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PHARMACOTHERAPEUTIC INNOVATIONS IN CEREBROVASCULAR ACCIDENT TREATMENT: A STUDY FROM THE ABIDJAN CARDIOLOGY INSTITUTE MEDICAL ICU

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Abstract: *Cerebrovascular accidents (CVAs), commonly known as strokes or "brain attacks," represent acute medical emergencies characterized by the obstruction or rupture of cerebral arteries, leading to the deprivation of blood supply to specific brain regions, resulting in cerebral infarction. These incidents manifest as rapid-onset neurological deficits lasting more than 24 hours, encompassing a spectrum of symptoms indicative of brain dysfunction. Among the most prevalent manifestations are sudden onset weakness or sensory loss in facial and limb muscles, typically unilateral, along with cognitive impairments such as confusion and difficulty in speech or comprehension. Visual disturbances, gait disturbances, dizziness, severe headaches, and loss of consciousness may also occur, underscoring the diverse clinical presentations associated with CVAs (Sagui, 2007; Kemnang et al., 2019).*

Keywords: *Cerebrovascular accidents, stroke, cerebral infarction, neurological deficits, brain dysfunction.*

INTRODUCTION

Sometimes referred to as a 'brain attack,' cerebrovascular obstruction or rupture of a cerebral artery, which leads to accidents (CVAs) are acute conditions resulting from the the death of a portion of brain tissue due to the loss of a proper blood supply (cerebral infarction). They are characterized by the rapid development of localized or global clinical signs of brain dysfunction, with symptoms lasting more than 24 h (Sagui, 2007). The most common stroke syndrome is sudden weakness or loss of feeling in the face or one or more limbs, usually on one side of the body. Other symptoms are mental confusion, difficulty speaking or comprehension, unilateral or bilateral decreased vision, difficulty in walking, dizziness, loss of balance or coordination, severe abnormal headaches, fainting or unconsciousness (Kemnang et al., 2019).

This condition is the second leading cause of death in the world, with 87% of cases occurring in developing countries (Sagui, 2007; Béjot et al., 2009). They are responsible for 52% of vascular deaths in Africa against 38% in Europe (Shanthi et al., 2011). In Côte d'Ivoire, in 2010, strokes constituted nearly 30% of the conditions encountered in neurological hospitalization services (Adoukonou et al.,

2010) with approximately 15,000 people suffering from the disease, including nearly 10,000 deaths and 9% of deaths in public hospitals were due to strokes in subjects aged 45 to 69 (Béjot et al., 2009).
Indeed, stroke-related morbidity and mortality depend on access to curative and preventive care in people at risk for the disease such as exposure to tobacco, diabetes, high blood pressure, obesity and lipid disorders (Rusinaru, 2010).
The medical management of cerebrovascular accidents must occur quickly and is mainly based on taking calcium channel blockers in the event of arterial hypertension (main factor of stroke), paracetamol in the event of fever, and phenobarbital in the event of an epileptic attack. Rapid and efficient care avoids death but also reduces complications related to the disease, the first step in care being to confirm the diagnosis of stroke and to specify whether it is an ischemic or hemorrhagic stroke.
In Côte d'Ivoire, the medical care of strokes is preferentially carried out at the Abidjan Cardiology Institute (ACI), the only hospital center specialized in the country in the care of patients suffering from cardiovascular diseases. This study was carried out in the intensive care unit of the Abidjan Cardiology Institute with the general objective of describing the pharmacotherapeutic strategy for cerebrovascular accidents.

MATERIALS AND METHODS

This involved carrying out a retrospective cross-sectional study with a descriptive aim at the outpatient department of the Abidjan Cardiology Institute. The study consisted of consulting the files of patients previously received in the said service from January 2019 to December 2021. Data collection was done between February and March, 2022.

Patient inclusion

The files included in the study were those of patients who had experienced a stroke, aged 18 or older, received in the service during the study period, and had at least one episode of stroke drug prescription documented in their files. The records of patients who were lost to follow-up during the study period were not retained for this study. The Abidjan Cardiology Institute archive register contained approximately 60 patients registered in the medical intensive care unit between 2019 and 2021. All of these patients were included in the study based on the aforementioned inclusion criteria.

Data source

A data collection sheet was used to collect information from patient files such as sociodemographic (age, sex, place of residence, profession), clinical (risk factors, types of strokes), and pharmacotherapeutic data correlated with the type of stroke of the patient (medical prescription, pharmacotherapeutic dispensation, administration of the treatment, monitoring of the treatment). The diagnosis of the type of stroke as well as the definition of the risk factors were carried out according to the Canadian recommendations for best practices in stroke care (Gladstone et al., 2022). A retrospective follow-up was carried out for patients with several prescription episodes in order to assess the evolution of the stroke, the occurrence or not of complications between the admission of patients to the ACI and the end of the study period and how patients are discharged by type of stroke. Also, a percentage of compliance with Canadian recommendations was determined using the prescriptions retained in the study.

Ethical considerations

Data were collected anonymously after approval by the ACI Ethics Committee.

Data analysis

The data in the form of quantitative variables were expressed as means ± standard deviations and those in the form of qualitative variables were expressed in counts and percentages. Statistical analysis was performed with R version 4.1.1 software. A Chi^2 test was used to compare the number of patients according to their mode of discharge. The differences were considered significant when the calculated Chi^2 was greater than the theoretical Chi^2 read in the Chi^2 table (ddl=2) =5.99.

RESULTS

Sociodemographic and clinical data

A total of 56 patient records were included in this study. The sociodemographic data are shown in Table 1. The sex ratio (M/F) was 1.54 with 60.7% men and 39.3% women. The average age was 65.2 ± 10.3 years with extremes ranging from 33 to 86 years. Patients aged between 70 and 80 years were more numerous. The majority of patients (66.6%) lived in Abidjan and had a professional activity in 27% of cases against 63% of retirees (Table 1).

Clinical patient entry data (Table 2) showed that ischemic strokes were the most frequently encountered (93%). In addition, all patients were exposed to the risk factors of the study with diabetes (92%), hypertension (90%), senility (61%), and possible history of stroke (57%) as the most cited factors (Table 2).

Table 1. Sociodemography and clinic of patients.

Sociodemographic data (n)	% of patients or (mean±SD) All patients	Patients with CVAI, n = 52	Patients with CVAH, n = 4
Age (year)	65.9±10.3	49.3±12.3	68.3±10.4
Sex (45)			
Male (28)	60.7	85.7	14.3
Woman (17)	39.3	94.1	15.9
Place of residence (8)			
Abidjan	66.7%	100	n/a
Outside of Abidjan	33.3%	100	n/a
Occupation (11)			
Professional activity	27.27	100	n/a
Non-working (unemployed, housewife)	0.10	100	n/a
pensions	63.63	100	n/a
Total, n (%)	56	52 (93%)	4 (7%)

SD: Standard deviation; CVAI: ischemic stroke; CVAH: hemorrhagic stroke; n = Number; Nd: Not available.

Table 2. Cardiovascular risk factors of ICA medical intensive care stroke patients.

Risk factors	% of patients		
	All patients	Patients with CVAI	Patients with CVAH
Modifiable risk factors			
hypertension (n=40)	90	89	11
Diabetes (n=36)	92	100	0
Dyslipidemia (n=22)	9	100	0
Obesity (BMI ≥ 30.0 kg/m²) (n=2)	50	100	0
Smoking (n=21)	5	100	0
Alcoholism (n=21)	14	100	0
Stress (n=22)	14	100	0
Sedentary lifestyle (n=24)	33	100	0
Unmodifiable or barely modifiable risk factors			

Senility (Age ≥ 60 years old) (n=56)	61	97	3
Genetic	n/a	n/a	n/a
History of stroke (n=28)	57	94	6

CVAI: Ischemic stroke; CVAH: hemorrhagic stroke.

Therapeutic data

All patients in the study received therapy according to the type of stroke (Table 3). The number of drugs used ranged from one to five in the two types of stroke, that is,
3.4% monotherapy, 1.8% dual therapy, 5.4% tri and quad therapy and 42.9% pentatherapy. On the other hand, therapies of more than six drugs were used only in ischemic strokes at a proportion of 41.1%.

Types of stroke therapeutic	**CVAI (%)**	**Type not specified (%)**	**CVAH (%)**	**Numbers**	**Percent**
Monotherapy	0	0	100	2	3.4
Bitherapy	100	0	0	1	1.8

Table	4Triple therapy	33	66	0	3	5.4	presents
the	Quadritherapy	33	66	0	3	5.4	
	Pentatherapy	78	13	9	24	42.9	
	Hexatherapy or more	82	18	0	23	41.1	
	Total	71	21	8	56	100	

categorization of the pharmacotherapeutic classes prescribed to patients. The pharmacotherapeutic classes used in the two types of stroke were limited to analgesics (3.0%), antidepressants (4.8%), and antihypertensives (10.4%). In the ischemic strokes, the presence of antiplatelet agents (54.0%),

Table 3. Distribution of types of stroke according to the type of therapy used.

CVAI: Ischemic stroke; CVAH: hemorrhagic stroke.

Table 4. Pharmacotherapeutic classes prescribed to patients.

Pharmacotherapeutic class	Active substances	Type of stroke		Compliance recommendations	
		CVAI	CVAH	CVAI	CV
Analgesics		4	2		
Level 1	Paracetamol	2	1	Yes	Y
Level 2	Tramadol	2	1	Yes	Y
Normolipemics		22	0		
Atorvastatin		21	-		
Rosuvastatin		1	-		
Antibacterials		11	0		
Betalactams + Inhibitors beta-lactamases	Amoxicillin + Clavulanic Acid	8	-	Yes	
Cephalosporins	Ceftriaxone	3	-	Yes	
Antidepressants		11	2		
Anticonvulsants	Valproic acid	4	-	Yes	
	Midazolam	2	1	Yes	Y
Benzodiazepines	Diazepam	3	1	No	N

	Clonazepam	2	-	No
Antihypertensives		112	6	
Diuretic	Furosemide	27	-	Yes
	Spironolactone	11	-	Yes

Table 4. Cont'd

ARA II	Candesartan	1	-	Yes	-
ARA II + IEC	Amlodipine + Valsartan or Perindopril or Valsartan	10	-	Yes	-
Beta blockers	Bisoprolol	29	1	Yes	Yes
	Nebivolol	6	-	Yes	-
IEC	Ramipril	9	-	Yes	-
	Perindorpil	12	1	Yes	Yes
ICA	Nicardipine	4	4	Yes	Yes
ARA II +Neprilysin	Valsartan + Sacubitril	3	-	Yes	
Platelet antiaggregants		31	0		54.0
COX-1 inhibitors	Aspirin	29	-	Yes	-
ADP receptor inhibitors	Clopidogrel	2	-	Yes	-
Anti-coagulants		21	0		9.7
Heparins	Calciparin	2	-	Yes	-
	Enoxaparin	9	-	Yes	-
	Heparin sodium	6	-	Yes	-

Oral anticoagulants	Acenocoumarol	2	-	Yes	-		
	Rivaroxaban	2	-	Yes	-		
Total		211	10	92%	86%	100	

CVAI: Ischemic stroke; CVAH: hemorrhagic stroke; *Canadian stroke best practice recommendations.

Table 5. Clinical and biological follow-up parameters of patients during retrospective follow-up.

Retrospective follow-up (n)	Values (Mean±Standard Deviation)	Normal values*
Clinical parameter		
Glasgow score (56)	12.37±2.3	>12.0
Body temperature (°C) (56)	38.01±0.80	36.00-37.50
Blood Pressure (mmHg) (56)	16.2/9.7±2.0/1.3	9/14
Biological parameter		
Capillary blood glucose (g/L) (56)	0.95±0.25	0.80-1.27
INR (3)	1.57±0.22	2.00-3.00
PT (%) (21)	73.10±7.57	> 70.00%
Hemoglobin (g/dL) (12)	13.00±1.33	12.00-16.00
Uremia (g/L) (7)	0.23±0.02	0.15-0.4[1]

*Canadian recommendations for best practices in stroke care and the National Compendium of Ivorian Therapeutic Protocols 2019 edition. [1]Normal values regardless of sex. INR = International Normalized Ratio; PT = prothrombin count.

Table 6. Distribution of patients according to mode of discharge during the retrospective follow-up.

Way out*	Type of stroke		
	All patients (%)	CVAI (%)	CVAH (%)

Residence	73	93	7
Deceased	23	92	8
Transfer	4	100	0

*Calculated Chi^2 = 0.1594 Theoretical Chi^2 = 5.99. CVAI: Ischemic Stroke; CVAH: hemorrhagic stroke; *Canadian Stroke Best Practice Recommendations.

Table 7. Distribution of patients according to complications observed during retrospective follow-up.

Complications	**Proportions (%)**
Pulmonary infection	2
Bedsores	6
Seizures	11
None	82

adults, the second cause of dementia after Alzheimer's disease, and the third cause of death (Haute Autorité de Santé, 2007). They therefore constitute a major public health issue through their incidence and the resulting medical, social, and economic consequences as well as through the mandatory involvement of the entire healthcare sector. This retrospective study of strokes identified 56 patients with stroke from 2019 to 2021 in the medical intensive care unit of the Abidjan Cardiology Institute.

During the study, 93% of registered patients were prone to ischemic stroke against 7% hemorrhagic stroke. Indeed, most strokes are ischemic (usually due to a clogged artery), but some are hemorrhagic (due to a ruptured artery) (Rusinaru, 2010). The average age was 65.17 years. This average age would be linked to the conditions of inclusion of hypertensive patients in the study, the threshold age of which was 18 years, but also to the pathological conditions of the disease which involve impairment of the elderly subjects. In The global burden of stroke, the average age of stroke was 70.8 years overall and 76.2 years for developed countries against 73.1 years for developing countries such as Côte d'Ivoire (Shanthi et al, 2011). It was noticed, throughout the study, an unequal distribution of age groups. A higher proportion of patients in the age group of 50 to 80 years was observed. Consistent with other studies, the incidence of stroke increases with patient age due to the aging of blood vessels, making this condition a disease that predominantly affects the elderly (Benilha et al., 2014). Regarding the incidence

of stroke by sex, data from the literature indicate a predominance of men over women in all countries, with a sex ratio of 1.25 (Gladstone et al., 2022). This trend was observed in the present study where the sex ratio was 1.54 in favor of men. Also, according to data related to the profession, retired patients are much more prone to stroke than those with a professional activity. The reason could be that these patients, in addition to being elderly, would be subject to several risk factors as observed in the study.

Diabetes (92%), high blood pressure (90%), senility (61%), history of stroke (57%), and obesity (50%) were the most frequent risk factors for complications encountered in stroke patients with at least three risk factors per patient in ischemic stroke. Complication risk factors such as arterial hypertension and history of stroke were found in all patients with ischemic and hemorrhagic stroke. However, patients with ischemic stroke had additional risk factors.

The high proportion of diabetes and hypertension in the overall study population is explained by a correlation between hyperglycemia, arterial hypertension and stroke. Indeed, the chronic increase in blood sugar leads to fat metabolism disorders and vascular lesions, consequences of the occurrence of stroke (Benilha et al., 2014). As for arterial hypertension, the repeated exposure of the arterial walls to high blood pressure causes them to harden and thicken.

These blood vessels thus become fragile and can then cause strokes (Benilha et al., 2014). A history of stroke also put patients at risk for new stroke.

Overall, several risk factors that can promote the occurrence of strokes have been recorded. Upstream management of these factors could therefore reduce the incidence of stroke in the elderly. In the absence of prevention and in the event of a stroke crisis, the establishment of comprehensive disease management becomes necessary.

Nowadays, in addition to the mechanical management which involves thrombectomy, pharmacological management is associated with the aim of improving the overall management of patients suffering from stroke. Thus, more than six drugs per therapy were recorded in the therapeutic protocols of the study with a predominance of pentatherapy (42.9%) followed by hexatherapy or more (41.1%). Therapies below four drugs were in low proportion (16%). In ischemic stroke, therapies featured at least two drugs. On the other hand, in hemorrhagic strokes, it was either monotherapy or pentatherapy. As in other studies carried out in geriatrics in Brest in 2012, or in the emergency room in Limoges in 2012, there was also an average of 5.25 drugs per prescription. Polytherapies in general and in particular, in patients with hemorrhagic stroke, combine at least five clinical signs present during the disease, the treatment of which seems obvious (Le Manuel, 2023; Kothari et al., 1997). This state is therefore correlated with taking several drugs in the management of the disease.

Drugs used in therapies included antiplatelet drugs 54%, antihypertensives 10.4%, normolipemiants 10%, anticoagulants 9.7%, antibacterials 5.1%, antidepressants 4.8%, and analgesics at 3%. In hemorrhagic strokes, the absence of normolipemiants, antibacterials, antiplatelet agents, and anticoagulants was noted.

Platelet aggregation inhibitors therefore constitute the most prescribed therapeutic class in stroke patients with more than half of the prescriptions and aspirin as the main molecule prescribed during the study. Indeed, according to several recommendations, aspirin is an appropriate first-line treatment in the presence of a low risk and most of the time after 21 days of double antiplatelet therapy with

clopidogrel (Wang et al., 2015; Lun et al,, 2022). Regarding antihypertensives, which represent the second most used therapy in stroke, their use would be justified by the involvement of arterial hypertension in 90% of strokes as risk factors. In a multicenter study carried out in the United States in 2014, arterial hypertension was involved in more than 40% of strokes (Willey et al., 2014). It is therefore one of the most important modifiable risk factors to address in order to prevent a subsequent stroke. While it remains unclear what the optimal blood pressure targets should be for systolic and diastolic blood pressure, it is known that maintaining blood pressure below 140/90 mm Hg reduces the risk of stroke (Goldstein and Simel, 2005). Normolipemiants are also a predominant category among registered therapies. Specifically, for lipid-lowering agents, a statin should be administered in all cases of minor non-cardioembolic stroke, provided there are no contraindications or adverse effects (Goldstein and Simel 2005).

Use of a high-dose statin (e.g. atorvastatin 80 mg/day or simvastatin 40 mg/day) is associated with a reduction in the absolute risk of subsequent stroke of 1.5 to 1.9% after median follow-up period of 2.5 years (Boulanger et al., 2018).

Anticoagulant therapy also reduces the relative risk of subsequent stroke by 66% in the presence of nonrheumatic atrial fibrillation after minor stroke (Wang et al., 2021).

In order to fight against urinary and skin infections, it is essential to use antibiotics, antifungals, and antivirals (Boulanger et al., 2018). In the study, antibiotics were prescribed during certain therapies with a predominance of amoxicillin associated with clavulanic acid. Regarding antidepressants which represented 5.58% of prescriptions, valproic acid, midazolam, diazepam, and clonazepam were the active ingredients prescribed. According to the Canadian Stroke Best Practice

Recommendations, no drug or class of drug has been

found to be superior in the treatment of depression after stroke. However, taking into account the side effects, selective serotonin reuptake inhibitors would be preferable in people who have suffered a stroke. The choice of an antidepressant will depend on the symptoms of depression, possible known side effects of the drug, particularly in children or the elderly, drug interactions with other drugs being taken at the time, and underlying medical problems (Agence Nationale de Sécurité du Médicament et des produits de santé, 2014). Generally, all of these drugs registered during the study are considered suitable for initiating and maintaining treatment, either as monotherapy or in combination with other drugs in the context of combined treatment regimens as observed in the present study. It was thus noted an overall compliance of 89% of the protocols prescribed by the doctors of the Abidjan Cardiology Institute with respect to the Canadian recommendations for optimal stroke care practices. This compliance rate would be correlated with the results of the clinical and biological follow-up carried out. Indeed, the parameters studied presented values close to normal values, indicating a good favorable evolution of the disease in the patients of the study. This evolution was favorable in 73% in cases with mortality of 23% due to the delay in treatment. In the event of a favorable evolution, the appearance of complications was noted, including convulsive crises, bedsores, and pulmonary infections.

Conclusion

The study made it possible to identify the therapeutic classes used mainly in the medical intensive care unit of the Abidjan Cardiology Institute. These were mainly antiplatelet agents, antihypertensive drugs, and normolipemia. The protocols used had a satisfactory level of compliance with, however, disparities concerning the choice of certain molecules, especially with antidepressants. The follow-up of the treatment made it possible to observe a favorable evolution with a greater proportion of patients presenting complications such as bedsores.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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