasm.

There is no record of any chemical angioplasty procedure for which we used only Papaverine (0%).

The administered dose of Nimodipine was, on average 1.70 mg per procedure (and 1.56 per each affected arterial bed). The average dose of Papaverine was 75 mg (75 mg per each arterial presenting spasm) and, in all cases, it was associated with Nimodipine in doses varying with the number of vessels involved.

There was no record of patients with vasospasm signs after angioplastic procedures which were classified as having reached total or subtotal reversal of vasospasm. The calculated values were obtained from data concerning these two groups of patients.

Our series accounted for the death of ten patients (2.07% of the patients admitted for s-SAH investigation/treatment):

– six (1.24 % *idem*) cerebral death diagnosis, four of these (66.67%) occurred after admission DSA (average of 5.25 days, minimum 0 and maximum 16 days). During hospitalization, the ward physicians never requested control DSAs;

– one cerebral death diagnosis (16.67%) was made at the admission DSA;

– for the remaining cases in which the patients died, the diagnosis was cardio-pulmonary arrest (two cases). Both occurred in patients whose neurological status had been stable (Hunt & Hess ≤ 3 and GCS ≥ 10). Another patient died of spontaneous cardio-pulmonary ar-

rest that occurred 30 minutes after ending the admission DSA, even though no abnormalities in cardio-pulmonary and neurological status were registered during or after the procedure. One patient died of acute lung failure.

Summarizing, in 100% of the reported cases of death, the causes were not directly related to any of the therapeutic procedures (endovascular or surgical).

Discussion

There are no articles/reviews available in the international literature on which to assess the percentage of cases in a series of patients diagnosed with vasospasm secondary to spontaneous subarachnoid haemorrhage that should be treated by each kind of endovascular angioplasty technique (mechanical or chemical). There is also no reference as to the dosage of Nimodipine that should be administered during intra-arterial angioplasty procedures.

This paper briefly analysed our series of s-SAH cases admitted for diagnostic and/or re-evaluation DSA to establish a mathematical relation between the number of intra-cranial arteries affected by vasospasm and the dose of Nimodipine used during angioplasty procedures performed to reverse it.

Our main findings are:

– control DSA were requested for every patient whose neurological status was worsening (lowering of the GCS ≥ 3) or whose GCS became persistently ≤ 10 after endovascular therapy/surgery for SAH;

– the incidence of vasospasm secondary to s-SAH was: 77,31% (48,91% post cca and 51,09% post coiling);

– the ratio of vasospasm by number of affected arteries was:

– one arterial bed - 50 patients (54,35% of all patients with reported vasospasm);

– two arterial beds - 30 patients (32,61% *ibidem*);

– three arterial beds - six patients (6.52% *ibidem*);

– six arterial beds - one patient (1.09% *ibidem*);

– diffuse - five patients (5.43% *ibidem*);

– ratio of different types of angioplasty performed:

– mechanical (7.61% of all patients admitted for angioplasty);

– chemical (35.87% *ibidem*);

- ratio of different types of drugs used for anti-vasospasm chemical angioplasty;
- we used only Nimodipine during the angioplasty procedure in 33,70% of the patients who required anti-vasospasm angioplasty;
- ratio of vasospasm reversal following intra-arterial selective Nimodipine:
 - total remission - 77.42%;
 - subtotal remission - 12.90%;
 - parcial - 9.68%;
 - 100% of the patients who repeated DSA showed signs of vasospasm. After endovascular treatment for vasospasm, the patients who were classified as having “total remission” and “subtotal remission” of vasospasm after angioplasty never had neurological status worsening after angioplasty;
 - the average dose of Nimodipine applied was 1.70mg per chemical angioplasty session (average 1.56mg per spastic vessel).
 - 100% of the registered deaths did not have a cause that we could relate to the DSA/angioplasty procedure.

Conclusions

Taking into consideration that:

- intra-arterial Nimodipine was proven effective in obtaining the remission of 90.22% of all vasospasm cases (which corresponds to the sum of “total” and “subtotal reversion”);
- no clinical incidents were caused by selective angioplasty with Nimodipine;

- this drug is effective for selective angioplasty in a dose 1.56 mg per spastic arterial bed or 1.70 mg per angioplasty session;
- this dose is effective in obtaining a remission of vasospasm after s-SAH without further recurrence of vasospasm;
- the percentage of diagnostic and therapeutic incidents was 0%, implying that this drug can be used safely for all patients with a reported reduction of GCS ≥ 3 or persistence of low neurological status (GCS persistently ≤ 10 , after having eliminated the cause of s-SAH (endovascular or surgical).

References

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