ORIGINAL PAPER/*ARTYKUŁ ORYGINALNY*

Pharmacotherapy prior to and in acute ischaemic 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 niedokrwiennym. Zastosowanie oraz wpływ leków na wyniki leczenia udaru niedokrwiennego mózgu w codziennej praktyce klinicznej – wyniki Szpitalnego Rejestru Udarów Mózgu w Polsce

Maciej Niewada[1], Iwona Marta Sarzyńska-Długosz[2], Marta Skowrońska[2], Bogumił Kamiński[3], Adam Kobayashi[1], Anna Członkowska[1]

[1]Katedra i Zakład Farmakologii Doświadczalnej i Klinicznej, Warszawski Uniwersytet Medyczny
[2]II Klinika Neurologiczna, Instytut Psychiatrii i Neurologii w Warszawie
[3]Zakład Wspomagania i Analizy Decyzji, Instytut Ekonometrii, Szkoła Główna Handlowa w Warszawie

Neurologia i Neurochirurgia Polska 2013; 47, 6: 509-516
DOI: 10.5114/ninp.2013.39067

Abstract

Background and purpose: Stroke is a preventable disease and acute ischaemic stroke can be effectively treated. Specific pharmacotherapy is recommended in either prevention or acute ischemic stroke treatment. We aimed to evaluate the use and the early and late outcomes impact of drugs administered before and in acute ischaemic stroke in a real world practice.

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

Streszczenie

Wstęp i cel pracy: Udarowi mózgu można skutecznie zapobiegać. Dostępne są efektywne metody leczenia ostrego udaru niedokrwiennego. Zarówno w profilaktyce, jak i leczeniu ostrego udaru niedokrwiennego zalecana jest specyficzna farmakoterapia. Celem badania była ocena farmakoterapii stosowanej przed zachorowaniem oraz w ostrej fazie udaru niedokrwiennego mózgu, w warunkach codziennej praktyki klinicznej.

Materiał i metody: Analizie poddano grupę chorych hospitalizowanych z powodu udaru niedokrwiennego 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 strukturyzowanego kwestionariusza internetowego z autoryzowanym dostępem. Do oceny wpływu leków (stosowanych przed zachorowaniem oraz w ostrej fazie udaru niedokrwiennego) na rokowanie wykorzystano wieloczynnikową analizę regresji z uwzględnieniem wpływu innych czynników rokowniczych. Wczesne wyniki

Correspondence address: dr hab. med. Maciej Niewada, Katedra i Zakład Farmakologii Doświadczalnej i Klinicznej, Warszawski Uniwersytet Medyczny, Krakowskie Przedmieście 26/28, 00-927 Warszawa, Polska, e-mail: maciej.niewada@wum.edu.pl
Received: 25.02.2013; accepted: 25.03.2013

Results: A total number of 26 153 ischaemic stroke patients (mean age: 71.8 years; females: 51.6%) was reported. The analysis of pharmacotherapy showed that preventive use of hypotensive agents, anticoagulants in atrial fibrillation, antiplatelets and statins is inadequate. Regression models confirmed some expected drug benefits and additionally revealed that antihypertensive drugs or aspirin used prior to stroke and oral anticoagulants or statins used in hospital were associated with better stroke outcome.

Conclusions: The prevention of ischaemic stroke needs to be monitored and improved. Evidence-based treatment of acute ischaemic stroke requires further promotion. The benefits of acute ischaemic stroke treatment with statins require to be confirmed in randomized controlled settings.

Key words: ischaemic stroke, pharmacotherapy, aspirin, oral anticoagulants, antihypertensives, statins.

Wyniki: Analizie poddano dane 26 153 osób hospitalizowanych z powodu udaru niedokrwiennego (średni wiek: 71,8 roku; kobiety: 51,6%). Wykazano niewystarczające profilaktyczne stosowanie leków hipotensyjnych, przeciwzakrzepowych u chorych z migotaniem przedsionków, leków przeciwpłytkowych i statyn. W modelach wieloczynnikowych odnotowano spodziewane korzystne efekty farmakoterapii. Wykazano dodatkowo, że leki hipotensyjne i kwas acetylosalicylowy stosowane przed zachorowaniem oraz leki przeciwzakrzepowe i statyny w trakcie hospitalizacji są związane z korzystnymi wynikami terapeutycznymi.

Wnioski: Farmakologiczna profilaktyka udaru mózgu i leczenie ostrego udaru mózgu wymagają dalszego monitorowania i poprawy. Korzyści z zastosowania statyn w leczeniu ostrego udaru mózgu powinny być potwierdzone w badaniach klinicznych z randomizacją.

Słowa kluczowe: udar niedokrwienny, farmakoterapia, leki przeciwzakrzepowe, kwas acetylosalicylowy, leki hipotensyjne, statyny.

Introduction

Stroke, as a one of the leading causes of mortality and disability, is also very preventable and curable disease. Oxford Vascular Study showed 40% decrease in the age-specific incidence of major stroke in Oxfordshire from 1981 to 2004 [1].Ten risk factors (i.e. history of hypertension, current smoking, obesity measured with waist-to-hip ratio, diet, physical activity, diabetes mellitus, alcohol intake, psychosocial stress and depression, cardiac causes and dyslipidaemias) are associated with 90% of the risk of stroke [2]. Some of these risk factors can be addressed with specific and effective drug treatment. Therefore, apart from non-drug prevention methods, pharmacotherapy plays an important role in prevention of first-ever stroke as well as secondary cerebrovascular accident. Current guidelines in the primary prevention of stroke recommend targeting some of the modifiable risk factors with a specific drug. Secondary prevention follows the primary management, although intensification of treatment is well recognized as some modifications. Current and previous Polish guidelines issued in 2003 and 2008 recommended in secondary prevention of stroke: antiplatelets (mainly aspirin and ticlopidine as clopidogrel was not reimbursed until 2007 and combined preparation of aspirin and dipiridamol is not available in Poland so far), anticoagulants in atrial fibrillation (AF) patients, statins and blood pressure lowering agents (the last two should be considered for all ischaemic stroke patients) [3,4]. Secondary prevention of stroke should be established before hospital discharge. More evidence is reported on benefits produced by effective control of risk factor that reduces not only incidence but also stroke severity and improves outcome.

Stroke is also a curable disease. So far, acute ischaemic stroke specific drug treatment proved effective in randomized controlled trials is aspirin and thrombolysis. Aspirin is an immediate treatment after an ischaemic stroke to reduce the likelihood of having another stroke. Patients allocated to recombinant tissue plasminogen activator (rt-PA) up to 6 hours after stroke, are more likely to be alive with less disability. Acute stroke complications also need specific pharmacotherapy including antihypertensives in very high blood pressure, antibiotics in infections and antipyretics in fever, low molecular weight heparins in prevention of deep vein thrombosis or insulin in severe hyperglycaemia.

We aimed to evaluate the use and the early and late outcomes impact of drugs administered before and in acute ischaemic stroke patients reported in the Polish Hospital Stroke Registry and hospitalized in 2007 and 2008.

Material and methods

Data on hospitalized stroke patients reported within third edition of Polish Hospital Stroke Registry covering time-frame from 1st March 2007 to 29th February 2008 were analysed. All neurological centres in Poland were invited to participate and voluntarily report fully anonymous stroke patients data. Stroke was defined according to WHO definition as a neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours.

Data were collected with standardized web-based questionnaire, specially designed to eliminate misreporting and based on Swedish Stroke Registry and WHO *STEPwise approach to Surveillance*. The access to registry was dedicated to each participating centre and protected from unauthorised use. Data were reported fully anonymously and, additionally, analysed with blinded information on patients' allocation to particular stroke centre. To ensure the quality of reported data, randomly selected centres were audited. The following information was reported for all patients: demographics (age, gender), cardiovascular risk factors, mRS prior to stroke, time of symptom onset (if unknown, the time patient was last seen symptomless), clinical status at admission (level of consciousness), hospital management, stroke outcomes (modified Rankin Scale [mRS] at discharge) and drugs used before stroke, during hospital stay and prescribed on discharge. The manual including all important terms and definitions and easily accessible on the official website of the Registry was provided. The history of cerebrovascular events was defined as documented hospitalisation due to confirmed stroke or TIA. Hypertension was reported for patients diagnosed before or during index hospitalization (by repeated blood pressure measurements after acute phase, i.e. first seven days); threshold values for hypertension were based on JNC VII report (systolic blood pressure > 140 mm Hg or > 130 mm Hg for diabetic or chronic renal failure patients; diastolic blood pressure > 90 mm Hg or > 80 mm Hg for diabetic or chronic renal failure) [5]. Atrial fibrillation encompassed paroxysmal, persistent and permanent arrhythmias. Ischaemic heart disease could have been only reported for patients objectively diagnosed with either interventional or non-interventional methods. The history of myocardial infarction was defined as acute coronary syndrome treated in hospital 30 days before stroke onset. Finally, dyslipidaemias could have been reported only if laboratory tests conducted 3 months preceding stroke onset or during first 24 hours were available for the following: total cholesterol (> 200 mg%) or LDL cholesterol (> 100 mg%) or triglycerides (> 150 mg%) or HDL cholesterol (< 40 mg% for males and 50 mg% for females). The following drug groups were distinguished: aspirin, other antiplatelets, rt-PA, blood pressure lowering agents, oral anticoagulants, heparins, insulins, oral antidiabetic drugs, vasoactive (i.e. nicergoline, vinpocetine) and neuroprotective agents (i.e. piracetam), statins, antibiotics. In the third edition of Polish Hospital Stroke Registry, unique Polish Resident Identification Number (PESEL) was used to track annual survival of stroke patients based on data collected by Department of National Central Evidences run by Ministry of Internal Affairs and Administration.

Statistical analysis

Data were analysed separately for ischaemic stroke following ICD-10 classification (I63). Calculations and estimations were conducted for the whole ischaemic stroke patients population and appropriate subgroups identified, i.e. target population for studied drugs. Data were presented as numbers and corresponding percentages.

Multivariate regression models were used to adjust for case-mix and evaluate the impact of drugs used prior to or in acute ischaemic stroke on outcomes. The early outcomes were defined as in-hospital mortality or poor outcome (death or dependency – mRS ≥ 3) at hospital discharge. The late outcomes covered one-year follow-up and the number of days from stroke onset to death for fatal cases. Logistic regression models and Cox proportional hazard model were applied for early and late outcomes, respectively. Dedicated models controlled for distribution of age, sex, cardiovascular risk factors, disability assessed with mRS prior to stroke, consciousness at admission and treatment centres.

Results

A total number of 123 stroke centres reported data on 26 153 ischaemic stroke patients in the third edition of Polish Hospital Stroke Registry, including 94 centres which registered at least 100 patients.

Mean age of patients was 71.8 years (95% confidence interval [CI]: 71.7-71.9). For patients with first-ever stroke, mean age was 71.6 (95% CI: 71.4-71.8). Females represented 51.6% of the registered population. Table 1 shows baseline characteristics, including cardiovascular risk factors. Hypertension was most prevalent stroke risk factor, followed by ischaemic heart disease, dyslipidaemias, atrial fibrillation and diabetes. At least third patient was admitted within 4.5 hours from stroke onset.

The detailed analysis of pharmacotherapy used in patients prior to and in acute ischaemic stroke patients for general patients population and subgroups is shown in the Table 2.

Regression models after adjusting for case-mix confirmed some expected drug benefits, i.e. aspirin used at hospital was associated with better early and late prognosis (in-hospital death: OR = 0.54 [95% CI: 0.49-0.61]; poor outcome at discharge: OR = 0.85 [95% CI: 0.78-0.92], one year mortality: OR = 0.78 [95% CI: 0.74-0.83]). Antihypertensive drugs used prior to stroke were associated with lower odds of early and late mortality. Both oral anticoagulants and statins implemented during hospital stay were related to lower in-hospital

Table 1. Baseline characteristics of ischaemic stroke patients reported in the third edition of Polish Hospital Stroke Registry

	N	%
History of stroke	5847	22.4
Hypertension	19 010	72.7
Atrial fibrillation	6168	23.6
Ischaemic heart disease	8305	31.8
History of myocardial infarction	2627	10.04
Diabetes	6141	23.5
Smoking	3489	13.3
Alcohol abuse	1389	5.3
Dyslipidaemias	6722	25.7
Modified Rankin scale score prior to stroke:		
0	13 678	55.1
1	3866	15.6
2	2843	11.5
3	1749	7.0
4	1583	6.4
5	1128	4.5
Time from onset to admission < 4.5 hours (including missing data or unknown time of onset)	8398	32.1
Consciousness disturbances:		
Alert	19 907	76.2
Drowsy	4095	15.7
Stupor	1297	5.0
Coma	819	3.1

Table 2. Pharmacotherapy prior to stroke and used during hospital stay

Drugs used prior to stroke	**N**	**%**
Blood pressure lowering agents in hypertensive patients	14 594	75.8
Blood pressure lowering agents in patient with history of stroke	4184	71.6
Antiplatelets in patients with history of stroke	3474	59.4
Antiplatelets in patients with history of MI or IHD	4704	52.3
Oral anticoagulants in patients with AF	668	10.83
Statins	4020	15.37
Statins in patients with history of stroke	1451	24.8
Statins in patients with history of MI or IHD	2290	25.5
Statins in patients with dyslipidaemias	2085	31.0
Vasoactive agents	1470	5.6
Neuroprotective agents	1895	7.3
Antibiotics	244	0.9
Drugs used during hospital stay	**N**	**%**
rtPA– thrombolysis	296	1.1
Blood pressure lowering agents	20 008	76.5
Blood pressure lowering agents in hypertensive patients	17 097	89.9
Aspirin	21 484	82.1
Other antiplatelets	2159	8.26
Oral anticoagulants in AF patients	1150	18.6
Heparins	8269	31.6
Statins	11 848	45.3
Insulin	3087	50.3
Antibiotics	7469	28.6
Vasoactive agents	6425	24.6
Neuroprotective agents	14 281	54.6

MI – myocardial infarction, IHD – ischaemic heart disease, AF – atrial fibrillation, rt-PA – recombinant tissue plasminogen activator

mortality and risk of poor outcome at discharge. The latter used prior to stroke, as well as aspirin before stroke onset, were associated with better functional outcome at discharge. Drugs used prior to or in acute ischaemic stroke and found in multivariate regression models statistically significantly associated with early and late outcomes are presented in Table 3.

Discussion

Drug utilisation before cerebrovascular accident and in acute ischaemic stroke is important in monitoring of the current medical practice. It can also show the benefit of pharmacotherapy in real world settings. Data from the Polish Hospital Stroke Registry provide a unique opportunity to both – the evaluation of the current practice and providing evidences on possible drug related benefit based on everyday clinical practice data.

The pharmacotherapy practice prior to and in acute ischaemic stroke

Antihypertensive drugs were used prior to stroke on average by three out of four patients with hypertension in the Polish Hospital Stroke Registry. Compared to findings from other national registries it is less than in England, Wales and North Ireland, where almost 82% of hypertensive patients were treated with blood pressure lowering agents before stroke onset, but substantially more than in Sweden (55% of hypertensive males and 59% hypertensive females) [6,7]. We lack data on effectiveness of blood pressure control with antihypertensive prior to ischaemic stroke in the Polish Hospital Stroke Registry. Almost 90% of hypertensive patients were treated with blood pressure lowering compounds during hospitalization. As blood pressure tends to fluctuate in acute stroke, the assessment of antihypertensive agents is limited. However, only three quarters of total ischaemic stroke population were treated with blood pressure lowering drugs while guidelines clearly state that treatment must be considered in every, including normotensive, stroke patient. As the secondary stroke prevention should be established during hospital stay and hardly ever hypotensive treatment needs late (after discharge) start, thus one can argue there is still room to improve secondary prevention with blood pressure lowering agents.

Antiplatelets before stroke onset were used only by half of patients with history of myocardial infarction or

Table 3. The statistically significant findings of multivariate regression models on the drugs associated with early and late ischaemic stroke outcome

Drugs associated with in-hospital mortality:	***p*-value**	**OR**	**95% CI**
Antihypertensives prior to stroke	0.009	0.859	0.766-0.963
Antihypertensives in hospital	0.005	0.836	0.750-0.933
Aspirin in hospital	< 0.001	0.544	0.489-0.607
Oral anticoagulants in hospital	0.027	0.764	0.600-0.966
Statins in hospital	< 0.001	0.518	0.464-0.577
Antibiotics in hospital	< 0.001	3.710	3.372-4.084
Drugs associated with functional outcome at discharge:			
Aspirin prior to stroke	0.004	0.898	0.833-0.967
Statins prior to stroke	< 0.001	0.822	0.746-0.906
Aspirin in hospital	< 0.001	0.849	0.780-0.923
Oral anticoagulants in hospital	< 0.001	0.540	0.457-0.638
Statins in hospital	< 0.001	0.932	0.873-0.996
Antibiotics in hospital	< 0.001	2.681	2.152-3.352
Drugs associated with one year survival:			
Antihypertensives prior to stroke	0.001	0.904	0.854-0.957
Aspirin in hospital	< 0.001	0.782	0.740-0.826

OR – odds ratio, CI – confidence interval

ischaemic heart disease and slightly more often in patients with secondary stroke. Aspirin, especially used within 24 hours from stroke onset, if thrombolysis is not implemented, is established stroke care quality indicator as it is the only one antiplatelet of evidence-based benefit confirmed also in our study results or other Polish trials [8-11].The use of aspirin in acute ischaemic stroke in Poland is very similar to other countries [12, 13]. Not only aspirin use, but the timing of its application (first 48 hours) is important and that needs further assessment in Polish clinical practice.

Low use of anticoagulants in AF patients prior to stroke needs special consideration as AF is important risk factor of stroke and anticoagulants are very effective in preventing it. Hardly every tenth ischaemic stroke patient with AF received anticoagulants prior to stroke and that is very similar to findings from Swedish Stroke Registry, Danish Stroke Registry for secondary stroke patients and international European study of first-ever stroke [14-16]. Only in SAFE II study, the corresponding anticoagulant use rate was 22.2% but it was reported for patients with diagnosed AF and confirmed in ECG within 24 months prior to stroke [17]. Anticoagulation in AF stroke patients is also established stroke care quality indicator. In acute ischaemic stroke, use of oral anticoagulants should be started within first 2 weeks – the later the more severe stroke is. It should be stressed that less than 19% of ischaemic stroke patients with AF had treatment with oral anticoagulants initiated during hospital stay and only 21% were prescribed these drugs at discharge (data not presented). Substantial inter-countries variability in oral anticoagulants ordered at hospital discharge of AF stroke patients is well documented. In Sweden one-third of patients (even 46% of patients discharged home) is offered oral anticoagulants at hospital discharge. In cited SAFE II study, the corresponding value was 58.1% (range: 40.8% for Italy to 67.5% for France), but authors concluded that anticipated percentage of patients eligible (with no contraindications) for long-term oral anticoagulation can reach even 80%. Therefore further monitoring and improvement in that aspect of preventive stroke pharmacotherapy is more than justified. The availability of new oral anticoagulants could probably contribute to better control of stroke risk in AF patients.

Thrombolysis, the only beneficial drug therapy in acute ischaemic stroke apart from aspirin, was used only for 1.1% of studied population but since 2005 dedicated registry to rt-PA in stroke was operating (*Tromboliza w Udarze Mózgu* – TUM) the Polish Hospital Stroke Registry was probably affected by underreporting of that treatment as specific data on its use was collected elsewhere.

Statins were used only for one fourth of patients with history of stroke or myocardial infarction and ischaemic heart disease. One can expect that availability of statins generics contribute currently to their higher utilization in clinical practice. Nevertheless, use of statins prior to stroke was more driven by dyslipidaemias than cardiovascular diseases and did not reflect clinical guidelines. Statins were used only in 45% of patients during hospital stay. Although statins are not recommended in acute ischaemic stroke treatment, they should be considered in secondary prevention for every patient, thus these drugs seem to be underused in the Polish Hospital Stroke Registry.

Almost one third of acute ischaemic stroke patients were treated with heparins as low molecular weight heparins were shown to be effective in prevention of deep venous thrombosis in bed-driven patients [18,19]. As data on type of heparin used were not available, the more in depth analysis was not possible, but it should be noted that high doses of heparins were not shown to be beneficial in stroke patients and unfractionated heparins are less popular in Poland as well as reported very rarely in Swedish Stroke Registry [20,21].

Antibiotics use reflects the risk of infectious complications and indirectly indicates the quality of acute stroke care. The prophylactic treatment with antibiotics is neither effective nor recommended [22]. Almost one third of ischaemic stroke patients in the Polish Hospital Stroke Registry was treated with antibiotics in hospital and that is in accordance with systematic review of 87 studies involving 137 817 patients, which estimated the overall pooled infection rate complicating acute stroke at 30% and even 45% for intensive care unit studies [23].

Finally, the vasoactive (i.e. nicergoline, vinpocetine) and neuroprotective compounds (i.e. piracetam) are still popular in the management of acute ischaemic stroke. These drugs have not been shown effective in randomized clinical trials. Although these drugs are less and less common in following edition of the Polish Hospital Stroke Registry (data not presented; in first edition of the Polish Hospital Stroke Registry the corresponding rate was 33.1 and 79.9%, respectively), they are still fairly popular. As a kind of negative indicator, the use of vasoactive and neuroprotective agents can be used to reflect the dissemination of evidence-based clinical practice. It should be stressed that these drugs were used

rarely prior to stroke and much more often during hospital stay, thus hospital management results in increased use of these drugs and therefore should be further monitored and improved.

The impact of drugs used before cerebrovascular accident or in acute ischaemic stroke on patients prognosis

The findings from the Polish Hospital Stroke Registry should be interpreted with caution as it is exploratory analysis and can be only used to generate hypotheses that need to be confirmed in randomized controlled settings.

The early and long-term survival benefit of antihypertensive agents used prior to stroke observed in our study was also noted for drugs blocking renin-angiotensin-aldosterone system and confirmed by Grabska *et al*. in the analysis of stroke patients admitted to 2nd Neurological Department of Institute of Psychiatry and Neurology in Warsaw [24-26].

In our study, statins used prior to stroke were associated with lower risk of poor outcome at discharge. The benefit of these drugs used before stroke was confirmed in systematic review of 13 clinical trials, especially for patients with diabetes, elderly and concomitant hypertension or other cardiovascular diseases as well as for those with normal LDL cholesterol concentration [27]. In meta-analysis, Cordenier *et al*. also noted beneficial impact of pre-treatment with statin on in-hospital mortality, but did not observe improvement on 3 month functional outcome [28].

Stimulating finding from our study, justifying future clinical trials, concerns the early benefits (reduced in-hospital mortality and improved functional outcome at discharge) associated with statin use during hospital stay. In Cochrane systematic review, 8 clinical trials on statin use within first 2 weeks from TIA or stroke onset were identified [29]. Authors concluded that data available from randomized trials are still insufficient to establish whether statins are safe and effective in cases of acute ischaemic stroke and TIA and further randomized clinical trials are needed.

The benefit of oral anticoagulants observed in our study reflects rather the quality of stroke care (as specific data on the quality of stroke care were limited we could not fully control for that confounder) then the real advantage of these drugs used in acute stroke.

Our study has a number of limitations, some of them were already mentioned. Main limitation is voluntarily reported, not fully representative, sample of registered patients and limited scope of collected data. Nevertheless it is so far the largest study on real world everyday stroke care in Poland.

Conclusions

1. The prevention of ischaemic stroke with blood pressure lowering agents, anticoagulants in AF, antiplatelets and statins is inadequate and needs to be monitored and improved.
2. Evidence-based treatment of acute ischaemic stroke, as reflected by more aspirin and thrombolysis and less neuroprotective drugs use, requires further promotion.
3. The benefits of acute ischaemic stroke treatment with statins require confirmation in randomized controlled settings.

Acknowledgements and funding

The chief acknowledgement is to the thousands of stroke patients who joined the Polish Hospital Stroke Registry and to their doctors who reported data voluntarily and complimentary.

The study was supported by unrestricted, scientific grant from Polish Ministry of Health, National Cardiovascular Disease Prevention and Treatment Program – POLKARD 2007-2008.

Disclosure

Authors report no conflict of interest.

References

1. Rothwell P.M., Coull A.J., Giles M.F., et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet* 2004; 363: 1925-1933.
2. O'Donnell M.J., Xavier D., Liu L., et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet* 2010; 376: 112-123.
3. Wytyczne Grupy Ekspertów Narodowego Programu Profilaktyki i Leczenia Udaru Mózgu dotyczące organizacji pododdziałów udarowych. *Neurol Neurochir Pol* 2003; 37: 11-16.
4. Grupa Ekspertów Narodowego Programu Profilaktyki i Leczenia Chorób Układu Sercowo-Naczyniowego POLKARD. Postępowanie w udarze mózgu. Wytyczne Grupy Ekspertów Narodowego Programu Profilaktyki i Leczenia Chorób Układu

Sercowo-Naczyniowego POLKARD. *Neurol Neurochir Pol* 2008; 42: S201-S288.
5. Chobanian A.V., Bakris G.L., Black H.R., et al. Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. *Hypertension* 2003; 42: 1206-1252.
6. Prepared on behalf of the Intercollegiate Stroke Working Party by Clinical Effectiveness and Evaluation Unit Royal College of Physicians of London. National Sentinel Stroke Audit Phase 1 (organisational audit) 2006 Phase 2 (clinical audit) 2006, kwiecień 2007; http://www.rcplondon.ac.uk/sites/default/files/org_and_clinical_2006_concise-stroke-audit-round-5_2007.pdf (accessed: 25.02.2013).
7. Appelros P., Jonsson F., Asplund K., et al. Trends in baseline patient characteristics during the years 1995-2008: observations from Riks-Stroke, the Swedish Stroke Register. *Cerebrovasc Dis* 2010; 30: 114-119.
8. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. International Stroke Trial Collaborative Group. *Lancet* 1997; 349: 1569-1581.
9. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. *Lancet* 1997; 349: 1641-1649.
10. Sandercock P.A., Counsell C., Gubitz G.J., et al. Antiplatelet therapy for acute ischaemic stroke. *Cochrane Database Syst Rev* 2008: CD000029.
11. Nowacki P., Bajer-Czajkowska A., Masztalewicz M. Clinical characteristics of early and late recurrent ischaemic stroke. *Neurol Neurochir Pol* 2010; 44: 123-130.
12. Sposato L.A., Esnaola M.M., Zamora R., et al. Quality of ischaemic stroke care in emerging countries: the Argentinian National Stroke Registry (ReNACer). *Stroke* 2008; 39: 3036-3041.
13. Barber A., Charleston A., Anderson N., et al. Changes in stroke care at Auckland Hospital between 1996 and 2001. *N Z Med J* 2004; 117: U797.
14. Glader E.L., Stegmayr B., Norrving B., et al. Large variations in the use of oral anticoagulants in stroke patients with atrial fibrillation: a Swedish national perspective. *J Int Med* 2004; 255: 22-32.
15. Jorgensen H.S., Nakayama H., Reith J., et al. Stroke recurrence: predictors, severity, and prognosis. The Copenhagen Stroke Study. *Neurology* 1997; 48: 891-895.
16. Lamassa M., Di Carlo A., Pracucci G., et al. Characteristics, outcome, and care of stroke associated with atrial fibrillation in Europe: data from a multicenter multinational hospital-based registry (The European Community Stroke Project). *Stroke* 2001; 32: 392-398.
17. Deplanque D., Leys D., Parnetti L., et al. Stroke prevention and atrial fibrillation: reasons leading to an inappropriate management. Main results of the SAFE II study. *Br J Clin Pharmacol* 2004; 57: 798-806.
18. Sherman D.G., Albers G.W., Bladin C., et al. The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke (PREVAIL Study): an open-label randomised comparison. *Lancet* 2007; 369: 1347-1355.
19. Sherman D.G. Prevention of venous thromboembolism, recurrent stroke, and other vascular events after acute ischaemic stroke: the role of low-molecular-weight heparin and antiplatelet therapy. *J Stroke Cerebrovasc Dis* 2006; 15: 250-259.
20. Sandercock P.A., Counsell C., Kamal A.K. Anticoagulants for acute ischaemic stroke. *Cochrane Database Syst Rev* 2008: CD000024.
21. Eriksson M., Stecksen A., Glader E.L., et al. Discarding heparins as treatment for progressive stroke in Sweden 2001 to 2008. *Stroke* 2010; 41: 2552-2558.
22. Chamorro A., Horcajada J.P., Obach V., et al. The Early Systemic Prophylaxis of Infection After Stroke study: a randomized clinical trial. *Stroke* 2005; 36: 1495-1500.
23. Westendorp W.F., Nederkoorn P.J., Vermeij J.D., et al. Post-stroke infection: a systematic review and meta-analysis. *BMC Neurology* 2011; 11: 110.
24. Fuentes B., Fernandez-Dominguez J., Ortega-Casarrubios M.A., et al. Treatment with angiotensin receptor blockers before stroke could exert a favourable effect in acute cerebral infarction. *J Hypertens* 2010; 28: 575-581.
25. Chitravas N., Dewey H.M., Nicol M.B., et al. Is prestroke use of angiotensin-converting enzyme inhibitors associated with better outcome? *Neurology* 2007; 68: 1687-1693.
26. Grabska K., Gromadzka G., Czlonkowska A. Prestroke antihypertensive therapy: effect on the outcome. *Clin Exp Hypertens* 2013; 35: 141-147.
27. Lakhan S.E., Bagchi S., Hofer M. Statins and clinical outcome of acute ischaemic stroke: a systematic review. *Int Arch Med* 2010; 3: 22.
28. Cordenier A., De Smedt A., Brouns R, et al. Pre-stroke use of statins on stroke outcome: a meta-analysis of observational studies. *Acta Neurol Belg* 2011; 111: 261-267.
29. Squizzato A., Romualdi E., Dentali F., et al. Statins for acute ischaemic stroke. *Cochrane Database Syst Rev* 2011: CD007551.