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Review article

Neuropathic pain in Mali: The current situation, comprehensive hypothesis, which therapeutic strategy for Africa?

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ABSTRACT

Introduction: According to the taxonomy of the International Association for the Study of Pain (IASP 2011), neuropathic pain (NeuP) is defined as "*pain caused by a lesion or disease of the somatosensory nervous system*". NeuP is currently well-defined clinically, despite a high degree of etiological variation, and it has become a significant public health problem. This work aimed to study the situation regarding NeuP in current practice in Mali, as well as to analyze the therapeutic environment of the patients.

Methodology: This was a retrospective and cross-sectional study, carried out in two phases: (1) compilation of the files of patients according to the ICD-11, over a period of 24 months (2) a second prospective phase regarding the Knowledge, Attitudes, and Practices (KAP) of general practitioners and neurologists in regard to NeuP. The focus of the first phase of the study was the files of the patients who had undergone a consultation at the Gabriel Touré UHC. The second phase of the study focused on the general practitioners (Community Health Centers (comHC) of Bamako) and neurologists (Malian or not).

Results: Over the period of the study, 7840 patients were seen in consultation in the Department of Neurology, of whom 903 for NeuP, thus amounting to a NeuP frequency of 11.5%. Women accounted for 58.9% (532/903), with a sex ratio of 1.4. Using a comparative normal law, the difference in frequency was statistically significant between males and females ($p < 10^{-7}$) and between two age groups (p $\langle 10^{-3}$). The 49–58 years of age group was represented the most. Diabetic NeuP (21%), lumbar radiculopathies (14%), HIV/AIDS NeuP (13%), and post-stroke NeuP (11%) were the most represented. The survey among the carers revealed: a need for training, a low level of compliance with the therapeutic guidelines, and the use of traditional medicine by the patients.

Discussion/conclusion: This work confirms that NeuP is encountered frequently in current practice, and its optimal management will involve specific training of carers and improvement of access to the medications recommended in this indication. In light of this issue, we revisit the debate regarding the concept of essential medications and the relevance of taking into account effective medications for the treatment of NeuP.

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1. Introduction

The incidence of neurological diseases is steadily increasing throughout the world [1]. In this context, neuropathic pain (NeuP), which is well-defined clinically despite a high degree of etiological variation, is presently a major public health problem [2,3]. It is estimated that 6% to 10% of adults in the world suffer from NeuP [4,5]. In Africa, this symptom is a common comorbidity of certain endemic pathologies on the continent such as diabetes, human immunodeficiency virus and acquired immune deficiency syndrome (HIV/SAIDS), infection by hepatitis C virus, leprosy, stroke, and traumatic lesions of the limbs and the spinal cord [6–10]. In Western Africa, its prevalence at Paraku in Benin has been reported to be 6.3% in the general population [11]. In Dakar (Senegal), it has been reported to be 7.1% in the geriatric population [12]. In Ouagadougou in Burkina Faso, it has been reported to be 49.5% in people with low back pain [13]. Furthermore, its prevalence is expected to increase with the aging of the population, the diabetes epidemic, and improvement in the survival of cancer and of the HIV/AIDS pandemic [12,14].

Moreover, NeuP is associated with a significant decrease in the quality of life and the socioeconomic well-being of patients, more so than non-neuropathic chronic pain [15,16]. Furthermore, its treatment in countries with low incomes such as Mali is subject to the problem of accessibility and availability of the recommended medications [17–20], thereby making management of this pathology in the world in general, and in Africa in particular, a challenge [21–24].

Despite the high prevalence of NeuP, this pathology has been particularly well-studied in Africa in subgroups of the population (diabetics, people with low back pain, leprosy, elderly individuals, and people with HIV/AIDS [6,9,10,12,13]. Despite its well-documented socioeconomic consequences, the extent of the phenomena induced by NeuP in the hospital environment remains unknown to date. There have been very few studies in Mali and in Africa regarding the care that is provided for NeuP. In light of this lack of information, we have hypothesized that a global analysis of the situation regarding NeuP constitutes an indispensable pre-condition for devising a strategy tailored to the health systems of poor countries. The aim of this preliminary work in regard to the summary of our data from consultations, in parallel with a KAP survey among sufferers, was to study the status of NeuP in current practice in Mali, as well as to analyze the therapeutic environment of patients through the opinions of the sufferers. In this work we discuss the determinants of the application in sub-Saharan Africa of a conceptual framework, tailored to the sociocultural realities, that will ensure effective treatment of patients suffering from NeuP. We also revisit the concept of essential medications, based on the model list of essential medications of the World Health Organization (WHO). Most countries in sub-Saharan Africa have adopted this model list. We have reflected on the relevance of a possible integration of effective essential medications in the treatment of NeuP.

2. Methodology

2.1. Operational definitions

2.1.1. DN4

a validated questionnaire for identification of neuropathic pain based on the score obtained for 10 questions to be answered per patient, each question being awarded one point. When the score is equal to or greater than 4/10, the test is positive (sensitivity of 82.9%; specificity of 89.9%) [26,27].

2.1.2. Probable NeuP

Patients exhibiting features suggestive of NeuP such as a type of paresthesia, tingling, numbness, electric shocks, etc., for whom the questioning and the clinical examination allow establishment of (1) prior incidents of neurological lesions or disease resulting in NeuP (diabetes, HIV, stroke, low back pain); (2) symptoms in keeping with an anatomical correlation compatible with nerve damage; and (3) testing (electrophysiological, imaging) suggesting neurological damage.

2.1.3. Certain NeuP

Patients exhibiting pain that is neuropathic in nature (paresthesia, tingling, numbness, electrical shocks, etc.) in a context of neurological damage in conjunction with a well-documented underlying pathology (imaging, electromyoneurography) and positivity of the DN4 questionnaire (a score greater than 4/10).

2.2. Type and timing of the study

This was a retro-prospective, descriptive, cross-sectional study carried out in two phases, A first retrospective phase regarding the status of NeuP in Mali in the Department of Neurology of the Gabriel Touré UHC of Bamako based on the compilation of patient files over a period of 24 months from January 1st, 2017 to December 31st, 2018. A second prospective phase comprising an evaluation of the knowledge, attitudes, and practices (KAP) of the general practitioners and neurologists in regard to the treatment of NeuP, which took place from January 2nd, 2019 to June 30th, 2019.

2.3. Site of the study

The Department of Neurology of the Gabriel Touré University Hospital of Bamako (GT UHC) constituted the main site of the study. It is a 3rd reference facility of the health pyramid of the country. This department is strategic in terms of training of general practitioners and specialists in neurology. Three-quarters of the neurologists of the department obtained formal training in regard to the diagnosis and management of pain from peripheral neuropathy during their syllabus in general neurology.

2.4. Population of the study

The focus of the first phase of the study was the files of the patients who had undergone a consultation at the Gabriel Touré UHC. The second phase of the study focused on the general practitioners (Community Health Centers (comHC) of Bamako) and neurologists (Malian or not).

2.5. Sampling

The sampling for the first phase included all of the files of the eligible patients. The sampling for the second phase of the study was carried out by random selection of general practitioners in each of the 57 comHC of Bamako. In this group, 45 general practitioners agreed to participate in the study. We undertook a simple random sampling of 60 neurologists who were members of the African Federation of Neurology (AFAN). We contacted these 60 neurologists individually by email and we sent them the KAP questionnaire. Given the number of respondents among the general practitioners, the research team decided to retain the first 45 participants who responded to our request out of the total of 53 neurologists who replied to the email. These comprised 20 West African neurologists from the following countries: Mali, Benin, Ivory Coast, Guinea, Senegal, Niger, Togo, and Nigeria; 13 neurologists from central Africa (Cameroon, Chad, Gabon, and Central Africa); nine (9) practitioners from the Maghreb (Morocco, Tunisia, and Mauritania); three neurologists from Eastern and Southern Africa (Djibouti and Kenya). The comparison between the two groups of practitioners involved the same number.

2.6. Criteria for inclusion

The first phase of the study included the files of the patients seen at the GT UHC who underwent an exhaustive clinical evaluation

(questioning and physical examination revealing a pathology resulting in NeuP; presence in the file of paraclinical examination necessary for the diagnosis). In the second phase, we surveyed health professionals (neurologists throughout Africa and general practitioners at 57 community health centers in Bamako).

2.7. Criteria for non-inclusion

Incomplete files or those for which the neuropathic nature had not been proven by the clinical elements and the diagnostic tool (the DN4 questionnaire) were not included in the first phase of the study.

2.8. Tools and procedures for collection of the data

The data for the first phase of the study were collected from patient files containing sociodemographic, clinical (questioning, neurological and physical examination), the data for the additional and the therapeutic examinations, and the follow-up data. The files were compiled according to the guidelines of the International Association for the Study of Pain (IASP) and the WHO. Files of patients suffering from NeuP were retained: persistent or recent pain lasting more than three (3) months [25]. The files were categorized according to the 11th edition of the International Classification of Diseases (ICD-11) [26,27].

The first questionnaire for the collection of data in the consultation registries was in regard to the sociodemographic characteristics of the patients, the typologies, the clinical data, and the type of treatment received.

The 2nd questionnaire was in regard to the knowledge, attitudes, and practices of the carers (general practitioners versus neurologists). This questionnaire was designed specifically for the practitioners: their sociodemographic data and their knowledge, attitudes, and their practices regarding NeuP, the place of pain/NeuP and the most common types of NeuP in their daily practices, and their opinions regarding their patients' behaviors, especially in terms of their treatment of NeuP.

2.9. Statistical analysis of the data

The data were collected and analyzed with Prism GraphPad version 8.0 software. Frequency tables were generated, and calculation of the means were undertaken. The Chi^2 and Fisher's exact test were used to compare the proportions, with a threshold of significance set at $p = 0.05$. Simple logistic regression was used for the measures of association, with presentation of the odds ratios and their 95% confidence intervals.

2.10. Ethical considerations

The data in the patient files were collected in a strictly anonymous manner and with approval from the relevant authorities of the UHC. The Medical Work Committee of the UHC, which oversees the ethics committee and has an advisory role regarding the management of clinical research activities provided approval for this study to be undertaken. For active involvement of the comHC, the national health board of Mali was informed in writing. The AFAN administration was informed of the study by email. The practitioners did not receive any payment for participation in the study. The practitioners were informed of the objective and the benefits of the study, and their free and informed consent was obtained by email prior to their inclusion.

3. Results

3.1. Epidemiological and clinical situation of patients with NeuP in our practice

3.1.1. Sociodemographic characteristics

During the two years of the study, 7840 patients were seen in outpatient consultation in the department, and 903 cases of the patients exhibiting NeuP were recorded, thus amounting to a frequency of 11.5%. Women were represented more, at 58.9% (532/903) of the patients, thus amounting to a sex-ratio of 1.4. The 49–58 years of age, the 39–48 years of age, and the 29–38 years age groups were represented the most at 25.7% (217/903); 24.1% (217/903); and 22.1% (200/903), respectively. Using a comparative normal law, the difference in frequency was statistically significant between men and women ($p < 10^{-7}$) and between two age groups ($p < 10^{-3}$) (Table 1).

3.1.2. The main types of neuropathic pain

Diabetic neuropathic pain was the most represented type, at 21% (186/903), followed by lumbar radiculopathies, at 14% (129/903). Toxic neuropathic pain linked to antituberculosis drugs, pain of infectious origin (leprosy, Zona virus); the so-called "rare" causes in our study (pain linked to diseases of the nervous system, hereditary, fibromyalgia, Pudendal neuralgia, Arnold's neuralgia, and glossopharyngeal neuralgia) were less represented, at 2% for each group (Fig. 1).

3.1.3. Clinical characteristics of the NeuP

Women were more represented in eight types of neuropathic pain. This predominance was much more the case for neuropathic pain linked to HIV, trigeminal neuralgia, entrapment syndrome, and diabetic neuropathy, at 73.1% (87/119); 72.9% (27/37); 70.9% (22/31), and 69.9% (130/186), respectively. There was a statistically significant difference between gender and the types of neuropathic pain (with $Chi^2 = 54.69$; $p < 0.0001$). With trigeminal neuralgia as the reference, there were more men suffering from all types of neuropathic pain than women. Post-stroke neuropathic pain (2.98 times), toxic neuropathic pain linked to antituberculosis drugs (4.63 times), lumbar radiculopathy (2.74 times), myelopathy (4.26 times), and alcohol and organophosphorus-induced neuropathic pain (3.45 times) were more frequent in men compared to women (Table 2).

A high intensity of neuropathic pain was associated with certain etiologies: diabetic neuropathic pain 38.6% (46/119), toxic neuropathic pain linked to antituberculosis drugs 54.3% (44/81), cervicobrachial neuralgias 57.9% (11/19), lumbar-radiculopathies 39.5% (51/129), myelopathies 40.3% (27/67), neuropathies of toxic origin 51.2% (21/41), entrapment syndromes 38.7% (12/31), and systemic or hereditary causes 56.3% (9/16) (Fig. 2). They were mainly considered to be moderate for post-stroke neuropathic pain and neuropathic pain linked to HIV at 41.7% (43/103) and 59.1% (110/186), respectively (Fig. 2). The pain was deemed to be very intense for neuropathies of infectious origin, at 52.9% (9/17), and trigeminal neuralgias, at 56.8% (21/37) (Fig. 2). A statistically significant difference was observed between the intensity of the pain and the various etiologies of neuropathic pain ($p < 0.0001$).

A burning sensation was the type of pain encountered most in diabetic neuropathies, at 42% (50/119) (Fig. 3). Paresthesia was the most frequently mentioned type of pain by patients suffering from post-stroke neuropathic pain, at 30.1% (31/103), and lumbar radiculopathies, at 48.1% (62/129) (Fig. 3). A burning sensation was encountered most

Table 1
Sociodemographic characteristics of the study population.

Sociodemographic characteristics		Files surveyed N (%)	95% CI	p
Gender	Women	532 (58.9)	[55.7–62.1]	10–7*
	Men	371 (41.1)	[37.9–44.3]	
	Sex ratio	1.4 in favor of female gender		
Age bracket in years	18–28	74 (8.2)	[6.5–10.1]	10–3*
	29–38	200 (22.1)	[19.5–24.9]	
	39–48	217 (24.1)	[21.3–26.9]	
	49–58	232 (25.7)	[22.9–28.6]	
	59–68	110 (12.2)	[10.2–14.4]	
	69–78	40 (4.4)	[3.2–5.9]	
	> 79	30 (3.3)	[2.3–4.6]	

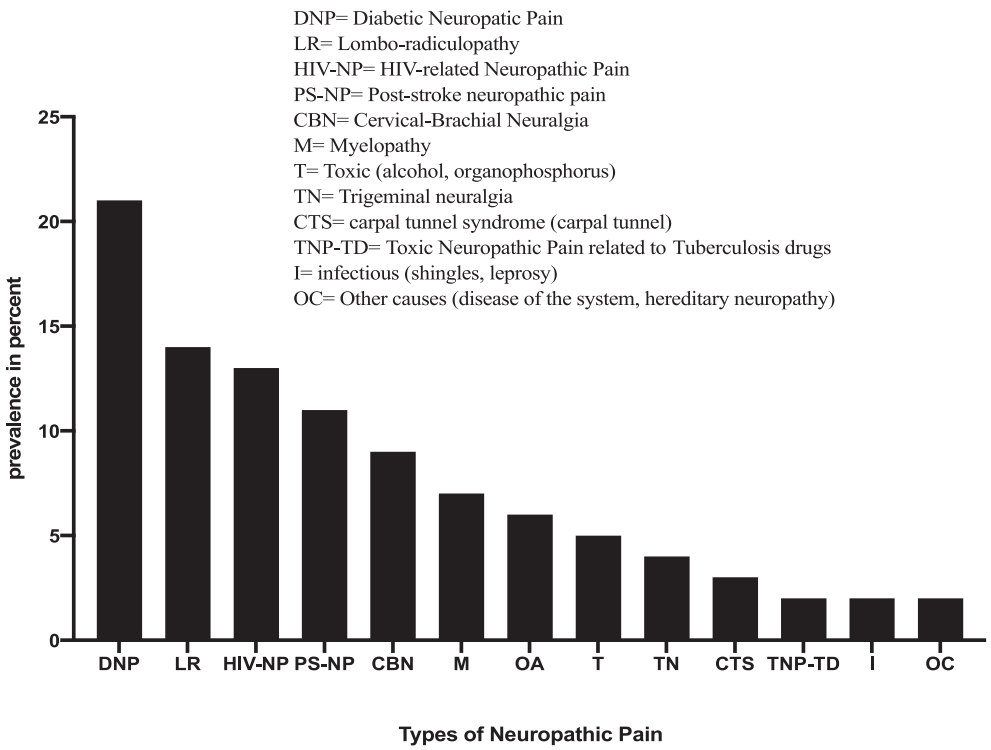

Fig. 1. Neuropathic pain typologies in our practice.

with toxic neuropathic pain linked with antituberculosis drugs, at 49.4% (40/81); neuropathies of infectious origin, at 47% (8/17); and trigeminal neuralgias, at 78.4% (29/37) (Fig. 3). Numbness was mainly encountered with neuropathic pain linked to HIV, at 39.8% (74/186); myelopathies, at 31.3% (21/67); neuropathies of toxic origin, at 36.6% (15/41); and entrapment syndrome, at 38.7% (12/31) (Fig. 3). With cervicobrachial neuralgias, a distribution of burning and numbness was noted, with 31.6% (6/19) each, as well as burning and searing pain, each at 10.5% (2/19) (Fig. 3).

3.1.4. Knowledge, attitudes, and practices (KAP) of the prescribers in regard to NeuP

The KAP survey involved 45 general practitioners and 45 neurologists representing participation rates of 79% and 75%, respectively.

3.1.5. Knowledge of the doctors regarding NeuP

The general practitioners and the neurologists mainly mentioned HIV and diabetes as the etiologies of neuropathic pain encountered in consultation. For the general practitioners, the frequencies were 31.1% and 26.7%, respectively versus 20% for each type for the neurologists (Table 3). Sleep disorders (28%) and anxiety (26.7%) were mentioned as

Table 2
Distribution of the various types of neuropathic pain according to gender.

Neuropathic pain typologies	Gender of the patients (%)			Odds Ratio	
	Files surveyed	M	F	OR [95% CI]	p-value
	N	n (%)	n (%)		
Post-stroke neuropathic pain	103	54 (52.4)	49 (47.6)	**2.98 [1.31;6.77]**	**0.008**
Diabetic neuropathic pain	186	56 (30.1)	130 (69.9)	1.16 [0.53;2.56]	0.71
HIV-linked neuropathic pain	119	32 (26.9)	87 (73.1)	0.99 [0.43;2.28]	0.99
Toxic neuropathic pain linked to antituberculosis drugs	19	12 (63.2)	7 (36.8)	**4.63 [1.42;15.08]**	**0.009**
Cervicobrachial neuralgia	81	32 (39.5)	49 (60.5)	1.76 [0.75;4.13]	0.19
Lumbar radiculopathy	129	65 (50.4)	64 (49.6)	**2.74 [1.23;6.12]**	**0.01**
Myelopathy	67	41 (61.2)	26 (38.8)	**4.26 [1.77;10.23]**	**0.0008**
Toxic (alcohol. organophosphorus)	41	23 (56.1)	18 (43.9)	**3.45 [1.33;8.94]**	**0.009**
Infectious (Zona, leprosy)	17	9 (52.9)	8 (47.1)	3.04 [0.92;10.06]	0.06
Other radiculopathies (lumbar spinal stenosis, post-surgery of the spinal cord)	57	23 (40.4)	34 (59.6)	1.83 [0.74;4.48]	0.19
Entrapment syndrome (carpal tunnel)	31	9 (29.0)	22 (71.0)	1.10 [0.38;3.19]	0.85
Other causes (nervous system disease, hereditary neuropathy, fibromyalgia, Pudendal neuralgia, glossopharyngeal. Arnold's neuralgia)	16	5 (31.2)	11 (68.8)	1.23 [0.34;4.42]	0.75
Trigeminal neuralgia	37	10 (27)	27 (73.0)	1 (ref)	–
Total	**903**	**371 (41.1)**	**532 (58.9)**		

Bold is to focus on the P that is significant.

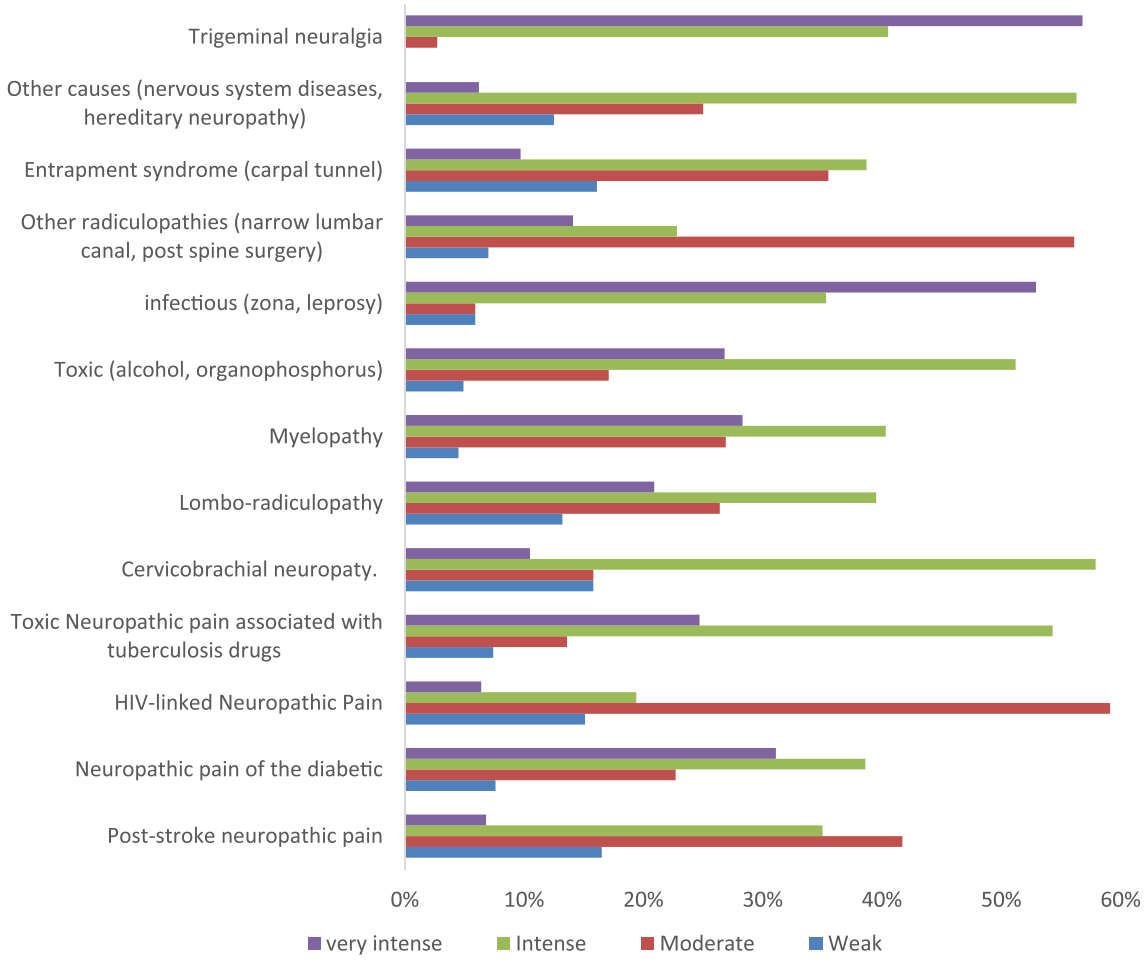

Fig. 2. Distribution of the intensity of the pain according to the neuropathic type.

the main consequences of the neuropathy by the neurologists, versus sleep disorders (24.4%) and a lower productivity (20%) for the general practitioners (Table 3).

At the therapeutic level, the neurologists mainly prescribe amitriptyline (26.7%), gabapentin (20%), and pregabalin (17.8%) as the three most effective drugs to treat neuropathy, versus amitriptyline (15.5%), carbamazepine (15.5%), and tramadol (13.3%) for the general practitioners (Table 3). The cost of the drug and its availability constituted the main criteria for the choice, both for the general practitioners (37.8% and 28.9%, respectively) and the neurologists (33.3% and 26.7%) (Table 3). The survey among the neurologists provided the price of several drugs in African countries that are currently used for NeuP, relative to the minimum wage (IGMW) of the country (Table 4).

Tolerability (safety) of a drug was raised by 15.5% of the neurologists as a criterion for the choice versus 6.7% of the general practitioners (Table 5).

3.1.6. Attitudes and practices in the treatment of NeuP

The majority of general practitioners (35.5%) stated that chronic pain was involved in more than 60% of their consultations, unlike the neurologists, of whom the majority (40%) asserted that this proportion ranged from 40 to 60% (Table 5). Headaches/migraines, low back pain and lumbar-radiculopathies, as well as neurological pain, were also mentioned as reasons for a consultation by 28.9%, 33.3%, and 15.5% of the general practitioners and 26.7%, 24.4%, and 24.4% of the neurologists, respectively (Table 5). There was a statistically significant difference between the neurologists and the general practitioners in the diagnostic approach (elements of orientation), with an odds ratio (OR) of 0.3 [0.1–1] and $p = 0.04624$ (Table 5). The majority of the general practitioners (64.4%) stated that they did not use any known diagnostic tool, unlike the neurologists, for whom the majority (77.8%) stated that they used the DN4 questionnaire as a diagnostic tool (Table 5). The neurologists were 22.6 [5.9–85.6] times more likely to use the DN4 questionnaire than the general practitioners. This probability was 67.7 [6.1–752.6] times for the use of other tools in addition to the DN4 questionnaire ($p = 0.001$). The intensity of the pain was evaluated during the questioning by the majority of the general practitioners (40%) and based on an analog scale (AS) by the majority of the neurologists (35.5%). The neurologists were 6.4 [1.8–23.1] and 6.7 [1.7–25.8] times more likely to use an analog scale and a simple visual scale (SVS), respectively, than the general practitioners ($p = 0.0046$ and $p = 0.00585$) (Table 5).

In terms of the views of the doctors regarding the therapeutic program of the patients, the majority of the general practitioners (84.4% or 38/45) and the neurologists (64.4% or 29/45) asserted that the patients used both conventional and traditional medicine. There was a larger number of general practitioners who stated cases of combinations of the two therapeutic methods, with an odds ratio of 0.4211 [0.2289–0.7472] and p-value of 0.003. The general practitioners, as well as the neurologists, for the most part, indicated that the beliefs of the populations were the main cause for the use of traditional practices, at 28.9% (13/45) and 33.3% (15/45), respectively. This attitude of the patients was tolerated by the majority of the carers who were questioned (general practitioners and neurologists). The most widely used traditional practice according

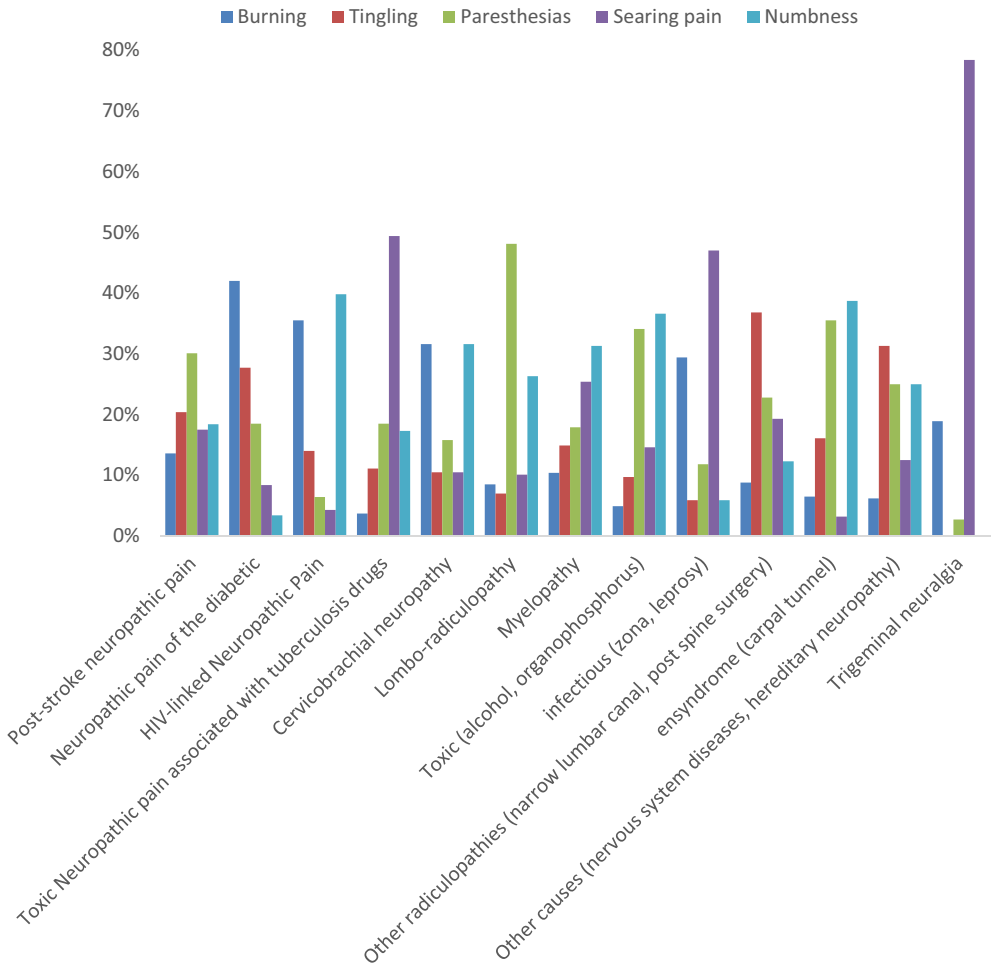

Fig. 3. Distribution of the type of pain according to the neuropathic type.

to the general practitioners was phytotherapy, at 26.7% (13/45), while for the neurologists, phytotherapy and scarification were designated as being the most widely used, at 28.9% (13/45) each (Table 6).

4. Discussion

4.1. NeuP is a prominent issue in current practice

This work, the first of its kind in Western Africa, was purposefully carried out in two phases (retrospective and prospective) to undertake a situational analysis of NeuP in our department and to carry out a KAP study of carers in terms of the treatment of NeuP, respectively. NeuP was, therefore, assessed from different perspectives in our context. Our results combined with the existing literature yielded preliminary data on the burden of NeuP in Mali and laid the foundation for context-tailored therapeutic strategies.

The use of validated tools minimized the common selection bias seen in NeuP studies [26]. Based on the ICD-11 guidelines, NeuP was categorized as peripheral or central. We included solely patient files with a valid neurological exam and a completed NeuP DN4 questionnaire, (if needed). The diagnosis of NeuP was based on a rigorous and purely clinical approach along with the use of diagnostic tools. These tools are relevant, but the clinical assessment remains the cornerstone of NeuP studies [27,28,29].

NeuP was presented as moderate to severe burning, paresthesias, tingling, searing pain, or numbness depending on the underlying causes, in keeping with the literature [12,30,31,36,37]. NeuP represented 11.5% of all outpatient visits in our Department of Neurology. We noted a relatively higher prevalence of NeuP (11.5%) compared to 6.3% in Benin [11] and 7.1% in Senegal [12]. This difference could be due to several reasons: (1) the hospital setting of our study, which took place in a department of neurology; (2) the expertise of our team was essentially comprised of neurologists, of whom ¾ had received specific formal training in regard to pain; and (3) current and frequent use of the DN4 questionnaire in our department. We emphasize that this questionnaire is easy to use and had a sensitivity of 80% and a specificity of 92%. [30]. In practice, our results were in keeping with the data in the world literature, for which the estimates of the prevalence of NeuP are between 6.5% and 17.9% [31]. These findings support the fact that the DN4 questionnaire, which is a more reliable tool than the painDETECT questionnaire, has been translated and validated in many languages in the world [32,33].

4.2. Sociodemographic characteristics

This work revealed that NeuP primarily affects working-age adults (i.e., individuals less than 60 years of age) and particularly women, with predictable socio-economic consequences. In this regard, our results confirm the data of the literature in Africa and in the world in general [11,31,34]. In France, Bouhassira et al. reported NeuP in 8% of women versus 5.7% in men, and 8.9% in patients over 50 years old versus 5.6% in those <49 years of age [35].

4.3. Etiologies of NeuP in our context

Many central and/or peripheral nervous system disorders can cause

Table 3
Knowledge of the carers regarding NeuP.

		GPs N (%)	Neurologists N (%)	Odds ratio (95% CI)	p
The main etiologies according to the carers	Lumbar radiculopathies	5 (11.1)	7 (15.5)	Ref	
	Diabetes	12 (26.7)	9 (20)	0.5 [0.1; 2.3]	0.39449
	HIV	14 (31.1)	9 (20)	0.5 [0.1; 1.9]	0.28293
	Alcohol	3 (6.7)	4 (8.9)	1 [0.1; 6.3]	0.95957
	Stroke	4 (8.9)	8 (17.8)	1.4 [0.3; 7.5]	0.67378
	Toxic	2 (4.4)	2 (4.4)	0.7 [0.1; 6.9]	0.77154
	Medications	4 (8.8)	3 (6.7)	0.5 [0.1; 3.5]	0.51663
	Deficiencies	1 (2.2)	3 (6.7)	2.1 [0.2; 27.1]	0.55608
Presumed impact on the quality of life according to the carers	Sleep impairment	11 (24.4)	13 (28.9)	Ref	
	Reduced productivity	9 (20)	5 (11.1)	0.5 [0.1; 1.8]	0.2754
	Anxiety	8 (17.8)	12 (26.7)	1.3 [0.4; 4.2]	0.69748
	Depression	9 (20)	11 (24.4)	1 [0.3; 3.4]	0.95592
	Dependence/ loss of autonomy	4 (8.9)	1 (2.2)	0.2 [0; 2.2]	0.19205
	Relationship problems	4 (8.9)	3 (6.7)	0.6 [0.1; 3.5]	0.59981
Drugs that are effective against NeuP according to the carers	Amitriptyline	7 (15.5)	12 (26.7)	Ref	
	Gabapentin	5 (11.1)	9 (20)	1.1 [0.2; 4.4]	0.94693
	Pregabapentin	4 (8.9)	8 (17.8)	1.2 [0.3; 5.3]	0.84241
	Antidepressant (IRS)	1 (2.2)	2 (4.4)	1.2 [0.1; 15.3]	0.9066
	Carbamazepine	7 (15.5)	4 (8.9)	0.3 [0.1; 1.6]	0.16262
	Opioids	2 (4.4)	1 (2.2)	0.3 [0; 3.8]	0.34834
	Cannabinoids	2 (4.4)	2 (4.4)	0.6 [0.1; 5.1]	0.62643
	Capsaicin patch	1 (2.2)	2 (4.4)	1.2 [0.1; 15.3]	0.9066
	Botulinum toxin	1 (2.2)	1 (2.2)	1.2 [0.1; 15.3]	0.9066
	Paracetamol	4 (8.9)	1 (2.2)	0.1 [0; 1.6]	0.11305
	Tramadol	6 (13.3)	2 (4.4)	0.1 [0; 1]	0.04828
	NSAIDs	5 (11.1)	1 (2.2)	0.1 [0; 1.2]	0.07202
Main criteria for choosing a drug in the treatment of NeuP	Cost	17 (37.8)	15 (33.3)	Ref	
	Efficacy	12 (26.7)	11 (24.4)	1 [0.4; 3]	0.94444
	Availability	13 (28.9)	12 (26.7)	1 [0.4; 3]	0.93273
	Tolerance	3 (6.7)	7 (15.5)	2.6 [0.6; 12.1]	0.20996

NeuP [41]. In 78.7%, NeuP was linked to a peripheral nervous system pathology such as diabetic neuropathy, neuropathy linked with HIV/AIDS, toxic neuropathy (antituberculosis drugs, alcohol, organophosphorus compounds), infectious neuropathy (Varicella Zona virus, leprosy), lumbar-radiculopathy, cervicobrachial neuralgia, lumbar spinal stenosis radiculopathy, postsurgery spinal radiculopathy, progressive polyneuropathy, genetic neuropathy, fibromyalgia, Pudendal nerve entrapment, trigeminal neuralgia, and Chiari malformation. In 19.2%, NeuP was linked to a central nervous system disease such as post-stroke neuropathic pain and NeuP in relation to a myelopathy. NeuP can also be idiopathic [31].

Diabetic NeuP (21%), lumbar-radiculopathies (14%), HIV/AIDS NeuP (13%), and post-stroke NeuP (11%) were the four most common etiologies of NeuP. Similar trends have typically been reported in the literature [35–40].

In 21%, NeuP was linked to diabetes due to its high prevalence in Mali and in Africa in general. In total, 7.1 million Africans currently suffer from diabetes, and this number is expected to increase to 18.6 million by 2030 [6]. Mali has a 7% prevalence of diabetes [42]. Diabetic polyneuropathy (DPN) with or without neuropathic pain potentially affects 50% of people with diabetes [43–45]. The prevalence of painful diabetic polyneuropathy was as high as 30.3% in a large multicentric study in South Africa [46].

In 14%, NeuP was linked to lumbar radiculopathy in our study. NeuP was found in 49.5% of the individuals with low back pain in Burkina Faso [13] and 40% in Germany [47]. In regard to NeuP, low back pain deserves more attention from the scientific community and the policy-makers as suggested in Lancet [48,49].

In 13%, NeuP was linked to HIV/AIDS in our study (Table 2) due to a 1.1% prevalence of HIV in Mali. Distal neuropathy has become very common with combined antiretroviral therapy [50]. It is not only severe but also often resistant to the currently available NeuP therapeutic arsenal [52,53]. In 2011, the prevalence of NeuP using the DN4 questionnaire in 600 patients with HIV was 20% [54,55]. In the Democratic Republic of Congo, 3.12% of the patients with HIV had neurological complications, and over 80% had NeuP [56]. NeuP can occur at any stage of the HIV/AIDS progression and it affects 55% of the patients taking ARV drugs for various reasons (the virus itself, HIV-related infections, ARV, and anti-TB drugs) [51,52]. It has been well-documented that ARTs result in NeuP, which negatively impacts the quality of life of patients. It is, therefore, important to facilitate patient access to drugs that are effective against NeuP through NeuP management programs. In addition to the effort to make ARVs widely available to patients with HIV, the potential to cause NeuP should be also considered [57].

In 11%, NeuP was linked to post-stroke outcomes in our study (Table 2). In a study in Nigeria, 50% of the patients exhibited post-stroke NeuP after a 3-month follow-up [62]. NeuP can affect up to 70% of patients after a stroke if properly diagnosed [63–68]. An increased prevalence of NeuP after stroke has been reported in low-income countries [58,59]. In sub-Saharan Africa, stroke has been increasing in prevalence in line with demographic transitions, lifestyle changes, and subsequent health risk factors (hypertension, diabetes, obesity, etc.) [60]. For instance, stroke is by far the primary cause of hospitalization stays and mortality in our neurology department [61].

Table 4
Cost of some of the drugs used in the medical treatment of neuropathic pain in 10 African countries relative to the minimum industrial wage of the countries (official sources).

Country	Drugs; Market price for one month of treatment (US dollars)					Minimum wage (US dollars)
	Neurontin® Gabapentin 300 mg	Lyrica 75 mg® Pregabalin 75 mg	Topalgic 100® Tramadol 100 mg	Laroxyl 25 mg® Amitriptyline 25 mg	Tegretol® Carbamazepine 400 mg	
Mali	48	62	68.70	7.17	9.29	80.69
Benin	39.49	83.05	19.85	5.46	9.46	80.28
Cameroon	–	51.03	4.19	5.31	9.45	72.53
Ivory Coast	68.50	52.99	8.32	5.34	11.14	119.99
Djibouti	61	38	5	7.50	9.14	85.89
Morocco	67.34	116.60	21.70	16.47	8.95	336.67
Niger	41.28	52.38	16.48	5.85	11.60	60.08
Senegal	87.36	65.65	16.64	5.50	8.70	95.39
Burkina Faso	45.80	44.27	6.10	4.58	10.68	64.42
Togo	53.78	48.12	4.26	6.30	10.20	69.99

4.4. Prominent place of NeuP in daily medical and neurology practices

NeuP represented over 40% of the outpatient visits for general medical practitioners (55.4%) and neurologists (71%) (Table 5), which suggests a relatively high prevalence of NeuP in Africa [69–72]. The current neurology curriculum at the medical school does not adequately prepare general medical practitioners to diagnose and refer NeuP patients for treatment. Postgraduate training is needed for this purpose. Similarly, young neurologists should be trained in the proper management of NeuP in clinical practice in "real life" [72].

4.5. Need for training in NeuP management

Most general medical practitioners in our study reported using the WHO list of essential drugs for the management of NeuP. However, they are often unaware that antidepressant and antiepileptic drugs could be used in NeuP in addition to their indication in depression and epilepsy, respectively [80,84]. Both the WHO and the International Association for the Study of Pain have emphasized the lack of qualified personnel as well as the paucity of diagnostic and therapeutic tools in Africa [2,22,24,73,74]. Patients with NeuP are cared for by poorly trained health professionals [75].

On the one hand, we found that the general medical practitioners (64.4%) and the neurologists (6.6%) were not aware of any diagnostic tool for NeuP. On the other hand, a patient satisfaction survey showed that less than one-third experienced over 30% pain relief [2]. The diagnostic and management of chronic pain/NeuP should be part of any effective continuing training for general medical practitioners and neurologists [72,76,77,78,79].

4.6. Limited compliance with current NeuP therapeutic guidelines in Mali

In our survey, amitriptyline, carbamazepine, and tramadol were the drugs most often prescribed by the general practitioners (Table 3), while for the neurologists these were amitriptyline; gabapentin, and pregabalin. Amitriptyline, which is the most available NeuP drug, is the only drug featured in the guidelines for general medical practitioners [2]. It is validated for treating NeuP and featured on the WHO model list of essential medications [80], despite its side effects [74,82]. For both the general medical practitioners and the neurologists in our study, amitriptyline was the most prescribed drug for patients with NeuP, which is in keeping with the literature [83]. General medical practitioners tend to prescribe the most accessible and the least expensive drugs for their patients [24]. No analgesic medications on this list of the

Table 5
Attitudes and practices of the carers in regard to NeuP.

Evaluation of the last 3 weeks of consultation		GPs N (%)	Neurologists N (%)	Odds ratio (95% CI)	p
Proportion chronic pain	Less than 20% of the consultations	4 (8.9)	4 (8.9)	Ref	
	Between 20 and 40%	13 (28.9)	9 (20)	1.1 [0.2; 5.4]	0.86681
	Between 40 and 60%	12 (26.7)	18 (40)	0.8 [0.3; 2.4]	0.6798
	More than 60%	16 (35.5)	14 (31.1)	1.7 [0.6; 4.8]	0.30211
Reasons for the consultation for pain	Headaches/migraine	13 (28.9)	12 (26.7)	Ref	
	Low back pain and lumbar radiculopathy	15 (33.3)	11 (24.4)	0.8 [0.3; 2.4]	0.68315
	Neurological pain	7 (15.5)	11 (24.4)	1.7 [0.5; 5.8]	0.3951
	Osteo-articular pain	4 (8.9)	5 (11.1)	1.4 [0.3; 6.3]	0.6974
	Oral facial pain	2 (4.4)	3 (6.7)	1.6 [0.2; 11.5]	0.6242
	Post-traumatic pain	3 (6.7)	1 (2.2)	0.4 [0.0; 0.4]	0.3904
	Psychogenic pain	1 (2.2)	2 (4.4)	2.2 [0.2; 27.1]	0.5412
Elements indicative of neuropathy	Context of the occurrence (notion of nerve injury)	7 (15.5)	16 (35.5)	Ref	
	Description of the pain upon questioning (burning, heat, discharge)	17 (37.8)	12 (26.7)	0.3 [0.1; 1]	**0.04624**
	Presence of discomfort/pain (numbness, tingling; paresthesias)	19 (42.2)	7 (15.5)	0.4 [0.1; 1.2]	0.09565
	Location of the pain (vicinity of a nerve)	2 (4.4)	10 (22.2)	0 [0; 0]	0.99938
Tools for diagnosis known and used	No tool	29 (64.4)	3 (6.7)	Ref	
	Yes (DN4)	15 (33.3)	35 (77.8)	22.6 [5.9; 85.6]	**0.0001**
	Other diagnostic tools in addition to the DN4	1 (2.2)	7 (15.5)	67.7 [6.1; 752.6]	**0.001**
Tools for evaluation of the intensity of the pain	Questioning	18 (40)	5 (11.1)	Ref	
	Numerical scale (NS)	11 (24.4)	11 (24.4)	3.6 [1; 13.2]	0.05276
	Analogue scale (AS)	9 (20)	16 (35.5)	6.4 [1.8; 23.1]	**0.0046**
	Simple visual scale (SVS)	7 (15.5)	13 (28.9)	6.7 [1.7; 25.8]	**0.00585**

Bold is to focus on the P that is significant.

Table 6
Opinions of the doctors regarding the therapeutic environment of the patients in regard to NeuP.

Opinions of the prescribers		GPs	Neurologists	Odds ratio (95% CI)	p
		N (%)	N (%)		
According to your experience, what is the proportion of your patients who have recourse to:	Strict conventional medicine	7 (15.6)	16 (35.6)	Ref	
	Traditional medicine associated with conventional medicine	38 (84.4)	29 (64.4)	0.421 [0.2289; 0.7472]	**0.0013**
According to your experience, what is the factor that explains recourse to traditional medicine by patients with chronic pain?	Beliefs	13 (28.9)	15 (33.3)	Ref	
	High cost of medications in conventional medicine	11 (24.4)	12 (26.7)	1.273 [0.5729; 2.885]	0.34
	High cost of consultations in conventional medicine	7 (15.6)	5 (11.1)	2 [0.8149; 5.291]	0.06
	The efficacy of traditional medicine	5 (11.1)	4 (8.9)	2.8 [1.038; 8.671]	**0.02**
	The accessibility of traditional therapists	7 (15.6)	4 (8.9)	2 [0.8149; 5.291]	0.06
	The difficulties obtaining a consultation in conventional medicine	2 (4.4)	5 (11.1)	7 [1.815: 45.48]	**0.001**
How do you view the use of traditional medicine by the patients?	I appreciate this practice	7 (15.6)	8 (17.8)	Ref	
	I tolerate this practice	16 (35.5)	17 (37.8)	0.5 [0.2025; 1.157]	0.05
	I believe in the efficacy of this practice	12 (26.7)	7 (15.5)	0.6667 [0.2595;1.639]	0.19
	I think that the association of this practice is better	5 (11.1)	4 (8.9)	1.6 [0.5173; 5.376]	0.2
	I do not appreciate this practice	3 (6.7)	6 (13.3)	2.667 [0.7298; 12.42]	0.07
	I recommend against this practice	2 (4.4)	3 (6.7)	4 [0.9249; 27.57]	**0.03**
According to your experience, what is the traditional practice most used by your patients with chronic pain/NeuP?	Phytotherapy	12 (26.7)	13 (28.9)	Ref	
	Recourse to marabouts (gris-gris, reciting Koranic verses	8 (17.8)	11 (24.4)	1.625 [0.6731; 4.125]	0.14
	Traditional manual methods (massage)	9 (20)	5 (11.1)	1.444 [0.6141; 3.52]	0.2
	scarification	5 (11.1)	13 (28.9)	2.6 [0.9505; 8.123]	**0.03**
	Prayers	11 (24.4)	3 (6.7)	1.182 [0.523; 2.709]	0.3

Bold is to focus on the P that is significant.

WHO are recommended as first-line treatment of NeuP [2,24,81], which hinders NeuP treatment [24]. Consequently, current health policies do not favor optimal management of NeuP in Africa because, except for amitriptyline, no other effective drugs against NeuP are listed as essential medicines, which limits the range of available drugs for the treatment of NeuP. The WHO should revise its list of essential medicines to accommodate drug-based treatment of NeuP [24,85–87].

In practice, a sufficiently strong therapeutic need and sufficient evidence have been shown to warrant inclusion of the additional medications recommended for the treatment of NeuP in the next editions of the model lists of the WHO [24,88]. This will certainly allow the medications to be cheaper and more accessible to patients with NeuP.

4.7. Optimal management of NeuP in the Malian and African contexts

Traditional medicine was reported to be an integral part of the therapeutic program of patients with pain in our study. It remains the first option for most people in rural Africa, whether or not they are literate [89,90]. Both general medical practitioners and neurologists tolerated its use because it is strongly embedded in our culture and because conventional medicines are also less affordable due to their cost. Patients with pain often resort to phytotherapy, fumigation, incantations, gris-gris, scarification, marabouts, and prayers, which stems directly from the cultural representations of pain. The disease is thought to be caused by occult forces in addition to natural causes [93,94], which may justify the simultaneous use of traditional and conventional medicines.

In NeuP, burning, electric discharge, tingling, and numbness are what mislead many patients and general medical practitioners in Africa. In Parakou (Benin, Western Africa), patients described NeuP as “unusual, odd, or even bizarre”. This unusual symptomatology could in part explain the alternative choice of traditional and herbal therapists [11]. In Nigeria, a study of musculoskeletal pathologies in people with HIV/AIDS revealed nearly systematic patient recourse to a combination of traditional medicine and conventional medicine [91]. Even in the U.S., indigenous populations (American Indians) generally rely on traditional medicine. A greater complementarity between conventional and non-conventional medicines could become standard in facilities that provide health care to multiethnic and racial groups [92]. American Indians explain pain in a very vague way compared to Caucasians. Therefore, currently used standard pain scales and questionnaires may not be a good match for these populations [94–96].

The next step in the management of NeuP in Africa will require contextualization of NeuP in the African setting and the validation of NeuP diagnostic tools in local languages. In recent years, we have assisted with the translation of these tools (DN4, Neuropathic Pain Questionnaire, S-LANSS; painDETECT) into various languages (Arab, Chinese, Spanish, Mongolian, etc.) for diagnosing NeuP [97–100]. African researchers hence ought to translate these tools into the main African languages (Kiswahili, Haoussa, Yorouba, Malinké, Lingala, Fulani, etc.). Furthermore, it is recognized that the cultural expression of suffering is based mainly on the words that are used to describe the pain [101]. Taking into account the wording is, therefore, useful in order to avoid erroneous interpretation of psychosocial distress as physical pain, which can lead to inappropriate treatments or to poor use of resources [102]. In this context, it has been shown that health interventions

regarding suffering and distress that take into account the sociocultural context by integration of linguistic aspects yield better results [103].

In this context of conceptualization, the physiological and neurobiological specificities, particularly the ethnic, racial, and genetic aspects of African patients should be integrated into the process of managing NeuP in Africa. The role of ethnic and racial disparities has been examined in models of North American studies. These studies are based essentially on the cultural differences between whites, African Americans, and Hispanics. Certain studies have also shown differences in perceptions (frequency, response to a given stimulus, pain threshold, and tolerance to pain) and the strategies for coping (strategies for dealing with the pain) between the various racial groups in the USA [104]. In this context, a review of 28 articles was able to show a higher prevalence of pain in minorities versus the white population in the United States. The authors of this study recommended implementation of a conceptual framework to better understand and treat pain experienced by ethnic and racial minorities [104]. In terms of an explanation, this ethnic and racial disparity appears to involve biological, sociocultural, and environmental factors [105]. For all of these reasons, some authors recommend the development of tools to measure pain that are culturally appropriate [106,107].

In terms of neurobiological aspects, one of the key elements to take into account with NeuP is genetic diversity. The discovery of genetic variants of ion channels constitutes compelling evidence for an influence of human genetics in the field of pain [108]. This genetic diversity appears to be the result of a complex interaction between environmental and genetic factors that alter both the vulnerability and the resilience of the somatosensory nervous system [108,109]. A better understanding of the genetic architecture of pain is, therefore, indispensable for optimal management of the issue of chronic and particularly neuropathic pain [109]. We are convinced that the African continent, with its great geographic, ethnic, and racial diversity, could provide a valuable contribution to this important step in the study and the treatment of pain.

Other than these considerations, these neurobiological aspects and beliefs constitute important elements to be integrated in relation to pain to devise therapeutic strategies. In this regard, North American studies have shown the relevance of integrating beliefs. For example, a study of cancer-related pain in Ojibway women (the third-largest autonomous group of American Indians in the United States and Canada) has allowed reticence to be shown based on the culture of discussing pain [108]. The authors of this work identified a common response to pain in Ojibway women that they labeled “blockage”. Thus, Ojibway are convinced that it is up to the carer to perceive and sense the pain of the patient in order to treat it. Moreover, Ojibway women described their interactions with the carers as being poor, unlike the white patients who found this interaction to be satisfactory [108].

In our experience, these erroneous beliefs tend to overestimate the capacities of practitioners of conventional medicine, who are often on equal footing as the healers in Mali and in Western Africa in general [92]. Following is the type of statements that African patients make regarding the carers *“if the doctor really has solid scientific know-how, they should be able to identify my illness/pain and cure it, as they are otherwise not in a position to be a carer. It is not up to me to tell them the nature of my illness*”. Moreover, we think that the acceptance and the success of certain so-called complementary practices (Chinese medicine, religion-based medicine, traditional practices) could be explained by this sociocultural imprint [110,111].

Based on our experience, the results of this work, and data in the literature, we call for cross-sectional and integrated management of chronic/neuropathic pain in Africa. Sociocultural adaptation of the health programs regarding pain would allow patients and their families to accept the interventions. The adaptation and the conceptualization will require win/win alliances between patients, researchers, clinicians, religious leaders, traditional therapists, and decision-makers. In our opinion, the implementation of this conceptual framework constitutes a crucial stage for effective management of neurological pathologies in general and chronic and neuropathic pain in particular.

5. Limitations of the study

The retrospective nature of the first part of our study (compilation of the patient data phase), despite the rigorous methodology for selection of the files, could lead to some information being lost, as all of the incomplete files or those for which the neuropathic nature was not proven were excluded. We, therefore, believe that our results have underestimated the extent of the phenomenon of NeuP in our practice. A prospective approach would be needed to provide an update. Regarding the second part, the selection of the 45 first responders resulted in others not being taken into account. In both cases, there could, therefore, have been selection bias.

6. Conclusion

This work allowed us to confirm the extent of NeuP in our context of low-income countries. In this context, characterized by a pronounced lack of technical platforms, simple and low-cost tools (such as the DN4 questionnaire) associated with rigorous clinical examination suffice to diagnose NeuP. The study of KAP among carers allowed us to note that optimal management of this pathology will involve: (1) better training of carers, and (2) improvement of the accessibility and the availability of medications. In light of this work, we have restarted the debate in Mali and in Africa in general regarding the concept of essential medications that should be tailored to the new epidemiological realities of the pathologies. Lastly, we believe that optimal management of chronic and neuropathic pain in Africa requires a process in which researchers will be engaged to customize and to contextualize the treatment of NeuP.

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