

INNOVATIVE PHARMACOLOGICAL TREATMENTS FOR CEREBROVASCULAR ACCIDENTS IN ICU: THE COCODY UNIVERSITY HOSPITAL EXPERIENCE

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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 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 (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.

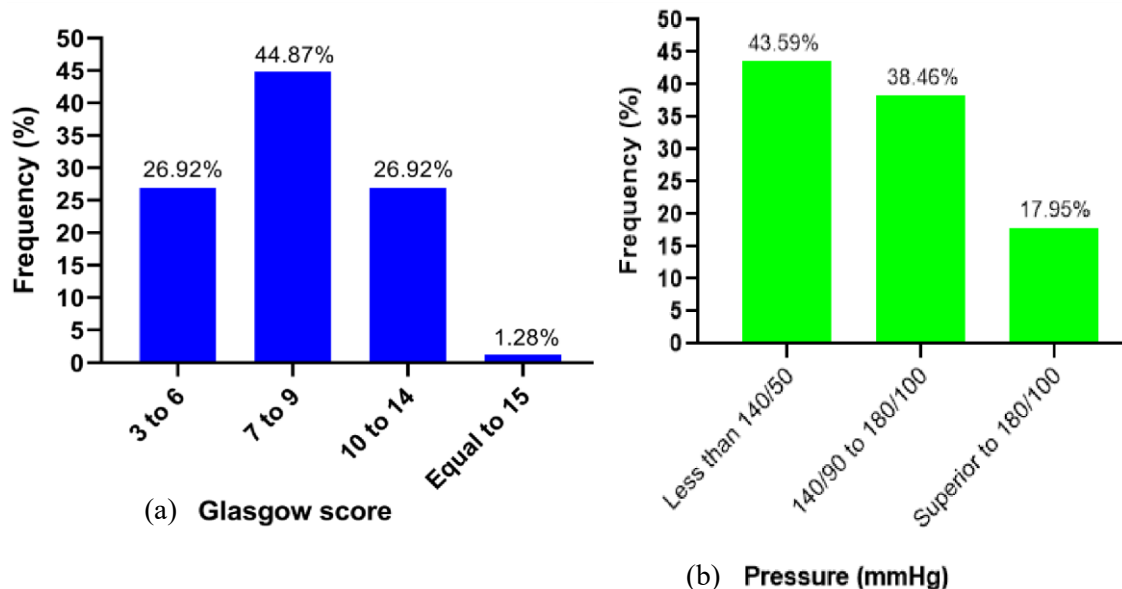


Figure 1. Patients distribution according to Glasgow score and blood pressure (mm Hg).

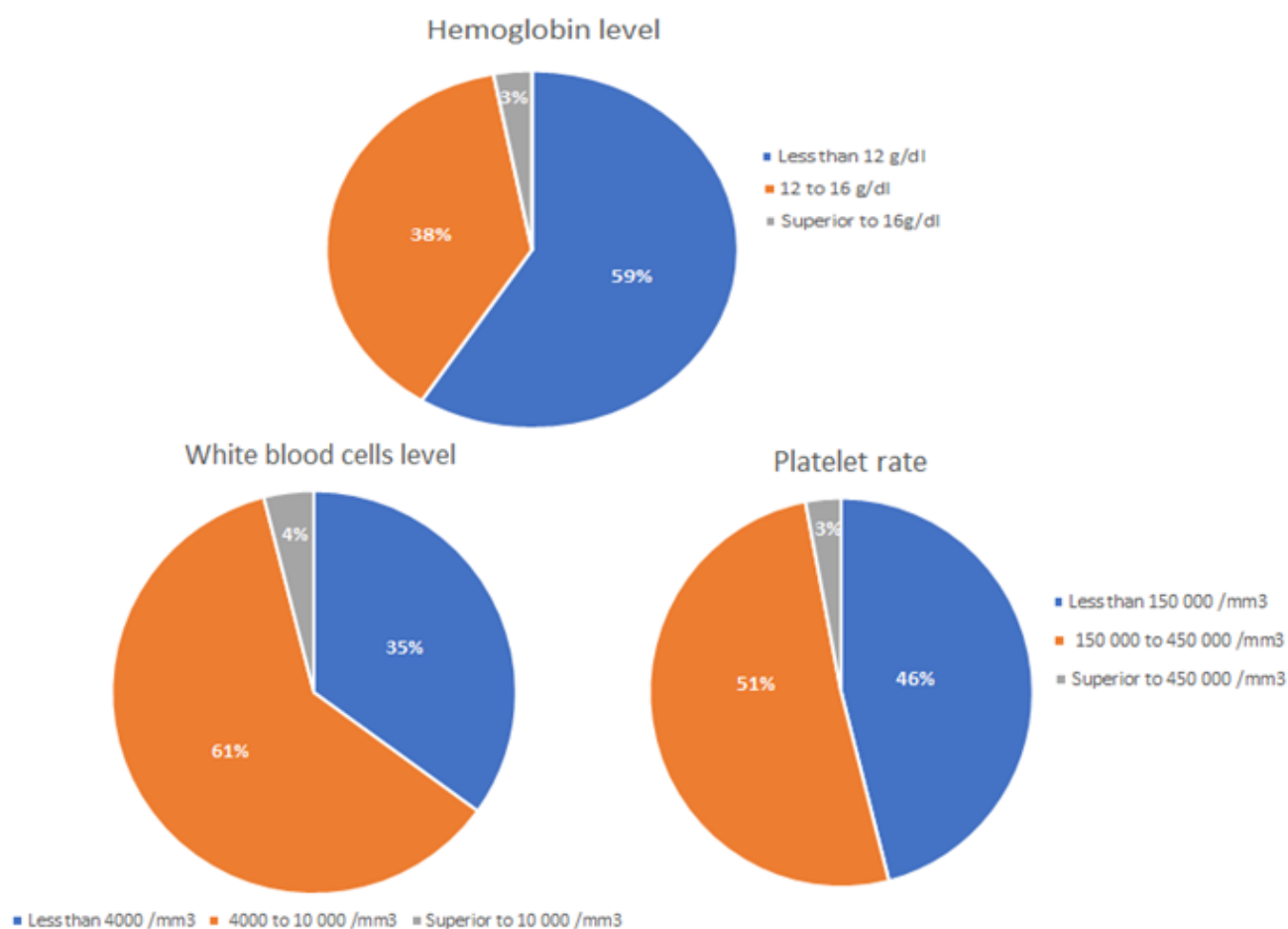


Figure 2. Patients distribution according to blood count.

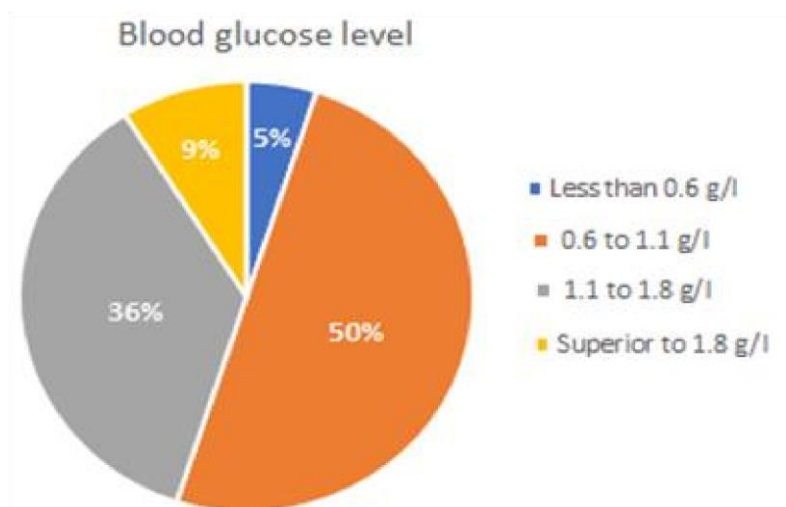


Figure 3. Patients distribution according to blood glucose.

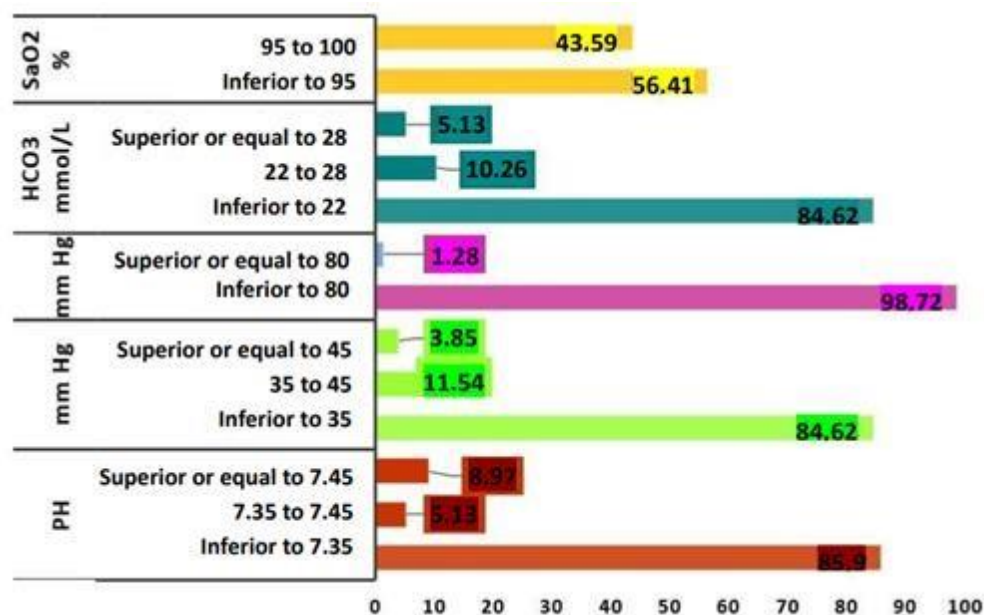


Figure 4. Patients distribution according to blood gas values.

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	
	Systemic hormonal		HO1	Pituitary and	HO1B	Hormone of the posterior pituitary	
	lobe Oxytocin 10 IU sol for inj		-				

H	preparations, except 100	hypothalamic hormones	
		and analogues except	
	sex hormones and		
		sex hormones and	Dexamethasone 4 mg inj amp
		-	
	insulins	Ho2 insulin	Ho2A Corticosteroids Betamethasone 4
	mg inj amp	-	
	Blood and	Bo1	Bo1A Antithrombotic Enoxaparin 4000 IU
	sol for inj Heparin calcium 5000 IU sol inj		
		Antithrombotic	
	hematopoietic	83.3 Bo2	Bo2A Antifibrinolytic
		Tranexamic acid 1g inj amp	- agents
	organs	Bo2	Bo2B Antihemorrhagic Phytomenadione
	10 mg inj amp	-	
B			
		Ao2	Ao2B Antulcerous Esomeprazole 40 mg inj
amp	Rabeprazole 20 mg inj amp		
	Digestif tract and	Ao3 Anti-acids, drugs for	Ao3B Belladonna and
	derivatives Atropine 0.25 mg inj amp	-	
		57.1 peptic ulcer and	
	metabolism	A12 flatulency	A12A Mineral/Calcium supplement CaCl ₂
	1g inj amp Calcium gluconate 1 g inj amp		
		A12	A12C Mineral/Magnesium supplement
	Magnesium sulfate 1g inj amp	-	
		Jo1	Jo1C B-lactamins Amoxicillin/Clavulanic
	acid 1g inj		
		Ceftriaxone 1g inj amp	
	Antiinfectives	Imipenem/Cilastatin 500 mg inj Jo1	Jo1D Other β-lactamins
	Cefixime 200 mg tablet	Antibacterials for Ceftriaxone/Sulbactam 1g inj amp	
J			
	for systemic use	55.5	systemic use

inj amp 200 mg sol for inf mg sol for inf	Amikacin 500 mg inj amp	J01	J01G Aminoglycosides Gentamycin 80 mg
		J01	J01M Quinolones - Ofloxacin
		J01 -	J01X Other antibiotics Metronidazole 500
inj amp	Paracetamol/Codeine 500 mg/30	No1	No1A General anesthetic Fentanyl 0.5 mg
		-	
		No2	No2A Opioids Tramadol 100
for inf	35.2	Anesthetics	mg inj amp tablets
			Paracetamol 500 mg sol for inf
			-
N Nervous system	-	No2	No2B Other analgesics Paracetamol 1 g sol
		-	
			Nefopam 20 mg inj amp
acid 500 mg tablet	No3		Phenobarbital 50 mg tablet
			Phenobarbital 100 mg tablet
			No3A Anticonvulsants - Valproic
			Clonazepam 2 mg tablet
			Levosulpiride 25 mg inj amp

Table 1. Contd.

No5	No5B	Anxiolytics	-	caps
No5	No5C	Hypnotics and sedatives	Midazolam 5	mg/ml inj amp
No6	No6D	Other anti-dementia		Ginko biloba 40
No7	No7A	drugs		mg tablet
		Parasympathomimetics		Neostigmine 0.5
				mg inj amp

C	Cardiovascular system	28.6	Cardiac therapy	Co1C	Co1C	Cardiac stimulant	-	Noradrenaline 8
							-	mg/6 ml inj amp
				Co2A	Co2A	Central antihypertensive	-	Methyldopa 500
								mg tablet
								Clonidine 0.15
								mg tablet
				Co3C	Co3C	Diuretic	Furosemide 20 -	
							mg inj amp	
				Co8C	Co8C	Calcium blockers	Nicardipine 10	Nicardipine 20
							mg inj amp	mg tablet
				Potassium clorazepate 10 mg				

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-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; Gonçalves 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

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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