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DOCTORATE STUDY
(PhD)

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Action of NIMOTOP on cerebrovascular spasm in subarachnoid hemorrhage aneurysm etiology

This study contains an analysis of two samples of patients having Aneurysm origin SAH, both by retrospective and prospective studies.

First sample consists in a number of 130 patients hospitalized between January 2005 and July 2009 at Neuro Surgery Clinic of D.Bagdasar-Arseni Hospita in Bucuresti – being diagnosed with SAH Aneurysm breakage. The diagnose was established using angiography examination IRM and CT.

Second sample consists in a number of 59 cases diagnosed as having Aneurysm etiology SAH – hospitalized in the same period of time at Neuro Surgery Clinic of University Emergency Hospital in Bucharest.

The purpose of this study is to underline the effectiveness of using Nimotop as a treatment of Vascular Spasm in SAH of Aneurysm etiology, in terms of:

- reduce the incidence of diffuse-moderate or severe vasospasm
- sequelae after delayed ischemic deficits due to vasospasm.

As a procedure, patients samples were subject of general clinical examination and neurological examination as well as of general and neurological paraclinical examination, in order to establish a correct diagnose and adequate treatment conduct.

Key words

- SAH = Subarachnoid hemorrhage – is a bleed at meningeal subarachnoid area.
- subarachnoid area – both cerebral and spinal are delimited on the interior by pia mater on the outside by the arachnoid.
- aneurysm (gr.aneurysma)= broadening ,expanding – Permanent arterial expansion , circumscribed , which has an increase tendency. It appears as a consequence of arterial wall weakening.
- Angiography vasospasm= contrast substance column thinning inside the cerebral arteries , usually localized but sometimes diffuse.

Results:

The results of the study for the patients sample having Aneurysm SAH from the clinic of Neuro Surgery from D.Bagdasar-Arseni Bucharest.

Out of the 130 de pacients, 74 (56,89%) were men and 56 were women (43,11%). Patients age was between 20 and 70 years. It has been observed that the incidence is greater for men than for women for the age of 3rd, 4th and 5th decade ; The ratio is changed for the 6th and 7th decade being even between men and women. Regarding the lead time between
desease start time and hospitalisation time it has been observed that 50 % of the pacients have been hospitalised on the first week after the start of the desease, 26,92% on the second week from the start and the rest of the pacients after the second week. All aneurysms were measured on arteriography films and categorised in three groups depending on dimensions: SMALL (up to 10 mm length), big (between 11 and 20 mm) and giant (over 20 mm in length).

The pacients with small aneurysm were 54,62% of total sample, big Aneurysms 43,85% and finally giant aneurysms 1,53%. In terms of localisation of the aneurysm, we have observed:

- 41 pacients had ACI aneurysm, aut of which 14 (34,14%) had a good recovery whilst 3 pacients (7,31%) have died.

-2 pacients having ACA aneurysm, aut of which one pacient has been recovered while the second died.

-12 pacients had ACM aneurysm; from these, 7 pacients had a good recovery (58,3%) and one pacient died (8,33%).

-75 pacients had ACoA aneurysm; aut of them 34 pacients have been recovered (45,33%) while 7 pacients (9,33%) deceased.

The pacients having ACM aneurysm had the biggest recovery ratio (58,3%) while the ones having ACA aneurysm, evolutive, had the biggest decease ratio.

The complication consisted in Vasospasm in SAH of aneurysmal origin; the same complication that generated the scope of the present study.

Cerebral arteriography has been performed for all 130 pacients from the study sample; the main criteria for being accepted for the study was the SAH diagnose proven by angiography of the aneurysm rupture; also condition of acceptance was that the pacient had not been under treatment with other Calcium blocking medicine except NIMOTOP. 32 pacients out of the 130 pacients sample have not been treated with Nimotop due to counterindications- being kept as comparison sample. Studying the effects of Nimotop over the vasospasm results were as follows:

83 pacients out of 130 persons with aneurysm origin SAH sample, were found having vasospasm categorized as:

Moderate vasospasm – with thinning of vascular lumen of 30-50% - two pacients;

Severe vasospasm at a number of 21 persons (focused – with a thinning of vascular lumen higher than 50%, and also involved a major vascular distribution);

Moderate diffuse vasospasm for a number of 12 pacients (thinning of the vascular lumen between 30% and 50% and involved more vascular distributions)
Severe – diffuse vasospasm at a number of 48 patients (thinning of vascular lumen with more than 50% and involved more vascular distributions);

From the 83 patients having vasospasm, 61 have been submitted for the Nimotop treatment while 22 patients consisted in the non treatment sample.

Comparing the two samples (Nimotop treatment 2 tablets every 4 hours) the results showed:

Moderate – diffuse vasospasm and severe – diffuse was observed at 70.48% of the Nimotop treated patients and at 77.27% of the non treated sample, slight but significant gap.

We have also studied the late ischemic deficit revealed at patients that were initially assessed as stable or improved status, followed by deterioration, but this deficit was considered to be caused by angiography vasospasm, as alternative causes like restart of bleeding, water on the brain or mistakes of medical care. Late ischemic deficit was noticed at 18.56% of the patients under treatment with Nimotop.

For the group of 32 non treated patients average age was 56 years, 67% were women and 33% were men.

We studied also a sample of 59 persons diagnosed with SAH, confirmed by angiography and IRM, hospitalised in Neuro Surgery Clinic of University Emergency Hospital Bucharest for the time period between January 2005–July 2009.

In these 59 cases 54.23% (32) were men and 45.76% (27) were women. Age of the patients varied between 20–70 years of age. It was observed that the incidence is bigger for the men than for the women for 3,4 and 6th decade of age; for the 7th decade the ratio reversed; In the mean time for 5th decade the ratio is even between men and women. Concerning the blood pressure, one of the main risk factors, we considered that all blood hypertension known patients have over 165 mmHg systolic pressure and a diastolic pressure over 90mmHg, as we observed that 61.02% (36) had normal blood pressure while 38.98% (23) had hypertension.

All patients were examined by angiography which revealed the presence of an aneurysm malformation of the carotid system, the most frequent localisation being at artery ACoA, 29 cases (49.15%), ACI 14 cases (23.72%), ACM 10 cases (16.94%) si ACA 6 cases (10.16%). All aneurysms were measured on angiography films and were categorized by the dimension of the aneurysm in three groups:

- Patients with small aneurysm 31 cases (52.54%)
- Patients with big aneurysm 21 cases (35.59%)
- Patients with giant aneurysm 7 cases (11.86%)

13.55% of the patients sample have not been done surgery on (8 cases) because of various reasons (Patient’s refuse, Family refuse, others) while surgery has been performed for a number of 51 patients (86.44%). When these persons left the hospital they were
categorized by the medical condition using Glasgow scale for 5 groups results, starting with 1st degree of recovery (best) till 5th recovery degree (deceased):

- 31 cases (53.00%) - 1st degree
- 11 cases (19.00%) - 2nd degree
- 8 cases (14.00%) - 3rd degree
- 6 cases (10.17%) - 4th degree
- 2 cases (3.83%) - 5th degree

The good recovery degree was higher for the patients of 1st and 2nd degree – Glasgow scale. Recovery of the patients, categorized by the age was as follows:

- 4 cases (3M+1F) - in 3rd decade
- 18 cases (10M+8F) - in 4th decade
- 16 cases (9M+7F) - in 5th decade
- 10 cases (5M+5F) - in 6th decade
- 11 cases (3M+8F) - in 7th decade

M=male F=female

The high percentage of good recovery was especially at 4th and 5th decade patients. Aut of 59 patients – study sample – 41 got Nimotop treatment; The rest of 18 patients did not receive treatment because of certain counterindications (various heart disease, kidney problems, liver disease) or simply intolerance after 3-4 days of treatment; this 18 persons sample consisted of the comparison sample against the persons who received the treatment with Nimotop. Depending on the radiological evaluation of the spasm revealed for the study of the patients from D.Bagdasar-Arseni Hospital in Bucharest the sample was categorized as: severe vasospasm, moderate vasospasm, absent, diffuse and focused; The evaluation results are the following: No vasospasm at the persons treated with Nimotop 7 cases (17.09%) and 2 cases from persons without Nimotop treatment (11.12%); Light Vasospasm 3 cases at people treated With Nimotop (7.31%) and 2 cases at the sample not treated (11.12%); Moderate vasospasm for 13 cases at persons treated with Nimotop (31.71%) and 7 cases – persons without treatment (38.88%); Moderate diffuse Vasospasm -12 cases – persons with treatment of Nimotop (29.26%) against 5 cases from people without treatment (27.77%); Severe – diffuse Vasospasm at 6 cases for people treated with Nimotop (14.63%) and 2 cases for people not treated (11.11%).

So, Moderate and severe - diffuse vasospasm has been observed at 75.60% of patients treated with Nimotop and at 77.76% of those without treatment. Difference is small but still significant.

Late Ischemic deficit appeared at 16.6% of the patients treated with Nimotop and at 25% of the group of patients that did not receive treatment.
Consequently it can be concluded that following Nimotop treatment, the late neurologic deficit caused by vasospasm appears less frequently.

**Conclusion**

1. S.A.H. occurrence is higher for men than for women aged at 3th and 4th decade, ratio being reversed for people at 6th decade, while at 7th decade ratio between men and women is almost even.

2. Concerning the lead time between start of disease and hospitalization, it was observed that most persons were hospitalized during the 1st week and least during second week (respectively 50% vs 23.08%).

3. Concerning the main risk factor for S.A.H.- Arterial HT –majority of the patients were normal blood pressure (84.6% of the first sample and 61.02% of the second sample) just few of them being hypertensive (15.38% of the first sample and 38.98% of the second sample).

4. Categorized depending on the neurologic status at the moment of hospitalisation they were grouped as per Hunt & Hess scale, it was noticed that most of the patients were at 2nd degree.

5. By performing cerebral angiography it was revealed the presence of an cerebrale aneurysmal malformation, most frequently on ACoA (49.15%) followed by AICI (23.72%).

6. All aneurysm have been measured as dimension on angiographic films and splitted into three groups: small – less than 10mm; big – between 11 and 20 mm; giant - over 20mm- most patients were included in small aneurysm category (54.62%) and the least into the giant aneurysm (1.53%).

7. At exiting of the hospital, patients of age at 4th and 5th decade had the highest recovery rate while the ones of age at 6th decade recorded the highest decease rate.

8. Depending on the SAH status at the moment of hospitalization and taking into account Hunt & Hess Scale it was revealed that patient sat first degree when hospitalized, had the best good recovery rate whilst the patients at degree 5 by hospitalization, had the highest decease rate.

9. Depending on the localization of the aneurysm, patients having ACM aneurysm, had the highest recovery rate, while the ones with ACA aneurysm had the highest decease rate.

10. Depending on the dimensions of the aneurysm, the highest recovery rate was observed at patients with small aneurysms, while the patients with big aneurysms recorded the highest decease rate.

11. Looking at the surgical treatment – we observed that patients that have been treated surgical had a high recovery percentage (54.62%) against the patients without surgery (9%)
and the decease rate for the patients that had not passed through surgery mare la cei care nu au fost operati (40%) against the operated patients (2.77%).

12. Concerning appearance of complications – subject of this study - the vasospasm from S.A.H. of aneurysmal ethiology - respectively the Moderate diffuse vasospasm and Severe was observed at 70.48% of the patients treated with Nimotop, and in 77.27% of the patients not treated with Nimotop, difference being small but significant.

13. The late ischemic deficit appeared at 18.56% of the patients treated with Nimotop and at 28% of those not treated.

14. So, It can be concluded that following the treatment using Nimotop, both Moderate – diffuse vasospasm and Severe – diffuse vasospasm as well as Late neurologic deficit caused by vasospasm were less frequent.

15. Finally, the present study clearly indicates that treatment with Nimotop is associated with an increase of the number of patients that had a good recovery and with a decrease of the number of patients that developed Late ischemic deficit. With certain limitations, the data obtained in this study can be used for planning and development of other clinical and paraclinical studies and also, by comparison with other studies may support a more accurate assessment of the patients prognosis.

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