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CRITICAL CARE IN STROKE: PHARMACOLOGICAL MANAGEMENT INNOVATIONS AT COCODY UNIVERSITY HOSPITAL ICU

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Abstract: *A cerebrovascular accident (CVA), commonly known as a stroke, presents a critical medical emergency characterized by the sudden disruption of blood flow to the brain, leading to neurological damage. This condition, if not promptly addressed within a narrow therapeutic window of 24 hours, can have grave consequences, ranging from death to irreversible impairment of brain function. Hepburn et al. (2018) highlight the severity of CVAs and underscore the urgent need for timely intervention to mitigate their debilitating effects.*
This abstract underscores the urgency and gravity of cerebrovascular accidents, emphasizing the critical importance of swift and effective intervention to prevent adverse outcomes. The 24-hour window following a CVA represents a crucial period during which medical interventions can significantly influence patient prognosis and outcomes. By providing timely and appropriate treatment, healthcare professionals can minimize neurological damage and improve patient survival and quality of life.

Keywords: *Cerebrovascular accident, Stroke, Neurological damage, Medical emergency, Intervention.*

INTRODUCTION

A cerebrovascular accident (CVA), characterized by an within 24 h, CVA can lead to death or cause irreversible interruption of blood flow, can result from a blockage of a neurological damage (Hepburn et al., 2018).
cerebral artery (ischemic stroke) or the rupture of a in industrialized countries, stroke ranks as the third cerebral artery (hemorrhagic stroke). Without treatment leading cause of death and the primary cause of physical disability. It can also lead to cardiovascular and respiratory disorders, seizures, and insomnia (Lopez, 2006; Sangha et al., 2015). In developing countries like Côte d'Ivoire, this critical situation accounts for approximately 45% of hospitalizations in neurology departments in Abidjan (Gnazegbo et al., 2018). A study conducted at the Abidjan Cardiology Institute (ICA) indicates a stroke prevalence of around 4% (Kouakou et al., 2015). The management of this condition relies on the rapid recognition of stroke symptoms in the early stages and prompts hospitalization in an intensive care unit to provide appropriate therapeutic care. This approach improves the vital prognosis and the quality of life for patients (Crozier, 2012). In the intensive care unit, effective management necessitates polypharmacy (Bollaert et al., 2010). The

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objective of our work was to describe the pharmacotherapeutic agents used in the Cocody Hospital Intensive Care Unit and verify the availability of drugs in the management of stroke.

MATERIALS AND METHODS

Study setting

Stroke patient files, between December 2017 and January 2020, were collected in Cocody University Hospital (CHU) intensive care unit. Included in this study were patients' files that had a stroke confirmed by medical imaging examination which contain sheets treatment. Records of patients who died before drug treatment start and incomplete files were excluded.

Study design

From January to June 2020, retrospective cross-sectional files study with descriptive purpose permit us to collect epidemiological, clinical, para clinical and therapeutic data. Also, from February to April 2020, information's collected from stock cards products and reports given by drugs stocks managers facilitated drugs availability estimation and description of molecules prescribed profile were performed using ATC classification guidelines (WHO, 1996). In order to have representative sample, the minimum number of patient files to collect was estimated according to Schwartz formula (Schwartz, 2006).

Ethical clearance

Data collection and analysis procedures performed were compliant with recommendations and guidelines involving human subjects (Public Decree No. 2017-884, Jarded, 2016; Le Louarn, 2018).

Data analysis

Data process and analysis was done using Excel© 2013 software, and GraphPad prism 8.0 through averages and percentages determination.

RESULTS

Eighty-five files were consulted in Cocody intensive care unit. Among these files, seventy-eight either 91.76% were retained.

Epidemiological data

Patients median age was 58 years (28 - 88 years) with 64.10% of them around 45 and 75 years old, Female were predominant (sex ratio: 0.95). Arterial hypertension (HTA) was most common risk factor (88.46%) followed in decreasing order by diabetes (60.26%), alcoholism history (15.38%), stroke history (14.1%), smoking (10.26%), contraception (3.84%) and cardiomyopathies (2.56%). Most patients admitted to intensive care came from emergency department (71%).

Clinical data

Hemorrhagic AVC was found in 71% of patients. Consciousness disorder was most common reason to admission (80%), followed by coma (12.82%). Clinical examination on admission found consciousness disorders with a Glasgow score (Jeret et al., 1993) between 7 and 9 in 44.87% of patients (Figure 1a). Neurological deficit was noted in 73% of patients and hemiplegia was the predominant focal neurological sign (77.78%). Blood pressure was mostly below 140/90mmHg and only 18% of patients had a pressure above 180/100mmHg (Figure 1b).

Heart rate was above 70 beats/min in 78% of patients; while respiratory rate was normal in majority of cases (64%) and only 3% of patients had permanent seizures. Depending on stroke type diagnosed by imaging, patients died respectively in 76% of cases from Hemorrhagic Cerebrovascular Accident

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(AVCH) and 44% for Ischemic Cerebrovascular Accident (AVCI). Other patients were either transferred to neurology department (AVCH: 18% and AVCI: 43%) or discharged from hospital.

Paraclinical data

Most imagery test realized was brain scan (97%). Blood count revealed anemia in 95% of cases and platelet and leukocyte levels were mostly normal (Figure 2). Urea/creatinine dosage gave results in accordance with standards in 50% of cases. Half (50%) of blood sugar levels were abnormal and 9% of patients had hyperglycemia above 1.8 g/l (Figure 3). The patients had hyponatremia in majority of cases (56%) and blood gases measured were mostly below normal values (Figure 4).

Drugs prescribed availability and profile

Drugs commonly prescribed in Cocody intensive care unit availability (Table 1) were around 48% and molecules used targeted several organs or system according to Anatomical Therapeutic Chemical (ATC) classification system (World Health Organization, 1996), especially: (i) Hormonal systemic preparations 100%: Oxytocin 10 IU injectable solution (inj sol), Dexamethasone 4 mg inj sol, Betamethasone 4 mg inj sol; (ii) Blood and hematopoietic organ drugs in a proportion of 83.3%: Enoxaparin 4000 UI inj sol, tranexamic acid 1g inj sol, Phytomenadione 10 mg inj sol; (iii) Medications of digestive system up to 57.1%: Esoméprazole 40 mg inj sol, Atropine 0,25 mg inj sol, Calcium chloride 1 g inj sol, Magnesium Sulfate 1g inj sol; (iv) Systemic Anti-infective drugs around 55.5%, with majority belong to β-lactamines family: Amoxicillin/ Clavulanic acid 1 g inj sol, Ceftriaxone 1g inj sol, Ceftriaxone/Sulbactam 1 g inj sol, Gentamicin 80 mg inj sol, Metronidazole 500 mg perfusion solution (perf sol); (v) Nervous system drugs up to 35.2%, most belong to hypnotics families, opioids, analgesics and antipsychotics: Fentanyl 0,5 mg inj sol, Tramadol 100 mg inj sol, Acetaminophen 500 mg perf sol, Acetaminophen 1 g perf sol, Nefopam 20 mg inj sol, Midazolam 5 mg /ml inj sol; (vi) Cardiovascular system medicines at 28.6%, namely diuretics and calcium channel blockers: Furosemide 20 mg inj sol, Nicardipine 10 mg inj sol.

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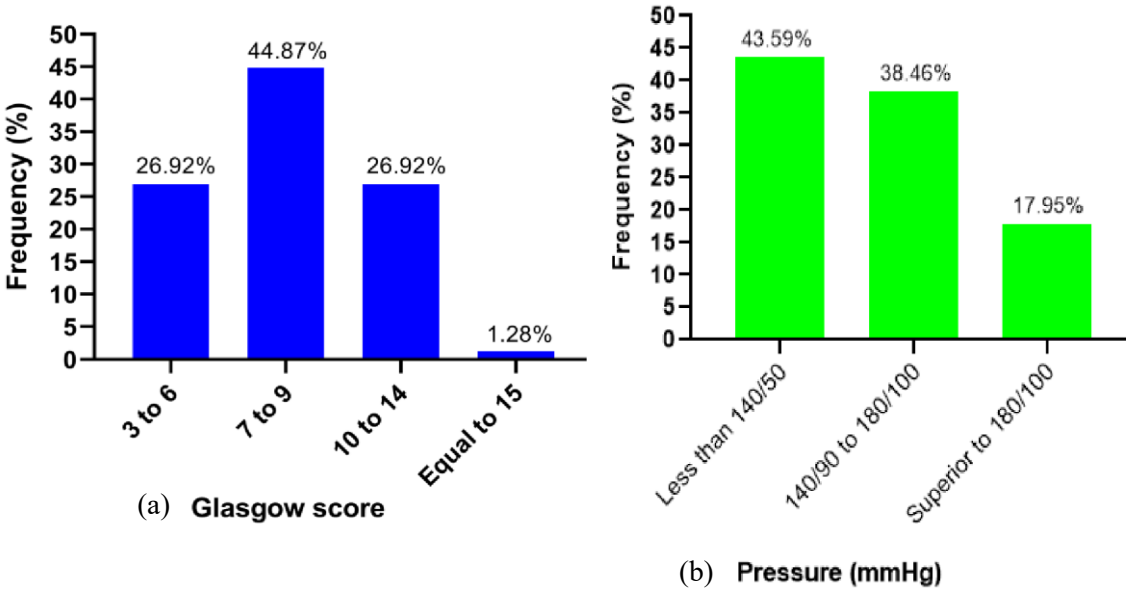

Figure 1. Patients distribution according to Glasgow score and blood pressure (mm Hg).

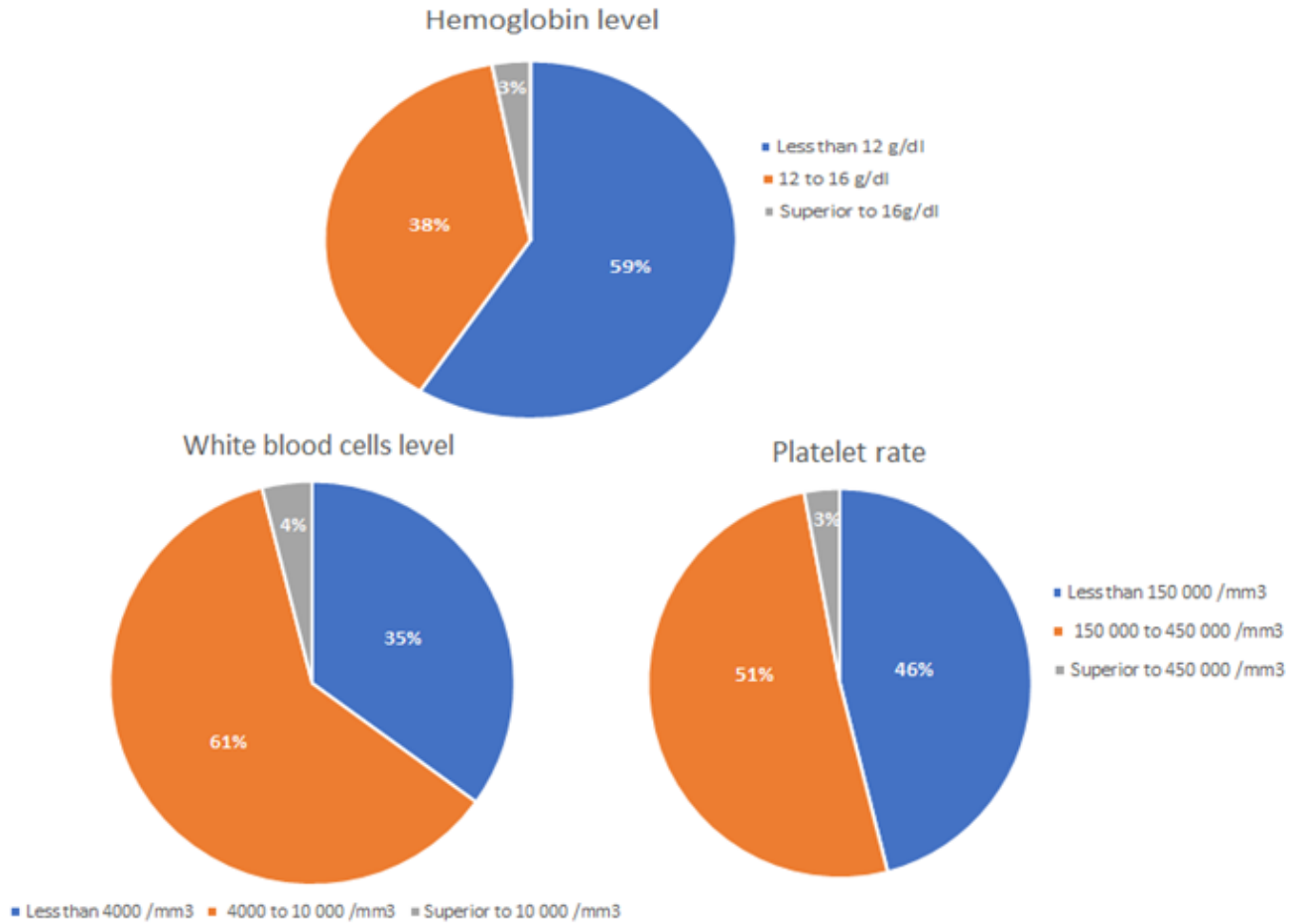

Figure 2. Patients distribution according to blood count.

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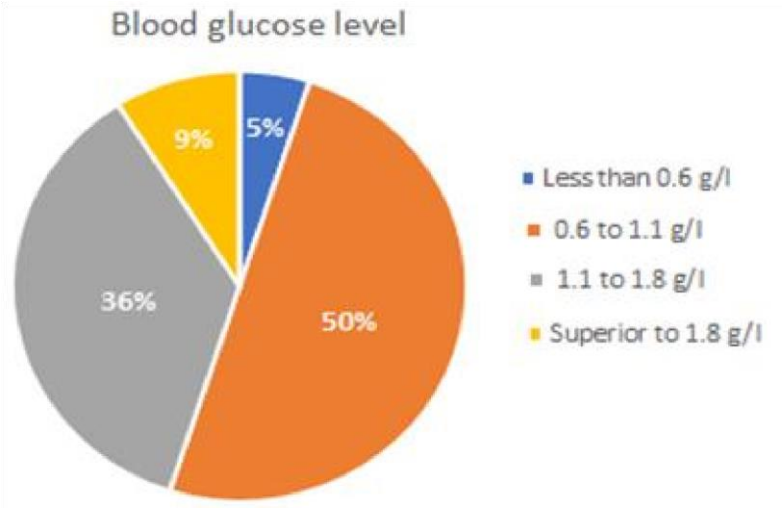

Figure 3. Patients distribution according to blood glucose.

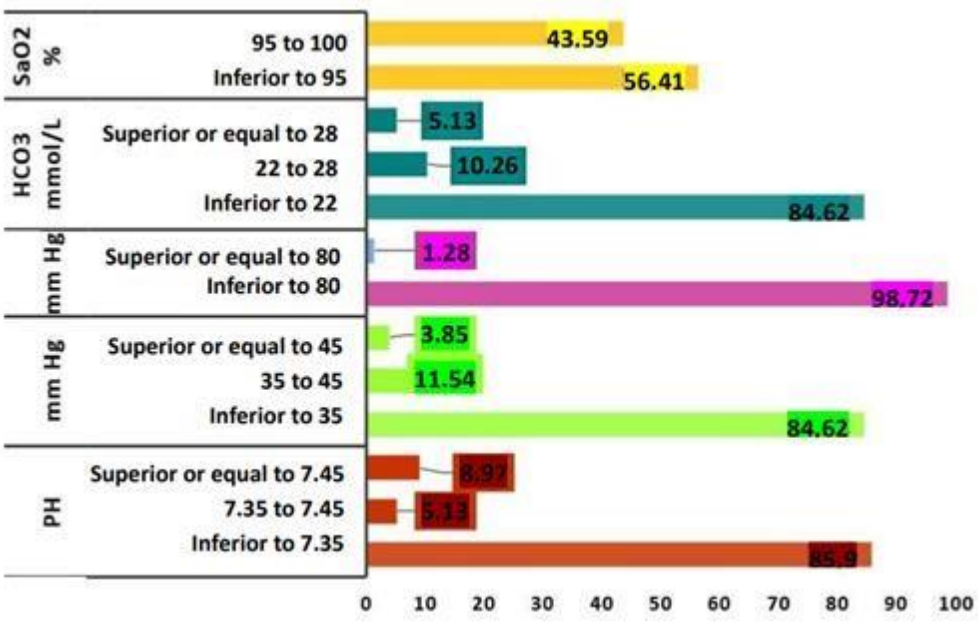

Figure 4. Patients distribution according to blood gas values.

Table 1. Drugs prescribed profile according to ATC classification.

System		Availability (%)	Pharmacologic group		Therapeutic class		Molecules available
ATC No.	Designation		ATC No.	Designation	ATC No.	Designation	

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	Systemic hormonal	H01	Pituitary and	H01B	Hormone of the posterior pituitary lobe	Oxytocin 10 IU sol for inj	-		
			hypothalamic hormones						
H	preparations, except	100	and analogues except						
	sex hormones and								
			sex hormones and			Dexamethasone 4 mg inj amp	-		
	insulins	H02	insulin	H02A	Corticosteroids	Betamethasone 4 mg inj amp	-		
	Blood and	B01		B01A	Antithrombotic	Enoxaparin 4000 IU sol for inj Heparin calcium 5000 IU sol inj			
			Antithrombotic						
	hematopoietic	83.3	B02	B02A	Antifibrinolytic	Tranexamic acid 1g inj amp	- agents		
	organs	B02		B02B	Antihemorrhagic	Phytomenadione 10 mg inj amp	-		
B									
		A02		A02B	Antulcerous	Esomeprazole 40 mg inj amp Rabeprazole 20 mg inj amp			
	Digestif tract and	A03	Anti-acids, drugs for	A03B	Belladonna and derivatives	Atropine 0.25 mg inj amp	-		
		57.1	peptic ulcer and						
	metabolism	A12	flatulency	A12A	Mineral/Calcium supplement	CaCl2 1g inj amp Calcium gluconate 1 g inj amp			
		A12		A12C	Mineral/Magnesium supplement	Magnesium sulfate 1g inj amp	-		
		J01		J01C	B-lactamins	Amoxicillin/Clavulanic acid 1g inj			
						Ceftriaxone 1g inj amp			
						Imipenem/Cilastatin 500 mg inj			
	Antiinfectives	J01	Antibacterials for	J01D	Other β-lactamins	Ceftriaxone/Sulbactam 1g inj amp			
						Cefixime 200 mg tablet			

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J		55.5				
	for systemic use		systemic use			
		J01		J01G	Aminoglycosides	Gentamycin 80 mg inj amp
						Amikacin 500 mg inj amp
		J01		J01M	Quinolones	- Ofloxacin 200 mg sol for inf
		J01		J01X	Other antibiotics	Metronidazole 500 mg sol for inf
						-
		N01		N01A	General anesthetic	Fentanyl 0.5 mg inj amp
						-
						Paracetamol/Codeine 500 mg/30
		N02		NO2A	Opioids	Tramadol 100 mg inj amp tablets
						Paracetamol 500 mg sol for inf
						-
		N02		N02B	Other analgesics	Paracetamol 1 g sol for inf
						-
N	Nervous system	35.2	Anesthetics		Nefopam	20 mg inj amp
	-					
						Phenobarbital 50 mg tablet
						Phenobarbital 100 mg tablet
		N03		N03A	Anticonvulsants	- Valproic acid 500 mg tablet
						Clonazepam 2 mg tablet
						Levosulpiride 25 mg inj amp

Table 1. Contd.

	N05	N05B	Anxiolytics	- caps
	N05	N05C	Hypnotics and sedatives	Midazolam 5 mg/ml inj amp -
	N06	N06D	Other anti-dementia drugs	Ginko biloba 40 mg tablet
	N07	N07A	Parasympathomimetics	Neostigmine 0.5 mg inj amp

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				C01C	C01C	Cardiac stimulant	-	-	Noradrenaline 8 mg/6 ml inj amp
				C02A	C02A	Central antihypertensive	-		Methyldopa 500 mg tablet
C	Cardiovascular system	28.6	Cardiac therapy						Clonidine 0.15 mg tablet
				C03C	C03C	Diuretic	Furosemide 20 mg inj amp	-	
				C08C	C08C	Calcium blockers	Nicardipine 10 mg inj amp	Nicardipine 20 mg tablet	

Potassium clorazepate 10 mg

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Source: World Health Organization (1996).

DISCUSSION

This study conducted in the Cocody Hospital Intensive Care Unit allowed us to observe a predominance of female patients, with a sex ratio of 0.95, and a median age of 58 years. This pattern is similar to that described in a study conducted at the Abidjan Cardiology Institute (ICA) (Kouakou et al., 2015). However, African literature, such as a study conducted at Bouaké University Hospital, has revealed a male predominance (Gnazegbo et al., 2018; Keita et al., 2005; Sène Diouf et al., 2006). Hypertension emerged as the dominant risk factor in both African and developed countries (Hajat et al., 2001). As for medical history, a majority of patients had at least one prior stroke, which aligns with the well-established possibility of stroke recurrence in these patients (Béjot et al., 2009;
Feigin, 2021; Pulit, 2016; O'Donnell, 2016). Most patients admitted to the intensive care unit were transferred from the CHU emergency services, particularly from the neurovascular units. This proximity allows for an effective commencement of care, ideally within the first 4 hours to yield favorable remission of symptoms (Lamblin et al., 2018).

The reasons for admission found in our study align with what is described in the literature (Diango et al., 2011; Kouakou et al., 2015), and AVCH (presumably a type of stroke) was more frequent than AVCI. Even if these two forms have same clinical symptoms and same progressions, only imaging can allow us to decide (OssouNguiet et al., 2013) and availability of a functional computed tomography scanner within Cocody University hospital has made possible to quickly make diagnosis. Our results are identical to those revealed by the team of Kouakou N'goran at ICA in 2015 (Kouakou et al., 2015). About 1% of patients had 15 Glasgow score, which suggests that they were misdirected to intensive care unit. High death rates have been noted in both types of strokes and in general, AVCHs are more redoubled than AVCIs. After AVC suffering, only 50% of patients survive and half of them have a significant disability (Keita et al., 2005). A study carried out in same department indicated a death rate around 70.89% (Mignonsin et al., 1992).

These still high death rates could be explained by occurrence of various complications due to late delay to start appropriate cure. In general, strokes management in intensive care unit was specific and non-specific strokes drugs. Among specific drugs, antihypertensive
(Nicardipine), antiplatelet agents (Aspirin) and anticoagulants (LMWH) were most used. Nonspecific drugs were represented by analgesics, fluid solutions and electrolytes, antiulcer drugs and anticonvulsants. Antiplatelet drugs and lipid lower agents were only used in AVCI patients.
Treatment protocols included: (i) Neurosedation by combining benzodiazepines anxiolytic (Midazolam) and morphine analgesics (Fentanyl) to avoid dangerous agitation and restore and equalized cerebral oxygen supply and consumption; (ii) Antihypertensive calcium. channel blocker with vascular tropism (Nicardipine) to lower blood pressure without cardiac effect; (iii) Cerebral antispasmodic treatment (Nimodipine) to prevent cerebral arterial spasm and hemorrhage complications; (iv) Hypoglycemic treatment (insulin) to lower blood sugar when it was above 1.4 g/l in order to avoid sugar excess deposit on the walls of weakened vessels; (v) Cerebral anti-edema treatment (Mannitol) to promote cerebral edema drainage, thus lower intracranial pressure; (vi) Anti-

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ulcer agent (Proton pump inhibitor) to prevent ulcer stress; (vii) Anticoagulant treatment (Enoxaparin) to prevent thromboembolic diseases; (viii) Anti-ischemic treatment (Ginkgo biloba) to induce good oxygenation favorable to cerebral hypoxia management; (ix)
Antiplatelet agent to allow clot lysis at ischemia origin; (x) Lipid-lower treatment (Statin) to lower cholesterol level involved arterial obstruction; (xi) Analgesic and antipyretic agent (Paracetamol, Tramadol, Nefopam) to stop pain due to invasive procedures. Thrombolysis was absent in AVCI management at Cocody intensive care unit.

Pharmacological agents used in intensive care unit complied in majority cases with learned societies recommendations, in particular with those of French Language intensive care Society (SRLF) (Bollaert et al., 2010). The SRLF recommends IV infusion to treat hypertension with Urapidil or Labetalol or Nicardipine, avoiding loading doses, and for AVCIs management, once-daily administration of acetylsalicylic acid (ASA) dosed at 160 mg-300 mg. In our study, ASA was prescribed at 100 mg daily dose, certainly to avoid medicines interactions. In addition, learned society recommends preventive anticoagulant treatment based on Low Molecular Weight Heparin (LMWH) for both types of strokes, but after 48 h for AVCH. Although molecules prescribed were compatible with each other, significant interactions, especially with glucocorticoids (Dexamethasone or Betamethasone) were possible in patients (Chong et al., 2014; Thesaurus, 2019; Gonçalve et al., 2020). The risks of adverse events due to combinations with antihypertensive (Nicardipine), hypokalemia diuretics (Furosemide), or antithrombotic (enoxaparin) are as follows: a reduction in the antihypertensive effect of Nicardipine due to water and sodium retention (HAS, 2013), an enhancement of the hypokalemic effect, and an increased risk of haemorrhage (Mondoloni et al., 2018). For Midazolam and Tramadol combination, sedation and respiratory depression risk could lead patient to coma or death, especially in elderly (Thesaurus Des Interactions Médicamenteuses, 2020). Management of all these undesired effects had required close clinical and biological monitoring by set out frequent measurements blood pressure, increased serum potassium monitoring and reduction as much as possible doses and duration of risk associations (Grillo et al., 2006; Bollaert et al., 2010).

One other difficulty encountered was drugs unavailability near 50% in hospital pharmacy. This low availability rate could be explained by various reasons as: (i) frequent stock-outs observed at the New Public Health Pharmacy (NPSP), only supplier of health products to public hospitals and the period during which this study was carried out coincided with the COVID-19 pandemic, where there had general slowdown in health products importation; (ii) prescription of drugs by clinicians not referenced on the national list of essential drugs; (iii) insufficient financials resources to purchase drugs, pushing prescribers often to refer patients to private pharmacies for get drugs.

Conclusion

The therapeutic management of strokes in the Cocody Hospital Intensive Care Unit is based on polypharmacy, with each drug used having a clear purpose and a justified indication. Our protocols adhere to international recommendations, with one notable exception being the practice of thrombolysis with AVCI's. In this unit, rapid and comprehensive diagnosis, followed by the initiation of selective and targeted treatments, could significantly improve the vital prognosis of our patients. Furthermore, increasing resources allocated to drug procurement, diversifying pharmaceutical product

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suppliers, and developing a health products booklet tailored to intensive care unit practices could greatly facilitate the work of clinicians.

CONFLICT OF INTERESTS

Authors declare that they have no conflicts of interest in relation with this article.

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