Advances in stroke evaluation and treatment

Avanços na avaliação e tratamento do acidente vascular cerebral

Flavio Augusto de Carvalho[1], Gisele Sampaio Silva[1]

ABSTRACT

One of neurology's most challenging and evolving fields, vascular neurology has been constantly calling for attention. From small breakthroughs to large randomized trials, the quest for new answers in stroke treatment has brought us many advances and keeps bringing problems and solutions as new trials are coming.

Keywords: Stroke; Neuroimaging; Reperfusion

RESUMO

A neurologia vascular é uma das áreas mais envolventes e um dos maiores desafios para o neurologista, e tem chamado constantemente a atenção. Desde pequenos estudos revolucionários até grandes ensaios randomizados, a necessidade de novas respostas no tratamento do acidente vascular cerebral tem trazido inúmeros avanços, problemas e soluções conforme novos estudos clínicos são publicados.

Descritores: Acidente vascular cerebral; Neuroimagem; Reperfusão

INTRODUCTION

Recanalization and reperfusion therapies in acute ischemic stroke

Succesfull recanalization, the Holy Grail of acute ischemic stroke therapy, is promisingly shown to be possible with several techniques[1]. Currently, intravenous thrombolysis with tissue plasminogen activator (rt-PA) in the first 4.5 hours for selected patients remains the standard of care with simultaneous transcranial Doppler ultrasound monitoring being advisable because this method can improve recanalization rates[1-3]. However, intra-arterial therapy up to 8 hours after stroke is increasingly being performed for patients whose vessels do not open with intravenous rt-PA or for those who are not eligible for systemic thrombolysis. Devices for mechanical thrombectomy, such as the MERCI retriever (Concentric Medical, Mountain View, California) and the PENUMBRA System (Penumbra, Alameda, California), provide excellent recanalization rates[4,5]. Just recently, the SOLITAIRE device (ev3, Plymouth, Minnesota), a self-expanding stent retriever, was approved by *Food and Drug Administration* (FDA) for stroke treatment based on the positive results described in the SWIFT trial. The SOLITAIRE device when compared with MERCI, achieved recanalization rates of 83.3 *versus* 48.1% ($p<0.0001$), respectively, also leading to other better results as lower mortality at 3 months, and lower rates of symptomatic intracranial bleeding[6].

Neuroimaging and stroke

The use of imaging methods to select patients for late recanalization therapies based on a penumbral pattern of magnetic resonance imaging (MRI) diffusion/perfusion mismatch is also under scrutiny. Despite negative results, recent trials have drawn the attention to this subject. One is the MR-RESCUE trial, an MRI based trial investigating the benefit of rescue mechanical thrombectomy in patients with diffusion/perfusion mismatch, which currently looks for evidence to this method. This trial has just stopped recruiting patients and its results will be announced in the near future[7].

Other imaging techniques are expected to play a role in the treatment of vascular diseases. Vessel wall imaging is currently being used to differentiate and identify several vascular conditions. Inflammation in atherosclerotic plaques can be identified by both [18F]-2-fluoro-2-deoxy-d-glucose positron emission tomography and MRI techniques[8,9]. Vessel wall enhancement on MRI is highly predictive of arterial

[1] Programa Integrado de Neurologia, Hospital Israelita Albert Einstein – HIAE, São Paulo (SP), Brazil; Department of Neurology and Neurosurgery, Universidade Federal de São Paulo – UNIFESP, São Paulo (SP), Brazil.

Corresponding author: Gisele Sampaio Silva – Avenida Albert Einstein 627, suíte 218 – Morumbi – Zip code: 05652-000 – São Paulo (SP), Brazil – Phone: (55 11) 2151-3340 – Email: giselesampaio@hotmail.com

Received on: Mar 23, 2012 – Accepted on: May 7, 2012

wall inflammation, and can differentiate between cerebral vasoconstriction syndrome and vasculitis[10].

Secondary prevention of ischemic stroke

If intra-arterial reperfusion therapies are still a matter of debate, secondary prevention with aspirin has been reascertained after the negative results of the PERFORM trial, which tested the selective thromboxane-prostaglandin receptor antagonist terutroban against aspirin[11]. On the other hand, never have we seen so many new possibilities for secondary prevention of stroke thanks to the development of three new oral anticoagulants for patients with nonvalvular atrial fibrillation. The RELY trial compared dabigatran, a direct thrombin inhibitor, with warfarin[12]. Similar bleeding rates and lower rates of stroke were observed with 150mg twice daily of dabigatran.

Recently, apixaban and rivaroxaban, two factor Xa inhibitors, also showed positive results in comparison to warfarin, as observed in the ARISTOTLE and ROCKET AF trials[13,14]. One can imagine that we should expect a raise in the number of succesfully treated individuals with the appearance of such options; however, the true impact of the use of those new drugs in the stroke prevention scenario is still to be analyzed.

Treatment of hemorrhagic stroke

Acute treatment of hemorrhagic stroke is also a promising field in vascular neurology. Not only do we understand better its potential complications (i.e. the spot sign can predict greater chances of hematoma expansion) but also are beginning to treat it better with more aggressive control of hypertension in the acute phase, as suggested to be safe in the INTERACT trial[15]. This approach is now under further investigation in the INTERACT 2 trial[16].

In addition, new ways to treat hemorrhagic stroke are coming to light. One is the use of minimally invasive surgery that is being evaluated by the MISTIE trial. Also the CLEAR trial has been evaluating the use of intraventricular rt-PA for clot lysis in intraventricular hemorrhages, what so far appears to be promising[17,18].

CONCLUSIONS

Evaluation and treatment of stroke has definitely improved over the last years, mostly due to well designed and patient oriented clinical trials. Although several questions remain unanswered, clinicians nowadays are able to manage patients with acute stroke and to conduct secondary stroke prevention using more evidence-based medicine than ever.

A remaining challenge right now is to implement efforts to assure that advances in stroke evaluation and treatment are going to be available for more and more patients, regardless of their geographical location and socio-economic status.

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