#### NEUROLOGIA I NEUROCHIRURGIA POLSKA 48 (2014) 85-90



Available online at www.sciencedirect.com

# **ScienceDirect**

journal homepage: http://www.elsevier.com/locate/pjnns



# Original research article

# Secondary prevention of stroke in elderly people in Poland—Results of PolSenior study

Beata Łabuz-Roszak a,\*, Michał Skrzypek b, Krystyna Pierzchała a, Agnieszka Machowska-Majchrzak a, Małgorzata Mossakowska c, Jerzy Chudek <sup>d</sup>, Iwona Mańka-Gaca <sup>a</sup>, Wojciech Bartman <sup>a</sup>, Andrzej Więcek <sup>e</sup>

## ARTICLE INFO

Article history: Received 8 August 2013 Accepted 24 November 2013 Available online 23 January 2014

Keywords: Stroke The elderly Secondary prevention Oral anticoagulant drugs Antiplatelet drugs Acetylsalicylic acid

#### ABSTRACT

Background and purpose: The purpose of the study was to evaluate the frequency of use of oral antiplatelet (OAP) and anticoagulant (OAC) drugs as secondary stroke prevention among older people in Poland and its association with sociodemographic factors, place of residence, and concomitant cardiovascular risk factors.

Material and methods: The study group consisted of 426 subjects with a history of a previous stroke (mean age of  $81.5 \pm 8.2$  years), participants of multicentre, population-based PolSenior study.

Results: Among the study group, 261 people (61.3%) used at least one drug as a secondary prevention. OAPs were regularly used by 237 people (55.6%), and OACs—by 25 people (5.9%). The most often used drug was acetylsalicylic acid. Ticlopidine was more frequently used than clopidogrel, and acenocoumarol was used more often than warfarin. Among all of the concomitant cardiovascular risk factors, congestive heart failure was mostly associated with OAP treatment, and a history of atrial fibrillation—with OAC treatment. Use of drugs did not depend on age, sex, place of residence (rural or urban), level of education and personal income, but it was associated with the region where the respondents lived.

Conclusions: Secondary cardiovascular preventive therapy in Poland is used too rarely in older people after stroke, and it especially concerns anticoagulant therapy in those with a history of atrial fibrillation. Structured educational programmes should be developed in Poland to improve usage of secondary preventive therapy in the elderly.

© 2014 Polish Neurological Society. Published by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

<sup>&</sup>lt;sup>a</sup> Department of Neurology, Medical University of Silesia, Zabrze, Poland

<sup>&</sup>lt;sup>b</sup>Department of Biostatistics, Faculty of Public Health, Medical University of Silesia, Katowice, Poland

<sup>&</sup>lt;sup>c</sup> International Institute of Molecular and Cell Biology, Warsaw, Poland

<sup>&</sup>lt;sup>d</sup> Department of Pathophysiology, Medical University of Silesia, Katowice, Poland

<sup>&</sup>lt;sup>e</sup> Department of Nephrology, Endocrinology and Metabolic Diseases, Medical University of Silesia, Katowice, Poland

<sup>\*</sup> Corresponding author at: Department of Neurology, Medical University of Silesia, ul.3-go Maja 13/15, 41-800 Zabrze, Poland. Tel.: +48 32 278 5326.

E-mail address: beatamaria.pl@hoga.pl (B. Łabuz-Roszak).

Table 1 – Frequency of use of particular medications in the study group ( $N=426$ ).				
	International drug name	Number of respondents using the drug n (%)		
Oral antiplatelet drugs (n = 237)	Acetylsalicylic acid Clopidogrel Ticlopidine	222 (52.1%) 6 (1.4%) 22 (5.2%)		
Oral anticoagulant drugs (n = 25)	Acenocoumarol Warfarin	25 (5.8%) 1		

## 1. Introduction

Stroke is a major cause of morbidity and mortality worldwide. The incidence of stroke in Poland is estimated at 175 per 100,000 for men and 125 per 100,000 for women and is similar to other European countries but the mortality is greater [1–5]. A history of a previous stroke is an important risk factor for subsequent cerebrovascular incidents. The most commonly used drugs worldwide in secondary prevention of stroke are oral antiplatelet agents (OAP), and among them – acetylsalicylic acid (ASA) [6]. The occurrence of cerebrovascular incidents has been reduced by 25% in patients regularly taking ASA [7,8]. Another group of medications used in secondary prevention are oral anticoagulant (OAC) drugs, especially recommended for prevention of recurrent stroke in people with atrial fibrillation [9].

The incidence of stroke increases significantly with age, and age is considered to be the strongest risk factor for cerebrovascular disease. Little is known about the usage of OAPs and OACs as the secondary prevention of stroke by the elderly in our country.

Thus, the purpose of the study was to evaluate the frequency of use of OAP and OAC drugs as secondary stroke prevention among older people in Poland and its association with clinical characteristics and concomitant cardiovascular risk factors.

## 2. Materials and methods

The study was based on the data collected during the implementation of a multicentre, publicly funded research project commissioned by the Polish Ministry of Science and Higher Education called 'Medical, psychological, sociological and economic aspects of ageing of people in Poland (PolSenior)' (PBZ-MEiN-9/2/2006). A detailed description of the project has been previously published [10,11]. The project was carried out from October 2008 to April 2012. It was approved by the Bioethics Commission of the Medical University of Silesia in Katowice.

The study group included respondents from the PolSenior project aged 65 years and older who answered positively to the question: 'Have you ever been hospitalized because of a stroke?' The following data from the general PolSenior database were used and analysed: age, sex, place of residence (village or city, or staying at a nursing home), level of education, personal income, a history of cardiovascular risk factors (coronary heart disease, previous myocardial infarction, congestive heart failure, pharmacologically treated hypertension, a history of atrial fibrillation, another previous stroke, pharmacologically treated diabetes, pharmacologically treated dyslipidaemia, active smoking), body mass index. The frequency of use of drugs was based on the data collected in the medical part of the questionnaire, including the international and trade names of drugs taken by participants.

Statistical data analysis was performed using SAS version 9.2 (SAS Institute Inc., Gary, NC). The level of statistical

Table 2 – Oral antiplatelet drugs (OAPs) and oral anticoagulant drugs (OACs) usage after stroke in different regions of Poland.					
Region	All the examined subjects n	OAP or OAC n (%)	OAP n (%)	OAC n (%)	
Central	92	48 (52.2%)	42 (45.7%)	6 (6.5%)	
South	76	51 (67.1%)	48 (63.2%)	3 (4.0%)	
East	85	59 (69.4%)	56 (65.9%)	4 (4.7%)	
North-West	62	35 (56.5%)	30 (48.4%)	5 (8.1%)	
South-West	49	27 (55.1%)	25 (51.0%)	2 (4.1%)	
North	62	44 (66.1%)	36 (58.1%)	5 (8.1%)	
p-Value		0.12	0.05	0.83	

Level of education	All the examined subjects	OAPs and/or OACs	OAPs	OACs
	n	n (%)	n (%)	n (%)
No declared education	7	3 (42.9%)	3 (42.9%)	0 (0%)
Incomplete elementary	56	31 (55.4%)	28 (50%)	3 (5.4%)
Complete elementary	187	121 (64.7%)	111 (59.4%)	11 (5.9%)
Professional	48	30 (62.5%)	27 (56.3%)	3 (6.3%)
High school	72	48 (66.7%)	40 (55.6%)	8 (11.1%
University	37	18 (48.7%)	18 (48.7%)	0 (0%)
p-Value		0.29	0.7	0.3

Table 4 – Association between personal income and oral antiplatelet drugs (OAPs) and oral anticoagulant drugs (OACs) usage (n = 297, not documented in 129).

Personal income zloty/mouth	All the examined subjects n	OAP or OAC n (%)	OAP n (%)	OAC n (%)
Less than 1000	126	77 (61.1%)	69 (54.8%)	9 (7.1%)
1001–1500	104	74 (71.2%)	64 (61.5%)	10 (9.6%)
1501–2000	45	28 (62.2%)	25 (55.6%)	3 (6.7%)
2001 and more	22	14 (63.6%)	14 (63.6%)	0 (0.0%)
p-Value		0.43	0.69	0.47

significance was  $p \le 0.05$ . The following tests were used: the  $\chi^2$  test, Fisher exact test, the Shapiro–Wilk test, the Student t-test, and the Wilcoxon rank sum test. A model of logistic regression was used to analyse the association between cardiovascular risk factors and treatment with OAP and/or OAC drugs.

# 3. Results

Among all the PolSenior participants aged 65 and older (n=4979), 426 people (8.6%) answered 'Yes' to the question: 'Have you ever been hospitalized because of a stroke?' and they were included in the analysis. The study group consisted of 236 men (55.4%) and 190 women (44.6%). The mean age of the examined subjects was  $81.5 \pm 8.2$  years, similar for men and women ( $81.1 \pm 8.7$  vs.  $81.9 \pm 7.5$  years p=0.33, respectively).

Among all the patients with a history of a stroke, 261 subjects (61.3%) used at least one drug as the secondary prevention. Oral antiplatelets were regularly used by 237 people (55.6%); 224 (94.5%) were taking one drug, and 13 (5.5%) were taking two drugs. Oral anticoagulants were regularly used by 25 subjects (5.9%) (one respondent was taking two OACs). Antiplatelet therapy and anticoagulant therapy were simultaneously applied by only one person (Table 1).

The percentage of women after stroke using OAPs and/or OACs (61.1%; n = 116) was similar to the corresponding percentage of men after stroke (61.4%; n = 145) (p = 0.93). Also

Table 5 – Frequency of concomitant cardiovascular risk factors in the study group (n = 426).

Risk factor	n (%)	Not documented n (%)
Previous strokes <sup>a</sup>	107 (25.1%)	28 (6.6%)
Pharmacologically treated hypertension	311 (73%)	-
Previous myocardial infarct	77 (18.1%)	21 (4.9%)
History of atrial fibrillation	105 (22.6%)	30 (7%)
Coronary heart disease (without myocardial infarct)	77 (18.1%)	22 (5.2%)
Congestive heart failure	69 (16.2%)	25 (5.6%)
Pharmacologically treated diabetes	89 (20.9%)	130 (30.5%)
Pharmacologically treated dyslipidaemia	153 (35.9%)	-
Current smoker	31 (7.3%)	4 (0.9%)
Overweight/obesity (BMI $\geq$ 25 kg/m <sup>2</sup> )	248 (58.2%)	82 (19.2%)

BMI, body mass index.

Table 6 – Frequency of oral antiplatelet drugs (OAPs) and/ or oral anticoagulant drugs (OACs) usage in association with presence (+) or absence (-) of concomitant cardiovascular risk factors (N = 426).

Risk factor	OAP or OAC	OAP	OAC
	n (%)	n (%)	n (%)
Previous stroke	es <sup>a</sup>		
(+)	70 (65.42%)	63 (58.88%)	8 (7.48%)
(-)	179 (61.51%)	162 (55.67%)	17 (5.84%)
p-Value	0.48	0.57	0.55
	ally treated hypert	ension	
(+)	219 (70.42%)	196 (63.02%)	24 (7.72%)
(-)	42 (36.52%)	41 (35.65%)	1 (0.87%)
p-Value	<0.01	<0.01	<0.01
Previous myoc	ardial infarct		
(+)	58 (75.32%)	50 (64.94%)	9 (11.69%)
(-)	189 (57.62%)	174 (53.05%)	15 (4.57%)
p-Value	<0.01	0.06	0.03
History of atria	al fibrillation		
(+)	73 (69.52%)	53 (50.48%)	21 (20.00%)
(-)	168 (57.73%)	164 (56.36%)	4 (1.37%)
p-Value	0.03	0.30	<0.01
Coronary hear	t disease (without 1	myocardial infarct)	
(+)	53 (68.83%)	45 (58.44%)	8 (10.39%)
(–)	195 (59.63%)	181 (55.35%)	15 (4.59%)
p-Value	0.14	0.62	0.06
Congestive hea			
(+)	52 (75.36%)	45 (65.22%)	7 (10.14%)
(-)	193 (58.13%)	178 (53.61%)	16 (4.82%)
p-Value	0.01	0.08	0.09
	ally treated diabete		C (C 70/)
(+)	64 (71.9%)	58 (65.2%)	6 (6.7%)
(-)	129 (62.3%)	114 (55.1%)	16 (7.7%)
p-Value	0.11 ally treated dyslipi	0.11	1.00
_	120 (78.4%)	106 (69.3%)	15 (9.8%)
(+)	141 (51.7%)	131 (48.0%)	10 (3.7%)
(–) p-Value	<0.01	<0.01	0.02
Current smoke		<0.01	0.02
(+)	18 (58.1%)	16 (51.6%)	2 (6.5%)
(-)	241 (61.6%)	220 (56.3%)	22 (5.6%)
p-Value	0.69	0.62	0.69
Overweight/ob		0.02	0.05
$(BMI \ge 25 \text{ kg/m})$	•		
(+)	163 (65.7%)	141 (56.9%)	23 (9.3%)
(-)	60 (62.5%)	58 (60.4%)	2 (2.1%)
p-Value	0.57	0.55	0.02
Sex			
Female	116 (61.1%)	102 (53.7%)	15 (7.9%)
Male	145 (61.4%)	135 (57.2%)	10 (4.2%)
p-Value	0.96	0.47	0.15

BMI, body mass index.

<sup>&</sup>lt;sup>a</sup> Two or more incidents of stroke.

 <sup>&</sup>lt;sup>a</sup> Two or more incidents of stroke; drugs, (+), risk factor present;
(-), risk factor absent.

Table 7 - Association of concomitant cardiovascular risk factors with oral antiplatelet drugs (OAPs) and/or	r oral
anticoagulant drugs (OACs) treatment ( $N = 426$ ).	

Risk factor	OAP or OAC		OAP		OAC	
	OR (95% CI)	p-Value	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Previous strokes <sup>a</sup>	1.22	0.6	1.24	0.55	0.82	0.78
	(0.58-2.57)		(0.62-2.49)		(0.21-3.31)	
Pharmacologically treated hypertension	1.85	0.11	1.73	0.14	3.87	0.27
	(0.87 - 3.94)		(0.83-3.6)		(0.35-43.26)	
Previous myocardial infarct	2.61	0.08	2.3	0.07	0.84	0.81
	(0.89-7.66)		(0.94-5.62)		(0.2-3.5)	
History of atrial fibrillation	1.11	0.79	0.38	0.01	31.47	< 0.01
	(0.51-2.42)		(0.18-0.78)		(6.59-150.16)	
Coronary heart disease (without myocardial infarct)	0.67	0.39	0.64	0.29	1.21	0.79
	(0.28-1.64)		(0.28-1.46)		(0.3-4.95)	
Congestive heart failure	3.02	0.05	2.69	0.04	0.46	0.32
	(1.02-8.88)		(1.06-6.8)		(0.1-2.12)	
Pharmacologically treated diabetes	1.74	0.12	1.73	0.1	0.61	0.49
	(0.86-3.52)		(0.9-3.33)		(0.15-2.48)	
Pharmacologically treated dyslipidaemia	2.35	0.01	1.27	0.46	10.91	< 0.01
	(1.18-4.65)		(0.68-2.38)		(2.4-49.65)	
Current smoker	0.65	0.39	0.72	0.5	0.73	0.81
	(0.24-1.75)		(0.28-1.87)		(0.06-9.39)	
Overweight/obesity	0.88	0.72	0.72	0.36	5.89	0.14
$(BMI \ge 25 \text{ kg/m}^2)$	(0.43-1.8)		(0.36-1.44)		(0.57-61.23)	
Sex (male/female)	1.69	0.16	1.89	0.06	0.36	0.16
	(0.82-3.49)		(0.96-3.7)		(0.08-1.51)	

OR, odds ratio: CI, confidence interval.

the age of the respondents did not affect the prevalence of secondary stroke prevention.

Most of analysed group lived in cities (61.2%; n=264). There was no difference in using OAP and/or OAC drugs between urban (61.4%; n=162) and rural (61.1%; n=99) residents (p=0.96). In the study group, there were 8 residents of nursing houses (1.9%) and 5 of them (62.5%) used OAP and/or OAC drugs.

We observed significant differences in the frequency of usage of antiplatelet drugs, depending on the province where the respondents lived. Oral antiplatelets were mostly applied by people from East (65.9% of respondents living in this region) and South (63.2%), while the lowest amount was applied by people living in Central region (45.7%), and North-West (48.4%). A detailed analysis of OAPs and/or OACs usage in different Polish regions is presented in Table 2.

No correlation was found between the frequency of use of OAPs and/or OACs after stroke and the level of education (Table 3) or personal income (Table 4).

The frequency of cardiovascular risk factors in the whole study group is shown in Table 5. The association between use of OAP and/or OAC drugs and presence or absence of cardiovascular risk factors is presented in Table 6. Among all of the cardiovascular risk factors, congestive heart failure was most associated with OAP treatment, and a history of atrial fibrillation—with OAC treatment (Table 7).

# 4. Discussion

The study was based on a countrywide representative sample of Poles aged 65 years or older and presented the prevalence of

secondary preventive therapy among a group of respondents after at least one episode of stroke. We found that in Poland about 60% of older people after stroke were applying secondary pharmacological prevention, and it seemed to be less than in other Western European countries [12–14], especially in people with atrial fibrillation [12]. Only one fifth of older Polish people with atrial fibrillation used OACs. According to the Swedish Stroke Register more than 30% of people after stroke with atrial fibrillation are applying OACs [12]. It should be stressed that the Swedish Stroke Register population was younger than in our study (mean age about 75 years).

Both worldwide and in Poland, the most popular drug used as secondary cardiovascular prevention is ASA. We also observed that ticlopidine was used more frequently in Poland than clopidogrel, probably because of the financial reasons (until recently, the preparations of clopidogrel in Poland were much more expensive than ticlopidine). Dual antiplatelet therapy was used by about 5% of respondents and the most common combination was ASA with ticlopidine.

We found that dipyridamole was not at all used in Poland. This drug is recommended in combination with ASA in patients after stroke who used ASA before or in patients after recurrent strokes [15,16]. The monthly cost of such combination is much higher than the therapy with ASA alone. In our country, not only the price, but also low availability of dipyridamole (it is not dispensed in Polish pharmacies), poses the problem. For instance, in Sweden it is prescribed in more than 10% of people discharged from the hospital after an ischaemic stroke [13].

We noticed that acenocoumarol was much more popular than warfarin in Poland, contrary to the situation in other

<sup>&</sup>lt;sup>a</sup> Two or more incidents of stroke.

countries [12–14]. In our opinion, it was also associated with low availability and high price of the drug for the patient in the period when the study was conducted.

Contrary to our previous paper [17], concerning general usage of OAPs and OACs in the whole PolSenior population, we found no association between applying of secondary cardiovascular prevention and age, sex, place of residence, level of education, and personal income.

However, our study revealed significant differences in the frequency of usage of analysed drugs, depending on the region where the respondents lived. In some regions, the prevalence of secondary pharmacological prevention was much lower than the average. It especially concerned Central region and North-West region. The number of people living in particular regions was rather low and it might influence the statistics but it should be checked in further examinations.

# 5. Limitations of the study

The reasons for abandonment of therapy (contraindications), the type of the stroke (ischaemic or haemorrhagic), and the time from the stroke could not be established because of the lack of data.

#### 6. Conclusions

- In Poland secondary cardiovascular preventive therapy is used too rarely in older people after stroke, and it especially concerns anticoagulant therapy in those with a history of atrial fibrillation.
- The frequency of use of OAPs and OACs as the secondary prevention in elderly people is not associated with age, sex, place of residence (urban or rural), level of education, and personal income.
- 3. The usage of OACs and/or OACs depends on the region where the respondents lived.
- 4. Among all the analysed drugs, the most popular is ASA. Ticlopidine is more popular than clopidogrel, and aceno-coumarol—than warfarin. Dipiridamole is not used in Poland as secondary prevention.
- 5. Among all of the concomitant cardiovascular risk factors, congestive heart failure was most associated with OAP treatment in the elderly after stroke, and a history of atrial fibrillation—with OAC treatment. Structured educational programmes should be developed in our country to improve usage of secondary preventive therapy in the elderly.

# **Conflict of interest**

None declared.

# Acknowledgement and financial support

Implemented under publicly funded project No. PBZ-MEIN-9/2/2006, Ministry of Science and Higher Education.

#### **Ethics**

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

#### REFERENCES

- [1] Sienkiewicz-Jarosz H, Głuszkiewicz M, Pniewski J, Niewada M, Członkowska A, Wolfe C, et al. Incidence and case fatality rates of first-ever stroke—comparison of data from two prospective population-based studies conducted in Warsaw. Neurol Neurochir Pol 2011;45: 207–12.
- [2] Mazurek M. Umieralność z powodu udarów mózgu w Polsce – rola badań obserwacyjnych opartych na danych z baz informatycznych. Wiad Lek 2005;58: 397–402.
- [3] Kral M, Herzig R, Sanak D, Skoloudik D, Vlachova I, Bartkova A, et al. Oral antiplatelet therapy in stroke prevention. Minireview. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2010;154:203–10.
- [4] Kwolek A. Rehabilitacja w udarze mózgu. Wydanie I. Wydawnictwo Uniwersytetu Rzeszowskiego, Rzeszów; 2009:33–6.
- [5] Kesteloot H, Sans S, Kromhout D. Dynamics of cardiovascular and all-cause mortality in Western and Eastern Europe between 1970 and 2000. Eur Heart J 2006:27:107–13.
- [6] Varon D, Spectre G. Antiplatelet agents. Hematology 2009;1:267–72.
- [7] Antithrombotic Trialists' Collaboration. Collaborative metaanalysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ 2002;324:71–86.
- [8] Shulga O, Bornstein N. Antiplatelets in secondary stroke prevention. Front Neurol 2011;2:1–6.
- [9] Hirsh J, Dalen J, Anderson DR, Poller L, Bussey H, Ansell J, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. Chest 2001;119(Suppl.):8–21.
- [10] Bledowski P, Mossakowska M, Chudek J, Grodzicki T, Milewicz A, Szybalska A, et al. Medical, psychological and socioeconomic aspects of aging in Poland. Assumptions and objectives of the PolSenior project. Exp Gerontol 2011;46:1003–9.
- [11] Mossakowska M, Więcek A, Błędowski P, editors. Aspekty medyczne, psychologiczne, socjologiczne i ekonomiczne starzenia się ludzi w Polsce. Termedia, Poznań: Monografia projektu PolSenior; 2012.
- [12] Asberg S, Henriksson KM, Farahmand B. Ischemic stroke and secondary prevention in clinical practice. Stroke 2010;41:1338–42.
- [13] Glader EL, Sjolander M, Eriksson M, Lundberg M. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke 2010;41:397–401.
- [14] Gao R, Li X. Risk assessment and aspirin use in Asian and Western populations. Vasc Health Risk Manag 2010; 6:943–56.
- [15] Verro P, Gorelick PB, Nguyen D. Aspirin plus dipyridamole versus aspirin for prevention of vascular events after stroke or TIA. Stroke 2008;39:1358–63.

- [16] ESPRIT Study Group, Halkes PH, van Gijn J, Kappelle LJ, Koudstall PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006; 367:1665–73.
- [17] Łabuz-Roszak B, Pierzchała K, Skrzypek M, Swiech M, Machowska-Majchrzak A. Oral anticoagulant and antiplatelet drugs used in prevention of cardiovascular events in elderly people in Poland. BMC Cardiovasc Disord 2012;12:98.