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An Analysis of Primary Prophylaxis in Middle-Aged and Elderly Stroke Patients with Atrial Fibrillation

Analiza pierwotnej profilaktyki udaru u chorych z migotaniem przedsionków w średnim i podeszłym wieku

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Abstract

Background. Atrial fibrillation (AF) is the cause of about 16–18% of ischemic strokes. The authors analyzed the preventive therapy applied in middle-aged and elderly patients with AF and completed ischemic stroke treated in three wards in a large city and a smaller town in Poland and the impact of the type of primary prevention on the death rate.

Material and Methods. Patients with strokes were divided into three groups: those with a high risk (284/349 patients), an average risk (43/349 patients), and a low risk of stroke (22/349 patients) in the course of AF.

Results. In the patients with a high risk of stroke, the primary prophylaxis was an antiplatelet drug (23.6%). Only in 7.4% (21/284) of those treated was an anticoagulant (AC) administered. The manner of conducting treatment was different from that recommended by stroke experts. Statistically significantly fewer patients (5.3%) taking an AC (acenocumarol, $p < 0.001$) died in comparison with those who did not (30.8%). The main cause of death was extensive ischemic stroke (72.6%) and in 7.1% of the cases it was secondary bleeding to an ischemic focus.

Conclusions. Due to improper primary prophylaxis in patients with AF with a high risk of ischemic stroke, the authors recommend a simple blood test to estimate the INR of proper treatment and prophylaxis and also recommend the MMSE test for patients in the group at high risk of stroke prior to the start of anticoagulant treatment. Prophylaxes should be applied according to the recommendations of experts (*Adv Clin Exp Med* 2009, 18, 2, 141–146).

Key words: atrial fibrillation, high-risk stroke, primary preventive treatment.

Streszczenie

Wprowadzenie. Migotanie przedsionków (AF) jest przyczyną około 16–18% udarów niedokrwiennych. Autorzy zanalizowali leczenie zapobiegawcze stosowane u osób w średnim i podeszłym wieku z migotaniem przedsionków i przebyłym udarem niedokrwiennym, leczonych w trzech oddziałach w Polsce (duże miasto i miasteczko), oraz wpływ rodzaju pierwotnej prewencji udaru na śmiertelność.

Materiał i metody. Pacjenci z udarem zostali podzieleni na trzy grupy: z wysokim ryzykiem udaru (284/349 chorych), średnim – (43/349 chorych) i niskim ryzykiem udaru (22/349 chorych) w przebiegu migotania przedsionków.

Wyniki. U chorych z wysokim ryzykiem udaru jako profilaktykę pierwotną stosowano lek przeciwplateletowy (23,6%). Tylko u 7,4% (21/284) stosowano antykoagulant (AC). Sposób prowadzenia leczenia różnił się od zaleceń ekspertów w dziedzinie leczenia udarów. Śmiertelność u chorych leczonych AC (5,3%) była mniejsza niż u chorych nieleczonych AC (30,8%), różnica była istotna statystycznie. Główną przyczyną śmierci był rozległy udar niedokrwienny (72,6%). U 7,1% chorych przyczyną śmierci było wtórne ukrwotoczenie ogniska.

Wnioski. Z powodu nieprawidłowej profilaktyki pierwotnej u chorych z AF i wysokim ryzykiem udaru autorzy zalecają proste badanie krwi, aby ocenić wskaźnik INR i skuteczność leczenia, a także przeprowadzenie testu MMSE z grupy wysokiego ryzyka udaru przed rozpoczęciem leczenia AC. Profilaktyka powinna być prowadzona według wytycznych ekspertów (*Adv Clin Exp Med* 2009, 18, 2, 141–146).

Słowa kluczowe: migotanie przedsionków, udar wysokiego ryzyka, profilaktyka pierwotna.

Atrial fibrillation (AF) affects nearly 0.9% of the general population. AF is the cause of about 15–18% of ischemic strokes [1, 2] and only 5% of patients with normal sinus rhythm [3]. The number of ischemic strokes increases with age, and in patients over 80 years of age this proportion rises to 36% [4]. Disorders of cognitive functions occur in about 25% of patients with AF [5, 6]. Due to the possibility of numerous complications in patients with AF, properly conducted preventive treatment has a great significance. Applying an anticoagulant (AC) in the primary prevention of an ischemic stroke decreases the risk of its occurrence by 44–86% and the death rate to about 26% [7, 8]; it also reduces the risk of the appearance of cognitive function disorders [9, 12].

According to American Heart Association (AHA) guidelines, antiplatelet (AP) therapy is recommended as a prophylaxis of stroke in AF patients up to 65 years old and without other ischemic stroke risk factors [10, 13]. Acetylsalicylic acid (ASA) at a dose of 325 mg a day decreases the risk of ischemic stroke and mortality by 26% and 10%, respectively [11, 14]. Preventing ischemic stroke in patients with AF is less expensive than treating its consequences.

In the present study the aim was to define the occurrence of AF in middle-aged and elderly patients suffering from ischemic stroke and with various degrees of stroke risk in three hospital wards in Poland and to analyze the impact of the type of primary prevention on the death rate.

Material and Methods

The retrospective analysis covered 349 ischemic stroke patients with atrial fibrillation (219 women and 130 men) out of 2234 ischemic stroke patients hospitalized in one of two municipalities. In all patients, CT was performed within 3 to 48 hours after stroke occurrence. The patients recruited for the test were being treated in two neurological wards (ward A, 138 patients, 77 women and 61 men, and ward B, 95 patients, 58 women and 37 men), both located in a city with a population of nearly 700,000, and in the internal disease and neurological wards of a district hospital (ward C, 115 patients) serving an area with 47,000 inhabitants. The registration of patients with stroke took place during their hospitalization. Every patient had an ECG done on the day of admission to the hospital which confirmed AF.

Data concerning prophylactic treatment prior to stroke occurrence were established on the basis of medical history from the patients, families, and caretakers and were analyzed afterwards. In order

to have objective data, medical staff, patients, family members, and the doctors in charge were not told how the information would be used. In cases of missing data in the history of the disease, the information was completed by means of telephone interview.

The patients with AF included in the analysis were divided into three groups: group I with a high risk, group II with a moderate risk, and group III with a low risk of stroke [4, 12]. Group I covered patients aged 75 and over and patients over 65 with the following factors of stroke risk: TIA or stroke, hypertension, diabetes, coronary artery disease, left ventricular dysfunction, and congestive heart failure. Group II consisted of patients aged between 65 and 75 years of age without risk factors of stroke and risk factors of cerebrovascular incident. Group III consisted of patients under 65 without risk factors of stroke or TIA in their medical history. A similar analysis was carried out in patients who died within 30 days after a stroke.

Statistical Analysis

Age, sex, number of deaths, and patients with high, average, and low risk of stroke occurrence were statistically analyzed. Primary stroke prophylaxes were compared in all the wards as well as in the risk groups and the death rate depending on the prophylaxis type was assessed. Frequency analysis was performed using the chi-squared test.

Results

Of the 2234 patients with a diagnosis of ischemic stroke treated in wards A, B, and C, 15.6% (349) suffered from AF. The ward A patients included in the study constituted 13.5% (138/1022) of their ward, ward B patients 15.1% (95/629), and ward C patients 19.9% (116/583). In group I, with a high stroke risk, were 284/349 (81.4%) patients with an average age of 76.8 years (range: 75–93), group II consisted of 43/349 (12.3%) patients with an average age of 70.2 years (range: 65–75), and group III 22/349 (6.3%) patients with an average age of 55 years (range: 50–64). The numbers of patients hospitalized in wards A, B, and C did not show any statistical differences. Only in ward B were patients with a high risk of stroke hospitalized more often (Table 1).

In 23.6% (67/284) of the patients with a high risk of stroke, acetylsalicylic acid at a dose of 75 mg a day constituted the primary prophylaxis. Clopidogrel was administered in only 4 patients. In all the risk groups, treatment with an AP was applied in 29.5% (103/349 patients). Anticoagulant drugs

Table 1. Risk of stroke and primary prevention in patients with AF**Tabela 1.** Ryzyko udaru i profilaktyka pierwotna udaru u chorych z AF

Risk of stroke (Ryzyko udaru)	High (Wysokie)	Moderate (Średnie)	Low (Niskie)	All (Łącznie)						
Mean age – years (Średni wiek – lata)	76.8	70.2	55.0	67.4						
Range (Zakres)	75–93	65–74	50–64	50–93						
Sex, F/M (Płeć)	178/106	31/12	10/12	219/130						
n (%)										
Ward A (Oddział A)	109 (79.0%)	17 (12.3%)	12 (8.7%)	138						
Ward B (Oddział B)	102 (87.9%)	11 (9.5%)	3 (2.6%)	116						
Ward C (Oddział C)	73 (76.8%)	15 (15.8%)	7 (7.4%)	95						
Total (Łącznie)	284 (81.4%)	43 (12.3%)	22 (6.3%)	349						
Prevention before stroke (Profilaktyka udaru)										
All (Łącznie)	284			43			22			n
	AP	AC	NP	AP	AC	NP	AP	AC	NP	
n (%)										
Ward A (Oddział A)	20 (7.0)	8 (2.8)	81 (28.5)	10 (7.2)	4 (9.3)	3 (7.0)	5 (22.7)	4 (18.2)	3 (13.6)	138
Ward B (Oddział B)	28 (9.9)	9 (3.2)	65 (22.9)	8(6.9)	3 (7.0)	0	1 (4.5)	2 (9.1)	0	116
Ward C (Oddział C)	19 (6.7)	4 (1.4)	50 (17.6)	9 (9.5)	3 (7.0)	3 (7.0)	3 (13.6)	1 (4.5)	3 (13.6)	95
Total (Łącznie)	67 (23.6)	21 (7.4)	196 (69.0)	27 (62.7)	10 (23.3)	6 (14.0)	9 (40.9)	7 (31.8)	6 (27.3)	349

AP – antiplatelet prevention, AC – anticoagulant prevention, NP – no prevention.

AP – z zastosowaniem leku przeciwplateletowego, AC – z zastosowaniem antykoagulantu, NP – bez profilaktyki.

were administered to 7.4% of the patients (21/284) in the group with a high stroke risk, and in all risk groups in 10.9% of patients (38/349) with an INR less than 2 on admission. There was no primary prevention in 69.0% of the patients (196/284) in the group at high risk. In all the groups of stroke risk, prevention was not administered to 59.6% of the patients (208/349). In the group with a moderate risk of stroke occurrence, AP was applied in 27/43 patients (62.7%) and AC in 10/43 patients (23.3%). In only 14% of these patients (6/43) was no primary prophylaxis applied. In the group of patients with a low stroke risk, AC and AP prophylaxes were applied in 16/22 patients (72.7%) and no prophylaxis was applied in 6/22 (27.3%) patients.

In the group with high stroke risk (group I), 26.4% of the patients died (75/284) within 30 days

after the stroke, in group II 11.6% (5/43), and in group III 18.2% (4/22). The death rate in the group at high stroke risk was significantly higher than in the group with moderate stroke risk ($p = 0.04$). Patients died significantly more often while in ward C (36/73) than in the other wards ($p = 0.001$) (Table 2).

Analysis of the death rate depending on the type of therapy indicated that of the 103 patients in whom AP was applied, 18 (17.5%) died in all risk groups. This death rate was statistically significantly lower ($p = 0.01$) than that of patients who did not receive AP. Of the patients receiving AC in the primary preventive treatment, 5.3% (2/38) died, and of the patients with no primary prophylaxis, 30.8% (64/208) died. The differences were statistically significant ($p = 0.001$). Treatment of AP with acetylsalicylic acid at a dose of 75 mg

Table 2. Risk of stroke and prevention before stroke in the patients who died**Tabela 2.** Ryzyko udaru i profilaktyka pierwotna udaru u zmarłych

Risk of stroke (Ryzyko udaru)	High (Wysokie)	Moderate (Średnie)	Low (Niskie)	All (Łącznie)					
Mean age – years (Średni wiek – lata)	79.8	73.2	63.0	72.1					
Range (Zakres)	75–93	66–74	61–64	61–93					
Deaths n (%) (Zgony)									
Ward A (Oddział A)	19 (17.4%)	1 (5.9%)	0	20 (14.5%)					
Ward B (Oddział B)	20 (19.6%)	1 (9.1%)	1 (33.3%)	22 (19.0%)					
Ward C (Oddział C)	36 (49.3%)	3 (20.0%)	3 (42.9%)	42 (44.2%)					
Total (Łącznie)	75 (26.4%)	5 (11.6%)	4 (18.2%)	84 (24.0%)					
Prevention before stroke (Profilaktyka udaru)									
	high risk			moderate risk			low risk		
	AP	AC	NP	AP	AC	NP	AP	AC	NP
Deaths n (%) (Zgony)									
Ward A	4 (20%)	1 (12.5%)	14 (17.3%)	1 (10%)	0	0	0	0	0
Ward B	5 (17.9%)	1 (11.1)	14 (21.5%)	1 (12.5%)	0	0	1 (100%)	0	0
Ward C	1 (5.3%)	0	35 (70%)	2 (22.2%)	0	1 (33.3%)	3 (100%)	0	0
Total	10 (14.9%)	2 (9.5%)	63 (32.1%)	4 (14.8%)	0	1 (16.7%)	4 (44.4%)	0	0
Death rate depending on therapy type (Odsetek zgonów w zależności od rodzaju leczenia)									
AP	AC			NP			all		
18/103 (17.5%)	2/38 (5.3%)			64/208 (30.8%)			84/349 (24.1%)		

AP – antiplatelet prevention, AC – anticoagulant prevention, NP – no prevention.

Ward A : Ward C, $p = 0.001$; Ward B : Ward C, $p = 0.001$; High risk : Moderate risk, $p = 0.04$.

AP : NP, $p = 0.01$; AC : NP, $p = 0.001$

AP – z zastosowaniem leku przeciwplateletowego, AC – z zastosowaniem antykoagulantu, NP – bez profilaktyki.

Oddział A : oddział C, $p = 0,001$; oddział B : oddział C, $p = 0,001$; wysokie ryzyko : średnie ryzyko, $p = 0,04$.

AP : NP, $p = 0,01$; AC : NP, $p = 0,001$.

a day was predominant in the primary prophylaxis; two patients were treated with ticlopidine and clopidogrel. In two patients treated with AC using acenocumarol, INR was below 2.

Discussion

AF is the most common persistent arrhythmia. In Poland it affects about 400,000 to 500,000 people. In approximately 50% of cases it is a persistent form. AF increases the risk of stroke five times [13, 14], doubles the risk of death [15], and

increases the costs of treatment. These are reasons for prophylaxis with anticoagulants or antiplatelet drugs. In patients with AF aged below 75 years of age, the recommended preventive treatment includes ASA at a daily dose of 325 mg or with anticoagulants if other risk factors coexist [16]. In all patients with AF aged 75 and older, anticoagulants are the only recommended drugs for prevention. These recommendations correspond with NSA [17], ACCChPh [18], and ACC-ESC [19] recommendations, which are based on long-term multicenter clinical studies. Recommendations of European experts on cerebral stroke suggest

decreasing the daily dose of anticoagulants in people over 75 years of age because of an increased risk of hemorrhagic complications [20].

In the analyzed groups of patients with AF, anticoagulant therapy was administered only in 7.4% of the group with a high stroke risk. In the USA, anticoagulants were used in the early 1980s as a primary prophylaxis in 7.1% of patients [21] and in the early 1990s in 32% [16]. In 1999, anticoagulant therapy was applied to 50% of patients with non-valvular AF [22]. In our analysis, the percentage of patients with AF receiving anticoagulant treatment as a primary prevention of ischemic stroke is on the level of the USA in the early eighties. It is, however, similar to other European countries: in Italy, 10% of patients receives anticoagulant drugs [23], in Hungary 9.5%, in the UK 10.1%, in Spain 11.1%, and in Germany 4.5% [2]. The SAFE II test showed that about 25% applied prophylactic anticoagulant treatment in patients with AF in Austria, Belgium, France, Portugal, and Italy [24].

The death rate depending on the type of preventive therapy was highest in the group which did not receive any primary prophylaxis (30.8%). In the group treated with AP it was 17.5%. The lowest death rate (5.3%) occurred in the group receiving AC. This is compatible with other test results [7, 8]. Most of the patients in the group at high stroke risk who died should have, according to recommendations, received anticoagulant treatment before stroke onset. The more severe general condition of the patients in ward C also contributed to the higher death rate there. The difference in mortality rate between a neurological ward in a city

and a neurological/internal disease ward in a town results from the specialist care in so-called stroke units within neurological wards. Among the factors mentioned which restrict the application of AC in patients with AF are poorly organized medical care, low patient awareness of the dangers resulting from stroke, and dementia present in 25% of the patients [5,6]. It is also possible that doctors adopt a conservative attitude, being afraid of hemorrhagic complications in these patients. However, the latest research indicates a small risk of hemorrhagic complications, equaling about 1.3% [25]. It is imperative to review the approach to primary prevention in patients with AF.

The results show improper primary prophylaxis in patients suffering from AF who are at high risk of ischemic stroke among the middle-aged and elderly. While waiting for new drugs, it would be advisable to introduce a fast and simple blood test that could be performed by the patient himself (like in diabetes) for assessing the INR. This would provide the necessary treatment monitoring and allow an increase in the safety of anticoagulant therapy. Data from professional literature indicating the presence of dementia in nearly one fourth of patients with AF [5, 6] may indicate a necessity of assessing cognitive functions on the MMSE scale [26] prior to the start of anticoagulant treatment. A widespread information campaign also needs to be carried out among patients about ways of preventing the complications of arrhythmias. Good cooperation between a family member or legal guardian and medical care providers also guarantees proper primary prophylaxis of patients with AF.

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