

## Pharmacotherapy prior to and in acute haemorrhagic stroke. The use of pharmacotherapy and drugs-associated outcomes in real-world practice – findings from the Polish Hospital Stroke Registry

### *Farmakoterapia w okresie poprzedzającym wystąpienie udaru i w ostrym udarze krwotocznym. Zastosowanie oraz wpływ leków na wyniki leczenia udaru krwotocznego mózgu w codziennej praktyce klinicznej – wyniki Szpitalnego Rejestru Udarów Mózgu w Polsce*

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Neurologia i Neurochirurgia Polska 2013; 47, 6: 517-524

DOI: 10.5114/ninp.2013.39068

#### Abstract

**Background and purpose:** Haemorrhagic stroke is associated with substantial mortality and disability, thus prevention and appropriate treatment of acute intracerebral haemorrhage is crucial. We aimed to evaluate the use and the early and late outcomes impact of drugs administered before and in acute haemorrhagic stroke in a real-world practice.

**Material and methods:** Haemorrhagic stroke patients hospitalized between 1<sup>st</sup> March 2007 and 29<sup>th</sup> February 2008 and reported in Polish Hospital Stroke Registry were analysed. Fully anonymous data were collected with standardized, authorized access, web-based questionnaire. Multivariate regression models were used to adjust for case-mix and evaluate the impact of drugs used prior to or in acute haemorrhagic stroke on outcomes. The early outcomes were defined as in-hospital mortality or poor outcome (death or dependency – modified Rankin Scale  $\geq 3$ ) at hospital discharge, while late outcomes covered one-year survival.

#### Streszczenie

**Wstęp i cel pracy:** Udar krwotoczny jest związany ze znaczną śmiertelnością oraz niepełnosprawnością chorych; wymaga zarówno skutecznej profilaktyki, jak i leczenia ostrej fazy. Celem badania była ocena farmakoterapii stosowanej przed zachorowaniem i w ostrej fazie udaru krwotocznego mózgu, w warunkach codziennej praktyki klinicznej.

**Materiał i metody:** Analizie poddano grupę chorych hospitalizowanych z powodu udaru krwotocznego mózgu od 1.03.2007 r. do 29.02.2008 r., zgłoszonych do Szpitalnego Rejestru Udarów Mózgu w Polsce. W pełni anonimowe dane gromadzono z wykorzystaniem sformatowanego kwestionariusza internetowego z autoryzowanym dostępem. Do oceny wpływu leków stosowanych przed zachorowaniem oraz w ostrej fazie udaru krwotocznego na rokowanie wykorzystano wieloczynnikową analizę regresji z uwzględnieniem wpływu innych czynników rokowniczych. Wczesne wyniki leczenia zdefiniowano jako śmiertelność wewnątrzszpitalną i niekorzystny efekt terapeutyczny (punktacja  $\geq 3$  w zmody-

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Received: 25.02.2013; accepted: 25.03.2013

**Results:** A total of 3111 haemorrhagic stroke patients (mean age: 68.9 years; females: 46.7%) was reported. The analysis of pharmacotherapy showed low preventive use of hypotensive agents in hypertensive patients, high consumption of antibiotics and still overuse of vasoactive or neuroprotective compounds in acute haemorrhagic stroke. Regression models confirmed expected negative impact on stroke outcomes associated with oral anticoagulants but not antiplatelets and inconsistent impact of statins used prior to or in acute haemorrhagic stroke.

**Conclusions:** Preventive underuse of hypotensive compounds contribute substantially to haemorrhagic stroke risk. The high consumption of antibiotics and neuroprotective or vasoactive compounds in haemorrhagic acute stroke reflect the need to improved quality and evidence-based clinical practice.

**Key words:** haemorrhagic stroke, pharmacotherapy, antihypertensives, oral anticoagulants, statins.

## Introduction

Haemorrhagic stroke, also named intracerebral haemorrhage (ICH), accounts for 10-15% of strokes, which translates into approximately 2 million new episodes of ICH worldwide each year [1]. It is associated with a 30-day mortality rate that approaches 50%, and only 20% of survivors are functionally independent at 6 months [2]. Haemorrhagic stroke is associated with a recurrence rate of 1-3% per year. Approximately half of the stroke recurrences after haemorrhagic stroke are in the form of another intracranial bleeding, with the other half corresponding to ischaemic stroke. Despite its substantial frequency and its major toll in terms of acute mortality and long-term disability, haemorrhagic stroke has been relatively understudied, especially with regard to treatment and the value of various measures for secondary prevention.

Haemorrhagic strokes are most often due to high blood pressure. Adequate control of blood pressure could prevent the majority of haemorrhagic strokes as untreated or poorly controlled hypertension increases the risk of intracranial haemorrhage by three to four-fold. Another risk factor is diabetes, although it slightly increases the risk of haemorrhagic stroke including intracranial bleeding following thrombolysis in acute

ischaemic stroke. Certainly, excessive alcohol consumption increases the risk of haemorrhagic stroke and light to moderate intake was not showed beneficial contrary to ischaemic stroke. Smoking and possibly migraine with aura are also another risk factors [3].

Oral anticoagulants are associated with mean annual rate of haemorrhagic stroke of 0.2% and either more severe stroke or worse prognosis. Anticoagulation resumption after intracranial haemorrhage is a challenge. Current guidelines for patients with a comparatively lower risk of cerebral infarction (eg. atrial fibrillation [AF] without prior ischaemic stroke) and a higher risk of amyloid angiopathy (eg. elderly patients with lobar bleeding) or with very poor overall neurological function recommend consideration of an antiplatelet agent for prevention of ischaemic stroke. While in patients with a very high risk of thromboembolism it may be reasonable to restart warfarin therapy at 7 to 10 days after onset of the haemorrhagic stroke [4]. Antiplatelets for prevention of ischaemic events after ICH are considered safe in general, but caution should be paid to patients with lobar bleeding suspected to be due to cerebral amyloid angiopathy. Statins are effective for prevention of ischaemic events but they seem to increase the risk of lobar ICH recurrence.

Medical therapy of acute haemorrhagic stroke is mainly focused on adjunctive measures to minimize

**Słowa kluczowe:** udar krwotoczny, farmakoterapia, leki hipotensyjne, leki przeciwzakrzepowe, statyny.

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