Aneurysmal Subarachnoid Hemorrhage and Cognitive Deficits: a Phenomenon Difficult to Analyze

Hemorragia subaracnóidea aneurismática e déficits cognitivos: um fenômeno difícil de analisar

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ABSTRACT

Objective: Discuss cognitive deficits caused by subarachnoid hemorrhage (SAH) after rupture of cerebral aneurisms, since about half of the patients have severe or at least striking declines in one or more functions of the cognitive domain. Methods: This paper presents a literature review on cognitive deficits secondary to aneurysmal SAH. There was no delimitation of periods of publications or the locality where it was applied. The bibliographic references were accessed through the database PubMed (http://www.ncbi.nlm.nih.gov/pubmed/). Results: There are three main etiologies for the development of cognitive worsening: the effect of the initial bleeding, the consequences of vasospasm and delayed ischemia and the secondary ones to the treatment. Aneurysms located in the anterior communicating artery and in the middle cerebral artery seem to be related to worse evaluations. As surgical treatment seems to contribute to cognitive worsening, at least when evaluated early. Conclusion: Defining the involved factors in this pathology is a great challenge, since the papers of literature use different tests (Glasgow outcome scale or neuropsychological assessments), evaluate the patients in several stages (before or after treatment, being early or late) and compare the SAH patients with different groups (population without pathology or patients with unruptured aneurysms).

Key words: Cerebral aneurysm; Cognitive deficits; Subarachnoid hemorrhage

RESUMO

Objetivo: Discutir os déficits cognitivos provocados pela hemorragia subaracnóide (HSA) após a ruptura de aneurismas cerebrais, visto que metade dos pacientes apresentam pelo menos marcantes, em uma ou mais funções do domínio cognitivo. Métodos: O artigo apresenta uma revisão literária sobre déficits cognitivos secundários à HSA aneurismática. Não houve delimitação dos períodos das publicações ou da localidade onde foi aplicada. As referências bibliográficas foram acessadas pelo banco de dados PubMed (http://www.ncbi.nlm.nih.gov/pubmed/). Resultados: Existem três principais etiologias para o desenvolvimento de piora cognitiva: o efeito do sangramento inicial, as consequências do vasoespasmo e da isquemia tardia e as secundárias ao tratamento instituído. Aneurismas localizados na artéria comunicante anterior e na artéria cerebral media parecem estar relacionados com piores avaliações. O tratamento cirúrgico parece contribuir para a piora cognitiva, pelo menos quando avaliado precocemente. Conclusão: Definir os fatores envolvidos nesta patologia trata-se de um desafio, pois os trabalhos utilizam testes diferentes (Glasgow outcome scale ou avaliações neuropsicológicas), avaliam os pacientes em vários estágios (antes ou após o tratamento, podendo ser precoce ou tardivamente), além de comparar os pacientes com HSA com grupos diferentes (população sem patologia ou pacientes com aneurismas não rotos).

Palavras-chave: Aneurisma cerebral; Déficits cognitivos; Hemorragia subaracnóide

INTRODUCTION

The subarachnoid hemorrhage (SAH) represents 5% to 10% of all types of cerebrovascular accident (CVA), affecting most people in the 5th decade of life. Among their etiologies are emphasized the intracranial traumatism and the intracranial saccular aneurysms, which are the main cause of spontaneous SAH. Despite advances in the treatment of cerebral aneurysm and the prevention of secondary complications of SAH, a review carried out in 1997 showed a mortality rate of about 50% and that one-third of survivors remain dependent.

Cognitive deficits caused by aneurysmal SAH either caused

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by the hemorrhage itself or by its treatment are widely documented in the literature. However, little evidence of which clinical or surgical factors may cause these commitments was established32.

Studies confirm that 30 to 55% of patients, suffering from SAH and treated, have severe or at least striking deficits in one or more functions of the cognitive domain29.

Due to the need of early treatment for occlusion of the aneurysm, many authors describe the presence of changes of these functions after the procedure that the individual has undergone for the treatment of the aneurysm21. For this reason, there is no way to establish whether the damage arising from the SAH would be arising from the hemorrhage itself or generated by the procedure, either surgical or endovascular.

**Material and Methods**

The paper presents a literature review on cognitive deficits secondary to aneurysmal SAH, a pretty comprehensive subject that, in comparison with reports about the forms of treatment and their clinical complications - vasospasm, rebleeding and/or hydrocephalus, is relatively little published.

There was no delimitation of periods of publications or the locality where it was applied. The bibliographic references were accessed through the database PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) using the following keywords: “subarachnoid hemorrhage”, “cognitive impairment”, “neuropsychological assessment”, “intracranial aneurysm” and “outcome”.

Thus, the present paper aims to discuss aspects related to general concepts of cognitive deficits related to SAH, as well as the probable etiologies of these changes, showing how difficult it is to define the form and ideal moment of the evaluation.

It also seeks to define the main factors associated with cognitive worsening after the rupture of a cerebral aneurysm, aiming to, in the end, spread the subject to provide a better approach and management of these patients. This review does not focus on addressing specifically neuropsychological tests, what analysis should be performed, neither on describing the ways of applying them.

**Cognitive Deficits Post Subarachnoid Hemorrhage**

After the rupture of a cerebral aneurysm, the final result may be influenced by the general conditions of the patient, such as severity of the initial hemorrhage, previous aneurysms, age, gender, duration of treatment, history of hypertension, atrial fibrillation, renal failure, among others8.

Characteristics such as size, location in the posterior circulation and morphological aspects of the aneurysm are factors that influence the prognosis30.

It can also be determined by the conduct of the staff and the experience of the hospital group, e.g., institutional conditions that the emergency unit must have for the most suitable care to patients with SAH.

In a four to seven years follow-up study of aneurysmal SAH patients, carried out in 1997, Ogden et al. found 41% of the individuals with memory complaints, 48.3% with personality changes and 20% of the individuals with a decrease in their professional skills30.

Although the cognitive changes represent a major clinical problem, there is still little knowledge about the factors that cause these alterations in SAH.

**Pathophysiology of Cognitive Changes**

Many speculations are made in world-wide literature about what causes the emergence of cognitive sequelae in SAH and the main hypotheses are: a) resulting from neurotoxic effects and the presence of widespread blood in the subarachnoid space43, b) secondary to vasospasm and ischemia17,37 and c) consequent to damage caused by surgical or endovascular procedures21.

The presence of blood in the subarachnoid space possibly provides alterations in higher brain functions43. This aspect is present in all types of spontaneous SAH, thus, researchers sought the relation between the general condition of patients with aneurysmal SAH and other SAH patients without etiology.

Hawkins et al.20 and Kawamura et al. 25 followed patients with spontaneous SAH of unknown cause. In both studies, the patients showed good general prognosis, however they did not focus on a neuropsychological assessment that would reveal the actual cognitive profile of these patients.
Hillis et al. compared the cognitive performance three months after the surgery of patients who have had the diagnosis of unruptured aneurysms and compared with aneurysmal SAH patients. Their results revealed a worse performance of the patients who had SAH. Therefore, they concluded that SAH would be responsible for cognitive impairment.

Type of Evaluation

The Glasgow Outcome Scale (GOS) created to measure the quality of survival of patients is still an instrument used in individuals with SAH.

With the advancement of neuropsychology, it was noted that many of the good results measured from the GOS of SAH patients were not trustworthy with cognitive losses the patient presented.

Fauvage et al. found memory impairments and depression problems in 65% of the patients who had a GOS score five. Changes regarding social and emotional habits often passed unnoticed at a first moment, but in functional activities and in the work environment they became incapacitating.

With the use of specific tests, it was found that the damage of SAH is much more disastrous. Of individuals with SAH, approximately 50% present permanent losses, being cognitive changes one of its main causes.

Cognitive changes were confirmed even when the patient had a good recovery and no evidence of neurological deficits, differentiating the GOS results from the neuropsychological tests.

The task of identifying and classifying a cognitive impairment in individuals presents several difficulties such as determining where to establish a suitable cut-off point, i.e. below which performance it can be considered significantly impaired. The score may be in confrontation with the premorbid state of the patient or from the trial of performance of a normal population.

Another challenge is the definition of which neuropsychological test is appropriate to evaluate certain cognitive functions in a specific population. An endless number of analysis may be influenced by more than one cognitive function and it is up to the examiner to classify from the faults found which of them may have influenced the result.

Therefore, we advise to always verify the type of analysis of cognitive deficit when assessing works, so that there is no comparison between studies using simpler scales with more complex neuropsychological tests, as well as what has been defined as cognitive decline: the comparison with a specific group or the paired evaluation of SAH patients.

Moment of Evaluation

The decision about the best moment to perform the neuropsychological tests remains in a broad debate in the literature. In general, patients could be evaluated before the therapeutical procedure, after treatment and late after the first three months.

As the treatment of aneurysmal SAH should be instituted early, within the first 24-48 hours of the initial symptoms, a neuropsychological assessment is impaired in this short period of time.

In literature, up to the publication of our group, there was no documentation of a research measuring the cognitive skills in the period prior to the treatment for occlusion of the aneurysm, and thus it would not be possible to characterize the losses arising from the SAH itself.

Therefore, the undertaken papers have carried out comparative studies of the cognitive functions between patients with SAH and the control population or with patients who have had the diagnosis of intracranial aneurysm before its rupture, with no preoperative evaluation.

Viera et al. demonstrated worsening of cognitive impairment when compared to assessments in pre- and post-treatment period by paired analyses, proving the deleterious effect of therapeutical intervention in the functions of language and memory.

As the carried out research presents different methods regarding the interval after the SAH for applying the cognitive test, making it difficult to reach a consensus on important information, Ogden reports that at the initial moment of SAH it is possible to identify a relationship between the location of aneurysm and the cognitive impairment.

The study of Papagno et al. confirms there is a relationship between these two variables even after three months of SAH, and in this same study they revealed that two groups of patients...
with aneurysm in ACOA, assessed at different moments, one after a month and the other after three months, showed cognitive differences between them.

On the other hand, the research presenting evaluations after a year of SAH showed no cognitive differences among groups with aneurysmal SAH in different locations\textsuperscript{11, 23, 38}.

**Associated Factors**

*Location of the aneurysm*

For some authors, there is no correlation between the location of the aneurysm and the cognitive decline\textsuperscript{11, 31, 38}. However, other studies relate and specify the cognitive deficits with the site of the aneurysm.

Thus, the aneurysms located in the posterior circulation would have a better prognosis for verbal and visual memory, whereas the anterior communicating artery aneurysms (ACOA), as well as the temporary occlusion of their vessels, during the surgical procedure would be related to losses in memory and executive functions\textsuperscript{44}.

There are several studies linking cognitive disorders in SAH with aneurysm of ACOA. This fact is due to its high prevalence, resulting from the association with anatomical variations in the anterior communicating complex, such as the A1 segment hypoplasia\textsuperscript{10, 36}, as well as ACOA is related to the circulation of the posterior region of the frontal lobe, mesial and subcortical frontal area responsible for controlling some cognitive functions such as executive functions, memory, attention and suppression of usual answers\textsuperscript{1, 13}.

Most of the results of cognitive performance, involving aneurysms in the territory of ACOA, show persistent alterations in memory and personality changes\textsuperscript{39, 42}.

In 1989, Barbarotto et al.\textsuperscript{2}, compared the cognitive performance of patients with aneurysm of the middle cerebral artery (MCA) and with posterior communicating artery aneurysm (PCOA), showing similar cognitive profiles with alterations in naming, verbal fluency and verbal short-term memory in patients with aneurysm of the left side and change in spatial memory when on the right side.

In the study of aneurysms in the MCA, Haug et al.\textsuperscript{19} compared the cognitive performance of patients with ruptured and incidental MCA aneurysm 3 months and 1 year after the treatment. In their results, the group with SAH showed greater difficulty to return to their professional activities and verbal memory impairment. However, both groups showed a reduction in the quality of life and in the performance of the cognitive functions.

In 1993, Ogden et al.\textsuperscript{29}, in a prospective study with 89 patients, found that the site of the aneurysmal lesion was not determinative of the type of neuropsychological alteration. Evaluating this relationship, the same result was seen in the research done at the University of Salamanca by Perea-Bartolomé et al.\textsuperscript{34}, when assessing cognitive functions of patients after an interval of four years of SAH.

Our results\textsuperscript{45} have proven significant differences between patients with SAH resulting from aneurysms in ACOA and MCA when compared with individuals considered normal. Patients with aneurysm at MCA show greater decline in some criteria in language when compared to those with aneurysms in ACOA. We did not find differences between the right and left side, when compared the MCA and PCOA aneurysms.

**Surgical or endovascular treatment**

The choice of the form of treatment may influence the final cognitive deficit, and the injury is bigger in the patients undergoing surgical procedure, because embolization has a less invasive nature, causing less damage to the brain\textsuperscript{6}.

Proust et al.\textsuperscript{35} found similar cognitive performance in almost all the analyses carried out between the two groups. However, surgical patients showed significant losses in verbal memory, associated with frontomedial lesions found in Magnetic Resonance Imaging (MRI) exams.

In patients with unruptured aneurysms, the group undergoing surgery showed reduction in the quality of life, whereas the embolized patients had after three months similar evaluation to the period prior to treatment\textsuperscript{4}. On the other hand, in a study with 237 patients with ruptured ACOA aneurysms, larger cognitive changes were found in the group of patients undergoing endovascular treatment\textsuperscript{12}.

In the research of Haug et al.\textsuperscript{18}, no differences were found between the cognitive performance of patients undergoing surgery and the embolized ones after a period of three months.
In 2012, our group carried out the comparative analysis between patients undergoing surgery or embolization. They were evaluated at two moments (pre- and post-treatment) being possible to reveal the presence of new alterations as a result of the therapy performed. Only the group undergoing surgery showed differences between the pre and post period in almost all carried out tests.

**CONCLUSION**

The difference among the forms of assessment of this deficit strongly influences the comparisons of the studies, not being possible to establish differences when using for example the GOS and specific neuropsychological tests.

The same principle is applied for the moment when the analyses have been carried out, most works study the post-treatment period and compare SAH patients with patients with unruptured aneurysm or with a control group.

Thus, setting factors associated with cognitive decline becomes difficult. Aneurysms located in the ACOA and in the MCA seem to be related to worse evaluations when analyzed the papers in literature. Surgical treatment seems to contribute to cognitive worsening, at least when evaluated early, still requiring long-term work to define this relationship.

The critical analysis of the works of the literature on cognitive changes secondary to aneurysmal SAH demonstrates that one should always be very cautious in assessing the results, avoiding comparisons among studies using different tests, analyzing at different moments and comparing different groups.

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