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INSTRUCTIONS AUX AUTEURS

Le Journal de l'épilepsie de l'Afrique du Nord et Moyen-Orient publie des articles originaux cliniques, scientifiques ou médico-sociaux sur l'épilepsie dans les pays d'Afrique du Nord et le Moyen-Orient, ou d'autres pays. Il publie également des éditoriaux, des articles de revue, des cas cliniques, des lettres à l'éditeur, des aperçus historiques sur l'épilepsie dans le monde et les histoires vécues par les patients atteints d'épilepsie, les médecins ou autres professionnels concerbés par cette maladie.

Il publie également des rapports des séances de travail des Sociétés, ligues et associations de l'épilepsie en Afrique du Nord et Moyen-Orient.

CONDITIONS DE PUBLICATION

Les articles ne doivent avoir fait l'objet d'aucune publication antérieure ni être simultanément soumis pour publication à une autre revue. Les textes sont rédigés en français ou en anglais. Les articles sont adressés, par le Comité de Rédaction, pour avis à des lecteurs qui restent ano- nymes pour les auteurs. En aucun cas la responsabilité de la Revue n'est engagée vis-à-vis des manuscrits qui lui sont adressés, avant la décision finale du Comité de Rédaction.

Les articles originaux ne doivent avoir fait l'objet d'aucune publication antérieure (à l'exception d'un résumé de moins de 400 mots), ni être simultanément soumis pour publication à une autre revue.

La mise en page des articles y compris résumés, références, tableaux et figures ne doit pas dépasser :

•10 pages dactylographiées pour les mises au point,•8 pour les articles originaux,

•5 pour les éditoriaux,•4 pour les cas cliniques,•4 pour les activités associatives,

•3 pour les aperçus historiques•3 pour les lettres à l'éditeur•Et 2 pour les témoignages de patients épileptiques.

Les manuscrits doivent être sous format Word ou RTF (avec en 3 fichiers, 1-comportant le texte, les figures et les tableaux, 2-Comportant les photos et toute autre illustration Et 3-Attestation cédant les droits d'auteur à l'éditeur, attestant que le manuscrit n'est pas accepté ailleurs ou en cours de soumission, que tous les auteurs ont lu et approuvé la version finale et que les aspects éthiques sont respectés) ; tous les fichiers doivent être envoyés ensemble par email à l'adresse suivante : je.submission@gmail.com

RECOMMANDATIONS GENERALES POUR LA PRESENTATION DES MANUSCRITS:

Liste des recommandations (à vérifier avant l'envoi du manuscrit) : Manuscrit

•Le manuscrit est dactylographié en double interligne avec une marge de 2,5 cm sur chaque bord, y compris la page de titre, le résumé, les remerciements, les références, les tableaux et les légendes des figures.

•Il est conseillé d'utiliser le minimum d'abréviations. Le terme en entier précède l'abréviation lors de sa première apparition dans le texte.

•La hiérarchie des titres et sous-titres est bien mise en évidence par une numérotation.

•La disposition des articles originaux doit suivre le plan suivant : page de titre, résumés et mots-clés, résumés en anglais et ses mots-clés, texte (avec introduction, matériel et méthodes, résultats, discussion), références, tableaux, figures et légendes.

•Les pages sont numérotées, en chiffres arabes en commençant par la page de titre.

Pour accélérer la publication des manuscrits soumis, il est demandé de se conformer stricte- ment aux recommandations ci-dessous.

Les recommandations suivantes sont conformes aux normes dites de Vancouver pour la prépa- ration des manuscrits soumis aux journaux biomédicaux.

Page de titre

La page de titre comporte :

•Le titre récis et concis mais informatif (en français et en anglais).

•Le nom de chaque auteur suivi de son prénom.

•Le nom des services et des institutions responsables du travail.

•Le nom et l'adresse de l'auteur responsable de la correspondance pour le manuscrit avec son adresse e-mail (impératif).

•les remerciements, les sources de financements et les conflits d'intérêts éventuels.

Résumés et mots-clés

•Un résumé en anglais, en français et en arabe (facultatif) de moins de 250 mots chacun sont inclus pour les articles originaux.

•Les résumés sont structurés avec 4 paragraphes (introduction, participants et méthodes, ré- sultats, conclusion).

•Les mots-clés doivent être indiqués (entre 3 et 6 séparés par des tirets).

•l n'y a pas d'abréviations ni de référence bibliographique dans les résumés.

Tableaux, figures

Les documents iconographiques – figures et tableaux – sont obligatoirement appelés dans le texte et conformes aux recommandations suivantes :

•Les figures sont numérotées en chiffres arabes, par ordre d'apparition dans le texte où elles sont appelées (figure 1).

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•Les médicaments doivent être mentionnés selon leur dénomination commune internationale ou leur nom chimique. Les noms commerciaux doivent être mentionnés entre parenthèses après la DCI.

•Les symboles, chiffres et textes des figures sont clairs et de taille suffisante pour que chaque élément soit parfaitement lisible.

•En aucun cas les figures ne doivent être intégrées directement dans le corps du texte.

•La publication d'illustrations en couleur est recommandée.

Références

Les références bibliographiques, limitées selon la rubrique retenue, sont portées en fin d'article, numérotées selon l'ordre d'apparition dans le texte.

Le nombre de références :

•Ne doit pas dépasser 40 pour les articles originaux et 60 pour les mises au point,

•Doit être entre 5 et 10 pour les cas cliniques et entre 4 et 6our les lettres à l'éditeur,

Toutes les références doivent être appelées dans le texte (y compris celles appelées dans les figures et tableaux) : le numéro de la référence bibliographique citée est mentionné entre crochets.

Les références d'articles parus dans un périodique doivent comporter le nom des 6 premiers auteurs avec les initiales des prénoms (suivis de "et al." à partir du 7e auteur), le titre complet de l'article dans la langue originale, le nom de la revue selon les abréviations de l'Index Medicus, l'année, le numéro du tome, la première et la dernière page abrégée du texte.

La présentation – style et ponctuation – suit scrupuleusement les 3 exemples suivants :

1-Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary preven¬tion programs for patients with coronary artery disease. Ann Intern Med 2005; 143: 659-72.

2-Champault A, Dagher I, Vons C, Franco D. Laparoscopic hepatic resection for hepatocel¬lular carcinoma. Retrospective study of 12 patients. Gastroenterol Clin Biol 2005; 29: 969-73.

3-Guilpain P, Chanseaud Y, Tamby MC, Mahr A, Servettaz A, Guillevin L et al. Pathogénie des vascularites systémiques primitives (I) : vascularites ANCA-positives. Presse Med 2005; 34: 1023-33.

•Les citations de livres doivent comporter les noms des auteurs, le titre du livre, la ville, le nom de la maison d'édition et l'année de

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La présentation – style et ponctuation – suit scrupuleusement les 2 exemples suivants :
3- Danowski RG, Chanussot JC. Traumatologie du sport. 7e ed. Paris: Masson; 2005.
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The review of epilepsy in northern Africa and the Middle East publishes original clinical, scientific or medical social on epilepsy in the countries of northern Africa and the Middle East, or any other the world. It also publishes editorials, general reviews, clinical cases, historical overviews on epilepsy in the world and stories experienced by patients with epilepsy, physicians or other other professionals involved in epilepsy.
It also publishes the minutes of the sessions of Societies, leagues and associations against epilepsy in northern Africa and Middle East.
Condition of Publication:
The articles must not have been published nor simultaneously submitted for publication in ano- ther journal. The texts are written in French or English. The articles are addressed by the Drafting Committee for its opinion to readers who remain anonymous to the authors. In no event shall the review is undertaken vis-à-vis the manuscripts sent to him before the final decision of the Editorial Board.
Original articles should have been no previous publication (with the exception of an abstract under 400 words), nor be simultaneously submitted for publication in another journal.
The layout of articles including abstracts, references, tables and figures must not exceed:
•10 for general reviews,•8 for original articles,•5 for editorials,•4 for case reports,•4 for association activities,•3 for historical overviews•3 for letters to the editor•And for the testimony of two epileptic patients.
Manuscripts should be in Word or RTF format (including 3 files, 1-with the text, figures and tables, 2-Including photographs and other illustrations and 3-yielding certificate of copyright to the publisher stating that the manuscript is not accepted elsewhere or under submission, all authors read and approved the final version and the ethical aspects are met), all files must be sent together by email to: **je.submission@gmail.com**

GENERAL RECOMMENDATIONS FOR MANUSCRIPTS SUBMISSION:

List of Recommendations (check before sending the manuscript):
•The manuscript is typed double-spaced with a margin of 2,5 cm on each side, including the title page, abstract, acknowledgments, references, tables and figure legends.
•It is advisable to use as few abbreviations. The full term precedes the abbreviation at its first appearance in the text.
•The hierarchy of titles and subtitles is highlighted by a dial.
•The layout of the original articles should follow the following plan: title page, abstract and keywords, text (with introduction, materials and methods,results,discussion), references,t**ables,figures and legends.**
•Pages are numbered in Arabic numerals, beginning with the title page.
To expedite the publication of submitted manuscripts are asked to adhere strictly to the re- commendations below.
The following recommendations are consistent with standards of Vancouver called for the preparation of manuscripts submitted to biomedical journals.

Title page

The title page includes:

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•The name of each author followed by his first name.
•Name of services and institutions responsible for the work.
•The name and address of the author responsible for correspondence for the manuscript with his e-mail address (mandatory).
•Acknowledgments, sources of funding and potential conflicts of interest.

Abstracts and Keywords
•A summary in English, French and Arabic (optional) with fewer than 250 words for each is included in the original articles.
•Abstracts are structured with four paragraphs (introduction, participants and methods, results, conclu- sion).
•The key words must be given (between 3 and 6 separated by dashes).
•No abbreviations or references in literature abstracts.
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•The Graphic - figures and tables - are necessarily called in the text and in accordance with the fol- lowing recommendations:
•The figures are numbered in Arabic numerals, in order of appearance in the text where they are called (Figure 1).
•Tables are numbered in Roman numerals, in order of appearance in the text: (Table I).
•The figure legends are made one after the other end of the article, on a separate sheet.
•The figures must be submitted each on a separate sheet, and provided as separate files in a file its reasons for figure and are all accompanied by a caption.
•Different explanations or notes are required to understand below each table.
•The reproduction of previously published material must be accompanied by permission of the pu- blisher or the author's copyright holder.
•Abbreviations should be avoided. If the figure and / or table contain abbreviations, they should explain in the legend.
Drugs should be referred by their international name or chemical name. Trade names must be listed in parentheses after the DCI.
•Symbols, figures and text figures are clear and large enough so that each element is perfectly readable.
•In any case the figures should be integrated directly into the text.
•The publication of color illustrations is recommended.

References

References, limited depending on the item selected, are brought to the end of the article, numbered in order of appearance in the text.
The number of references:
•Must not exceed 40 for original articles and 60 for general reviews
•Must be between 5 and 10 clinical cases and between 4 and 6 for letters to the editor
All references must be cited in the text (including those referred to in the figures and tables): the number of the references cited is mentioned in brackets.
•References to articles in a journal should include the name of the first 6 authors with the initials of the first name (followed by «et al.» From the seventh author), the full title of the article in original language, the name of the journal abbreviations as cited in the Index Medicus, the year the number of the volume, the first and last page.
The presentation - style and punctuation - closely follows the three following examples:
[1]Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention Programs for patients with coronary artery disease. Ann Intern Med 2005; 143: 659-72.
[2]Champault A, Dagher I, Vons C, Franco D. Laparoscopic hepatic resection for hepatocellular carci- noma lular. Retrospective study of 12 patients. Gastroenterol Clin Biol 2005, 29: 969-73.
[3]Guilpain P Chanseaud Y, Tamby MC, Mahr A, Servettaz A, Guillevin L et al. Pathogenesis of systemic vasculitis primitives (I): ANCA-positive vasculitis. Presse Med 2005; 34: 1023-33.
•Citations of books should include authors' names, book title, city, name of publisher and year of publication.
The presentation - style and punctuation - closely follows the two following examples:
[3] RG Danowski, JC Chanussot. Sports traumatology. 7th ed. Paris: Masson, 2005.
•The Editorial Board reserves the right to return manuscripts to authors who do not comply with the recommendations outlined above before submitting them to the readers.

Editorial

Dr. Lilia Núñez-Orozco
President of Mexican IBE Chapter
Ambassador for Epilepsy

EDUCATION IN EPILEPSY

Epilepsy is a problem with several aspects: the disease in and of itself, requiring prompt medical attention; the emotional reactions that need psychological or psychiatric interventions; and, importantly, the stigma and social rejection which are consequences of ignorance and misconceptions.

Education is necessary to eradicate ignorance in order to foster better collaboration with people with epilepsy (PWE), their relatives and the society in general, in order to improve patient quality of life.

Everybody needs education about epilepsy, but the approach is different for PWE and relatives, physicians and health workers, school teachers, employers and society, because of the different roles they play vis-à-vis the person with epilepsy.

1.EDUCATION FOR PEOPLE WITH EPILEPSY:

The goals are to provide knowledge about their condition, which are the real limitations and expectations for the future, and the need to adhere to treatment, including medication and non-pharmacological measures.

The burden of the disease is heavy, but PWE are not alone, because epilepsy is very frequent and they need to share experiences with other PWE in order to accept and cope with the disease, and return to life and develop their abilities.

2.EDUCATION FOR FAMILY

Relatives also need to have a good knowledge about epilepsy and understand the need for adherence to treatment (medication and non-pharmacological measures) and the importance of supervising the adherence, no matter the age of the PWE. They also need to accept and cope with the disease, encourage PWE to develop their abilities and avoid overprotection/rejection.

PWE can have husband/wife and children; women with epilepsy can deliver healthy children with adequate treatment, but they need to have information about the risks of inheritance and of teratogenicity with antiseizure epileptic medication.

It is also very important to assign and respect PWE to play his/her corresponding role in the family.

There are different means of education: the main one is through informative sessions in a meeting room, where the concepts can be explained and people can ask questions to receive answers in an understandable language. As such, a schedule is required to perform a kind of permanent course about epilepsy. Other ways are pamphlets and handbooks on certain topics about the disease, mainly about what to do or not to do in daily activities when a person has epilepsy.

3.EDUCATION FOR PHYSICIANS AND HEALTH WORKERS.

Although they studied Medicine or health-related topics, the knowledge about epilepsy is very limited because of the current programs of the career in different universities. The general practitioner therefore usually also has wrong concepts about epilepsy and lacks the skills to diagnose and initiate a good antiepileptic treatment. The practitioner might not always know when it is necessary to refer PWE to the neurologist.

Education for physicians includes modification of the medical school curriculum in order to improve knowledge on epilepsy in Universities and participation in Continuous Medical Education (CME) courses. Elementary concepts are definition of epilepsy as a chronic brain condition with propensity to elicit seizures with neurobiological, cognitive, psychological and social consequences. It is furthermore important to know how to diagnose seizures and epilepsy, and the classifications, as well as how to start a comprehensive treatment with antiepileptic drugs and detect and treat psychosocial aspects of the disease.

It is also very important to teach physicians and health workers how to provide information about epilepsy to non medical persons, in order to help them grasp the concepts and obtain their cooperation for the treatment and care.

4.EDUCATION FOR SCHOOL TEACHERS

Education is a Human Right, so, children with epilepsy and no intellectual disability have to attend school and participate in all activities, including sports.

It is necessary to educate school teachers on how to attend to a generalized seizure so as to avoid the fear of a seizure for ignorance about first aid measures. Teachers are not to reject children with epilepsy in schools because of this fear. It is also important to teach them as well as students to show solidarity and respect to PWE and avoid stigma.

The good capacitation of PWE, will allow a better future in productive life.

5.EDUCATION FOR EMPLOYERS

Work is a Human Right. PWE in their productive years, need to have a job and be independent, to have social insurance, medical attention and medication.

Employers should be taught which jobs (almost all) can be performed by PWE and what the real risks are in order to accept PWE in their companies, thus allowing PWE to have an income and social insurance to be able to better attend to their illness.

6.EDUCATION FOR SOCIETY

Organizations of people with epilepsy and lay and professional persons who want to help PWE, have been founded in many countries to work in different aspects: giving psychological support, providing medical attention and medication, but mainly providing education to PWE, relatives and society, in order to improve adherence to treatment, understanding the disease and all the possibilities that they have to develop their abilities and be independent, with a good quality of life.

These organizations follow the aims of the International Bureau for Epilepsy (IBE) in more than 100 countries worldwide, working directly with PWE.

In order to improve education for health workers, the IBE can promote the participation of IBE chapters and associations in local and regional Epilepsy congresses along with representatives of international league against epilepsy (ILAE) to offer comprehensive programs that include patients, relatives and society at large.

Education is the axis of a better attention and adaptation to epilepsy and, as such, of a better quality of life for PWE.

All associations that belong to IBE have this very aim, pursuing several means to achieve their goals. Communication among the associations (to share ideas, programs, exchange educational materials, etc.,) can make this endeavor easier.

Associations work mainly with voluntary collaborators. Educational programs often need only the opportunity and space to be enacted and not necessarily a budget.

The associations can also use modern technology: Websites with information about the association and about epilepsy. Facebook, Twitter, channels of YouTube and podcasts are helpful resources in spreading information to interested people and the public in general.

All in all, education is a basic need for PWE and for all persons related to them. Epilepsy education has huge benefits on quality of life.

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Problem of accessibility to antiseizure drugs for patients suffering from epilepsy in Bangui. Central African Republic

Problème d'accessibilité aux antiépiletiques pour les patients souffrants d'épilepsie à Bangui. République Centra Africaine

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Conflicts of interest: None

Abstract

Introduction: Epilepsy is the most frequent severe chronic neurological disease of various etiologies characterized by the repetition of seizures. It affects more than 50 million people worldwide. In developing countries (DEP), 80-90% of people do not have access to treatment, for several reasons.

Goal: Assess patient accessibility to antiepileptic drugs in Bangui.

Methodology: It was a 3-month cross-sectional prospective study, from October 1 to December 31, 2018, within all the pharmaceutical structures in Bangui, recognized by the Ministry of Health.

Results: We visited a total of 32 structures and interviewed a total of 32 people. The average age of the respondents was 29, with a female predominance of 65.6%. Most worked as cashiers or accountants. The majority had no epilepsy training (84.4%) and was only aware of the generalized tonic tone (65.6%). The main cause of epilepsy was brain damage (56.3 %). The non-contagiousness of the disease was recognized by 71.9% of the respondents. The majority of those surveyed considered epilepsy to be incurable (62.5%), even pharmacists. More than half of the structures were sales units (56.2%). Among the 32 structures visited, 19 had antiepileptic drugs (59.6%). Phenobarbital was the most available (53.1%) followed by Carbamazepine (37.5%), Valproic Acid (37.5%), and Phenytoin (9.4%). These 4 major antiseizure medication were mostly found in pharmacies. Phenobarbital was the most prescribed and the most in short supply. Drug stock outs were frequent and it took a long time to restock them. The cost of antiseizure medication was very high.

Conclusion: The lack of trained personnel, the inadequacy of pharmaceutical structures, the insufficient availability of antiepileptic drugs and their very high cost are factors limiting the accessibility of antiepileptic drugs for patients.

Keywords: Epilepsy- Therapeutic accessibility- Antiseizure- Pharmaceutical structures- Bangui, Central African Republic.

Introduction

L'épilepsie est une maladie neurologique chronique sévère la plus fréquente, d'étiologies diverses caractérisée par la répétition des crises convulsives. Elle touche plus de 50 millions de personnes dans le monde. Dans les pays en voie de développement (PED), 80-90% des sujets n'ont pas accès au traitement, et ce pour plusieurs raisons.

Objectif

Evaluer l'accessibilité des patients aux médicaments antiépileptiques à Bangui.

Méthodologie

Il s'agissait d'une étude prospective transversale de 3 mois, allant du 1er octobre au 31 décembre 2018, au sein de toutes les structures pharmaceutiques de Bangui, reconnues par le ministère de la santé.

Résultats :

Nous avons visité au total 32 structures et interrogé au total 32 personnes. L'âge moyen des répondants était de 29 ans, avec une prédominance féminine de 65,6%. La plupart exerçait la fonction de caissières ou des comptables. La majorité n'avait pas reçu de formation sur l'épilepsie (84,4%) et ne connaissait que la forme tonicoclonique généralisée (65,6%).La principale cause de l'épilepsie était la lésion du cerveau (56,3%). La non contagiosité de la maladie était reconnue par 71,9% des enquêtés. La majorité des enquêtés considérait l'épilepsie comme incurable (62,5%), même les pharmaciens. Plus de la moitié des structures étaient des unités de vente (56,2%). Parmi les 32 structures visitées, 19 détenaient des antiépileptiques (59,6%). Le Phénobarbital était le plus disponible (53,1%) suivi de la Carbamazépine (37,5%), Acide Valproïque (37,5%), et la Phénytoine (9,4%). Ces 4 antiépileptiques majeurs se trouvaient pour la plupart dans les officines. Le phénobarbital était le plus prescrit et le plus en rupture. Les ruptures de stock des médicaments étaient fréquentes et le réapprovisionnement mettait beaucoup de temps. Le coût des antiépileptiques était très élevé.

Conclusion

Le manque de personnel formé, l'insuffisance des structures pharmaceutiques, la disponibilité insuffisante des médicaments antiépileptiques et leur coût très élevé sont des facteurs limitant l'accessibilité aux médicaments antiépileptiques pour les patients.

Mots-clés : Epilepsie, accessibilité thérapeutique, antiépileptiques, structures pharmaceutiques, Bangui, Centrafrique.

Introduction

Epilepsy is a chronic brain condition that affects all populations of the world, regardless of race, religion, sex, age, or social status. It reaches more than 50 million people worldwide, including 10 million in Africa. The prevalence varies from 4-10% o in developed countries, while in sub-Saharan Africa, it is estimated at 15% o [1,2]. In the Central African Republic, according to studies carried out in schools in Bangui and in the general population in Berberati in the west of the country, the prevalence of this condition varies from 2.8% o to 11.73% o [3,4]. If in developed countries, patients have easy access to antiseizure , in developing countries, 80-90% of epileptic subjects do not have access to treatment: Either by lack of infrastructure, or by insufficient availability of antiepileptic drugs, either due to the shortage of well-trained medical personnel or to traditional concepts on epilepsy. Antiepileptic drugs are not available for the majority of epileptics, for geo

graphic, financial or cultural reasons [5]. Studies on the accessibility, availability and cost of medicines have been carried out in certain regions of the world [6-10]. In the Central African Republic, no information is available on the supply, availability and accessibility of antiepileptic treatment by patients. Thus, we carried out this work in order to assess the accessibility of patients to AE drugs in Bangui, capital of the country.

Methodology

Our study took place in the city of Bangui, capital of the Central African Republic, located in the south of the country at 4° north latitude and 16° east longitude. The climate is equatorial and has a short dry season from December to March and a rainy season from April to November. The city of Bangui has 903,268 inhabitants, according to the 2018 projection, or 17.2% of the country's population. It covers an area of 100 km2. The main economic activities of the city are based on commercial enterprises and market gardening; but the military-political events in the city have damaged the economic fabric.

In terms of health, the city of Bangui is located in health region No. 7, divided into 3 districts:

-The Bangui I Health District: The Central District office is based in Lakouanga. Its area of responsibility covers the administrative districts of the 1st, 2nd and 7th Arrondissements.

-The Bangui II health district: The central district office is based in Beavers and covers the administrative districts of the 3rd, 5th and 6th Arrondissement.

-The Bangui III health district: The central district office is based in Bédé Combattant. Its area of responsibility covers the administrative districts of the 8 th, 4 th Arrondissement.

It is served by 4 central hospitals (National University Hospital Center of Bangui, Community University Hospital Center, University Hospital Center of Sino-Central African Friendship, Pediatric University Hospital Complex of Bangui), seven urban health centers distributed in the various districts of the city, private health centers and a clinic and several private medical offices.

This Table I shows the Distribution of pharmaceutical structures in the city of Bangui. To be called in the previous text

Districts	Pharmaceutical structures			Total
	wholesaler	pharmacy	sales units	
1er	3	6	4	13
2e	0	1	2	3
3e	0	0	1	1
4e	0	1	4	5
5e	0	3	2	5
6e	0	0	2	2
7e	0	0	2	2
8e	0	0	1	1
Total	3	11	18	32

Figure 1: Administrative map of Bangui (districts and districts).

It was a cross-sectional and exhaustive prospective study over a period of 3 months, from October 1 to December 31, 2018, covering all the pharmaceutical structures in Bangui recognized by the Ministry of Health. All subjects of both sexes with the qualification of heads of structures or dispensers of drugs were included. Not being part of the mini pharmaceutical kiosks and the drug sales structures having no sales authorization from the Ministry of Health. The data were collected using a previously established survey sheet, entered with Excel 2010 software, and analyzed with Epi info software version 3.5.4.

Results

During this study, 32 structures were visited, including 17 public (53.1%) and 15 (46.9%) from the private sector. Most of the pharmaceutical structures visited were sales units (56.2%) followed by pharmacies (34.4%). In our series, 32 people were interviewed ranging in age from 25 to 60 years old. The most represented age group was 25 to 34 years old (43.7%). The average age was 29 years old. There was a female predominance (65.6%) with an F / M ratio of 1.9. Almost half of our respondents had less than 5 years of practice.

More than half of them (53%) were cashiers or accountants followed by pharmacists (31%) and state nurses (13%). As far as knowledge of epilepsy is concerned, 84.4% of those surveyed are not trained in epilepsy and 65.5% only knew about the generalized toncicoclonic crisis. For 71.9%, epilepsy is not a contagious condition. Etiologically, brain damage was cited in 56% of cases followed by hereditary causes (25%). The majority (62.5%) of those surveyed considered epilepsy to be an incurable condition. Most respondents (68.80%) admitted to giving advice to people with epilepsy. Phenobarbital (87.1%) was the most well-known antiepileptic drug in the survey, followed by Carbamazepine (51.68%). In terms of drug safety, 48% of those surveyed did not know if these drugs have been validated by the pharmaceutical management. The majority of respondents (65.7%) had no idea about the frequency of pharmaceutical management monitoring visits. For the availability of EAWs, among the 32 pharmaceutical structures visited, 19 (59.6%) held antiepileptic drugs at the time of the visit. The main molecules available were Phenobarbital in 17 structures (53.1%), Carbamazepine in 12 of them (37.5%), Valproic Acid in 12 structures (37.5%), Phenytoin in 3 pharmacies (9.4%).

The AEs found in public structures were generics. It should be noted that among the 3 wholesalers visited; only one had be noted that among the 3 wholesalers visited; only one had antiepileptic drugs. During our survey, some pharmacies held more than one specialty of EA for the same active ingredient. Of the 19 structures that held AE, 15 often had stock outs, or (78.9%). The duration of stock-outs of AEs varied from 1 month or more than 2 months. The frequency of rupture was once per semester (40%) or once per year (40%) for the majority. The replenishment of AE could go up to more than 2 weeks in certain structures (73.3%). Phenobarbital was the most prescribed (73.7%) and most discontinued (63.2%) EA followed by Carbamazepine (31.6%) and Benzodiazepine (21.1%).

Discussion

During this study about accessibility to antiseizure medications in Bangui, the most represented age group was 25 to 34 years old (43.7%) with an average age of 29 years. This result is close to that found in Mali [11] in the city of Kati (30 years old). On the other hand, inferior to certain data found in Africa [12-14]. This predominance of young people in our population could be explained by the fact that they are mainly represented in the general population [15].

We note in our work a female predominance of respondents (65.6%). This result is close to that found in Niger [14] and different from that found in Bangui [12] and Mali [11]. This could be explained by the emancipation and promotion of women in the field of work.

The duration of exercise in the profession was less than 5 years. It is lower than those reported for Kati in Mali [11] and Sakoira in Niger [14]. The majority of respondents were neither pharmacists, state nurses (IDE), nor state graduate midwives (SFDE). For the most part, there were cashiers or accountants. This shows the negligence of the managers of certain pharmaceutical structures who hire people, most often close relatives, who have no idea about the products they distribute to patients.

We found during our study that the majority of respondents (84.4%) had not received any training on epilepsy. But 65.6% were aware of the generalized tonicoclonic form. This result is close to those found in Mali [16,17] and lower than those of certain African authors in Bamako and Bangui [4,11,12,18]. This high percentage of knowledge of this generalized tonicoclonic form is justified by the fact that, on the one hand, this form is the most frequent in developing countries (developing countries), especially in sub-Saharan Africa (60%) [2,19], and on the other hand, CTCGs are remarkable and spectacular manifestations for patients and those around them and their diagnosis is easier to demonstrate even for a non-specialist in comparison with other clinically less expressive epilepsy attacks [20].

Regarding the etiology, 56.3% believe that epilepsy is due to brain damage. This result is almost similar to the data of certain authors in Africa [4, 11,13,16].

Regarding contagiousness, 71.9% thought that epilepsy is not a contagious disease. This is different from the study carried out in Berberati in the west of the Central African country and in Mali [4,16,21]. This difference could be explained by the fact that the people hired and placed at the level of pharmacies received health training and even if they did not follow modules on epilepsy, they at least heard of this affection during their internships in the various departments where they went. Furthermore, saliva was the main route of transmission, and 62.50% of those surveyed said that epilepsy is incurable. This strong belief in contagiousness and incurability demonstrates their under-information on epilepsy and encourages them to create a communication and information framework like the Central African League against epilepsy.

We noticed during our study that pharmacists think epilepsy is a non-contagious and incurable disease. This claim of incurability can be explained by the fact that they are content to provide medication to their patient and in no way care about their future. While collaboration should exist between clinicians, pharmacists and all health personnel on the future of people on treatment; whether related to adverse drug reactions or clinical course. This is one of the WHO pharmacovigilance regulations [22].

During this series, the four major antiepileptics were known to the respondents, phenobarbital was the best known (87.1%), some did not know any. This could be explained by the fact that some people had no idea about the medical management of epilepsy, since traditional treatment remains the first option for some in Africa.

During our study, 48% of the respondents declared that they did not know if the drugs were validated by the pharmaceutical management. In addition, 65.7% of the cases did not know about the follow-up visits. Ensuring the safety of medicines is one of the essential points of pharmacovigilance. It is the responsibility of the national government to ensure that the medicines put on the market are safe, effective and of good quality, and that they are used properly. [22] According to the WHO, pharmacovigilance should be priorities in all countries where there is a public health program to fight the disease [22]. Unfortunately this is not the case in our country; Hence the risk of exposure of the population to the harmful consequences of the products on the organism.

During our investigation, the four major antiseizure medications (Phenobarbital, Carbamazepine, Valproic acid, Phenytoin and Diazepam, listed on the 12th list of essential medicines by the WHO [23] were found in 19 pharmacies (59.6%). This result is identical to that reported in Vietnam [6], with the exception of Phenobarbital used for drug addiction in this country which prompted the Vietnamese authorities to limit its accessibility drastically. It should also be noted that the respondents were not always health workers. The lack of knowledge about epilepsy and antiepileptics (AE) could influence our result. These 5 AEs are also available in all other African countries [24]. Their availability varied according to the pharmaceutical structures. The main source of availability of AEs was private structures, more specifically pharmacies.

In our study, Phenobarbital was the most available (53.1%) and the most prescribed (73.9%) EA, and its breakdown was 63.2% of cases. This result corroborates the data reported by certain African authors [25,26,27]. This explains why Phenobarbital is for WHO the anticonvulsant of choice in developing countries [28], where it is the most frequently prescribed drug for epilepsy [29]. In contrast to Antananarivo, Jost et al. found that Valproic Acid was the most available EA [7]. This result is similar to those reported in studies elsewhere [8,30]. In contrast, in Southeast Asia, Carbamazepine was the most widely available AE [6]. EA stock-outs were quite frequent and the structures took too long for replenishment.

The characteristics of the AEs available during our study were different. Most of them were not generics but specialty products. Phenobarbital was sometimes the only AE found in most sales units, in generic form. Generics were more affordable, sometimes free, especially Phenobarbital. The price of a tablet of Phenobarbital 100 mg in pharmacies (115.5 CFA francs) was three times the generic form (36.4 CFA francs). The latter is 7

times the price found in Benin [25] and 5 times in Togo [9]. But it remains the cheapest EA compared to the others. We find that the prices of these AEs are higher than those found elsewhere in Africa [31]. This is due to the isolation of the country, the very high taxes, the lack of competition in the market, the military-political crisis that the country has known for more than 10 years during which most of the infrastructure was destroyed.

Conclusion

This study enabled us to note that there exist within the pharmaceutical structures of the capital certain unqualified personnel responsible for dispensing the drugs. Those with qualified personnel have not received training in epilepsy. The cost of AE drugs was very high compared to other countries in the subregion and in sub-Saharan Africa. This is a limiting factor in the accessibility of EI for patients. Hence the need to put in place a policy of supply, quality control, and reduction in the cost of EI in order to relieve the suffering of the thousands of epileptics in the Central African Republic who seem to be left behind.

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Hippocampal sclerosis – Etiopathogenesis of drug resistant Temporal lobe epilepsy and current perspectives

Sclérose hippocampique - Etiopathogénie de l'épilepsie du lobe temporal résistante aux médicaments et perspectives actuelles

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Abstract:

Hippocampal sclerosis (HS), the most frequently seen histopathological finding in drug resistant temporal lobe epilepsy, is characterised by loss of neurons and gliosis, especially in the CA-1 and CA-4 regions of the hippocampus. The earliest descriptions of hippocampal sclerosis in epilepsy date back to early 19th century. With the advent of EEG in 1935, the role of HS was finally established in the causation of mesial temporal lobe epilepsy. Tremendous research has been undertaken in past decades to identify the causes and pathogenesis of hippocampal sclerosis. A significant cerebral insult (or initial precipitating injury) occurring early in life, such as a febrile or prolonged seizure, head injury, genetic polymorphisms, congenital cortical/ hippocampal malformations, autoimmune mechanisms and neuro-infections are all implicated as the etiological factors. Hippocampus itself is quite vulnerable to damage by seizures. Epileptic activity causes activation of glutamate receptors, NMDA (N-methyl-D-aspartate) receptors and AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors which puts the downstream signalling pathways in motion, in turn activating the caspases and leading to neuronal death. Studies have shown hippocampal sclerosis to be both cause as well as result of epilepsy. The pathomechanisms involved in HS are complex. Understanding the etiological and pathogenetic factors will help in undertaking interventions at appropriate time to prevent the development of HS and also in deciding the best surgical approach to achieve good seizure control. Hence, we present this review of the classification, etiology, pathogenesis and morphology of HS.

Keywords: Hippocampal sclerosis- Mesial temporal lobe epilepsy- Mossy fibre sprouting.

Introduction:

The commonest form of epilepsy in adults is temporal lobe epilepsy (60-70%), which is of two types. The common one, known as mesial temporal lobe epilepsy involves the medial or internal structures of the temporal lobe and the other one, called neocortical temporal lobe epilepsy, involves the outer portion of the temporal lobe. Mesial temporal lobe epilepsy (MTLE) often begins within the hippocampus or its surrounding structures and accounts for almost 80% of all temporal lobe seizures [1]. Hippocampal sclerosis (HS) is characterised by loss of neurons and gliosis in the CA-1 (CA refers to 'cornu Ammon', Latin for Ammon's horn) and subiculum region of the hippocampus [2]. In patients having drug-resistant temporal lobe epilepsy, it is the most common histopathological finding. In one of the European studies, out of 5,392 patients who underwent surgical resection for epilepsy due to various etiologies, HS was identified in 33.6%, and 5.1% of the cases showed dual pathology, that is, HS along with cortical malformations, vascular lesions, scars and tumours [3].

Almost two centuries have elapsed since the time when hippocampal sclerosis was first recognised in the patients with epilepsy. Bouchet and Cazauvielh, in 1825, were the first ones to describe HS in epilepsy. They published a series of 18 patients with epilepsy, 8 of who had HS [4]. In 1880, Sommer published a series of 90 post mortem cases of epilepsy in which he described neuronal loss mainly in the section of the hippocampal pyramidal cell layer immediately adjacent to the temporal horn of the lateral ventricle; this region was called Sommer's sector (now termed CA1) [5]. Jackson, in 1889, was the first to describe the clinical symptoms of temporal lobe epilepsy (TLE) [6]. It was however much later in 1935, that Stauder correlated HS with TLE [7]. In 1953, with the advent of electroencephalography (EEG), Sano et al published their study in which they associated HS with EEG evidence of temporal lobe seizures [8]. These findings led to the conclusion that HS was the cause of TLE.

Classification:

Several attempts have been undertaken in the past to classify the various patterns seen in HS. In 2013, ILAE (International League against Epilepsy) proposed a classification system for HS based on semiquantitative hippocampal cell loss patterns that can be applied by neuropathologists in any histopathology laboratory. The purpose of this classification scheme was to ensure uniform diagnosis of surgical specimens of patients with MTLE so that inter laboratory comparisons can be done. ILAE classified HS into 3 types based on histomorphology (Figure 1A). Standard stains were used i.e., H&E (hematoxylin & eosin) and crystal violet with luxol fast blue and IHC (immunohistochemistry) for GFAP (glial fibrillary acidic protein) and NeuN (neuronal nuclei).

In HS ILAE type 1 severe neuronal cell loss and gliosis is seen predominantly in CA1 and CA4 regions. CA1 predominant neuronal cell loss and gliosis is seen in HS ILAE type 2 and CA4 predominant neuronal cell loss and gliosis in HS ILAE type 3. In some surgical hippocampus specimens obtained from patients with temporal lobe epilepsy (TLE), normal content of neurons with only reactive gliosis is seen and this is

referred to as no HS [9]. Classifying HS is important as studies have shown that identification of HS/TLE phenotypes could account for clinical variability. HS subtypes may be predictive of seizure-free outcomes following surgery and subtypes of HS and patterns of subfield neuronal loss have been associated with specific memory impairments, either pre- or postoperatively, that can occur with TLE. No hippocampal sclerosis but gliosis and the type 2 hippocampal sclerosis have been seen to have the poorest outcomes (40% completely seizure free with 2- year follow-up) as compared with type 1 hippocampal sclerosis in which 70% seizure free outcome have been seen [10]. However, HS type, in the study by Jardim PA et al was not predictive of memory dysfunction or decline, which instead was seen to be associated with multiple factors like neuronal and hippocampal pathway integrity, regenerative capacity and degenerative changes [11].

Pathophysiology of Epilepsy:

Latest research shows that there are three basic phases that can be described in the process of epileptogenesis: first phase is of initial insult or acute brain damage, second is the latent period in which "maturation" of the epileptic focus occurs, and final one is the actual epilepsy, where secondary epileptogenesis takes place (Figure 1B). The most important etiological factors responsible for acute brain damage include severe craniocerebral trauma, stroke, epileptic state, recurrent and prolonged febrile convulsions, cerebral thrombosis and neurological infections [12]. A weak or sub threshold stimulus, if repeated, is capable of producing epileptic discharges at the place of stimulation. After a certain time, a process of progressive change begins: at first local, short epileptic discharge is caused by the stimulus but if the stimulus is given continuously or repeatedly, the discharges last longer and spread to larger areas of the brain, thus eventually giving rise to clinical epileptic seizures. If the condition is not treated, the duration between successive attacks decreases over time.

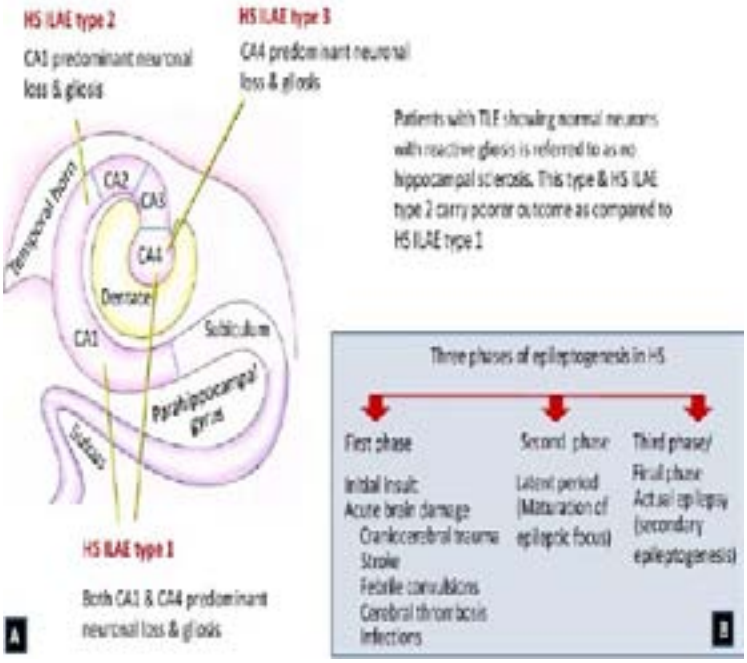

Figure 1: ILAE classification of hippocampal sclerosis (Figure 1A). Various phases in the process of epileptogenesis in hippocampal sclerosis (Figure 1B).

Following the initial insult, neurons get activated and there occurs intracellular accumulation of calcium ions which then activate the downstream pathways of secondary messengers, eventually leading to activation of gene expression and protein synthesis. In the following days inflammatory processes take place at the site of injury with the release of mediators of inflammation, and activation of glial and endothelial cell responses. At a later stage of epileptogenesis, the sprouting of new axons, synaptogenesis and angiogenesis are seen. All these processes eventually lead to reorganization of nerve tissue microarchitecture. In experimental and clinical studies, structural, biochemical and molecular changes have been identified between tissues from normal subjects and patients with epilepsy. The time during which these structural and molecular changes occur is usually a clinically silent period. Sometimes these changes are sufficient to bring about the clinical manifestation of epilepsy, and sometimes a second hit is necessary. It may be an external factor, like head injury or infections, or it may be the processes of neuronal apoptosis and necrosis and gene expression occurring since the initial insult, if they cause sufficient level of neuronal damage [12].

Etiology of Hippocampal Sclerosis:

Hippocampal sclerosis has been the topic of research for last several decades but whether hippocampal sclerosis is a cause or a result of seizures is still unclear. Role of both genetic and environmental factors have been implicated in the etiology of HS (Table 1). A significant cerebral insult (or initial precipitating injury) occurring early in life, such as a febrile or prolonged seizure, is the most frequently cited cause of HS. This initial insult is believed to irreversibly damage or alter the hippocampus and thus primes the hippocampus for progression to sclerosis following a latent interval [12]. Experimentally induced febrile seizures have been shown to cause severe pathological changes in the rat hippocampus [13]. In retrospective studies, a history of febrile convulsions has been reported in 30-50% cases with hippocampal sclerosis [14, 15]. In the FEBSTAT study (2014) 10% of children with febrile status epilepticus developed HS at a later date [16]. However, HS does not develop in all cases of febrile convulsions suggesting that this cannot be the only mechanism. There is a possibility that febrile seizures convert pre-existing congenital abnormalities of the hippocampus into HS [15, 17].

Table1: Etiological factors implicated in hippocampal sclerosis.

Important etiological factors in hippocampal sclerosis
Febrile convulsions (Conversion of pre-existing congenital abnormalities of hippocampus into hippocampal sclerosis)
Head injury (neuronal and interneuronal loss)
Genetic alterations involving SCN1A & ApoEε4
Congenital abnormalities of hippocampus
Cortical malformations
Vascular malformations
Low grade glioneuronal tumors
Infections (neurocysticercosis, viral encephalitis)
Voltage gated potassium auto antibodies

Head injury can cause hippocampal sclerosis. The head injury causes neuronal and interneuronal loss which is accompanied by increased excitability of the hippocampus, and eventually leads to spontaneous seizures [18]. The risk of developing epilepsy following head injury ranges from 2 to 25%, depending upon the severity of trauma [19]. The genetic basis of HS is not yet clearly defined. Some genetic variants like polymorphisms in the genomic region coding for sodium channel subunits, in particular SCN1A, have been linked with the occurrence of febrile seizures and hippocampal sclerosis and ApoEε4 (apolipoprotein E ε4) genotype has been associated with bilateral HS [20,21]. As mentioned above, congenital abnormalities of the hippocampus could predispose to hippocampal sclerosis and also to febrile seizures. Persistence of calretinin positive Cajal-Retzius cells has been found in the sclerosed hippocampus [22]. They secrete reelin, which plays a critical role in neuronal organization in the developing brain [18]. These cells are also seen in the cortex in cortical abnormalities like polymicrogyria [23] and microdysgenesis [24]. So, this could possibly mean that excess Cajal-Retzius cells represent a hippocampal malformation [18, 25].

Hippocampal sclerosis also occurs in association with more severe cortical malformations like cotical heterotopia, vascular malformations, and low-grade glioneuronal tumors [26, 27]. It is postulated that the extrahippocampal lesion generates seizures or subclinical seizure activity that results in neuronal loss in the hippocampus [18]. Such patients are said to have dual pathology, seen in 5-30% of patients with drug resistant TLE [26]. Best postsurgical seizure free outcome is achieved in these cases only when both the lesion as well as the abnormal hippocampus is removed [27]. Infections are also one of the etiological factors implicated in hippocampal sclerosis [18]. Association with neurocysticercosis [28], viral encephalitis [29] and herpes virus [30] have been described. More recently, voltage-gated potassium channel autoantibodies have been found in patients with HS [18, 31]. These autoantibodies result in acute or subacute encephalitis with enlargement, increased T2- weighted signal, and restricted diffusion of the mesial temporal lobe structures on MRI and can cause hippocampal sclerosis at a later date [32].

Pathogenesis:

Studies have shown that in prolonged seizures physiological compromise that occurs during status epilepticus, such as hypoxia, hypoglycemia, and hypotension, causes some neuronal damage but a significant amount of the damage is not due to these factors but due to excitotoxicity, in which the epileptic activity activates glutamate receptors and mediates neuronal death. Excessive influx of calcium primarily through NMDA (N-methyl D-aspartate) receptors, and also through specific AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptor subtypes, along with activation of metabotropic glutamate receptors causes activation of downstream signalling pathways (Figure 2). These result in activation of extrinsic and intrinsic caspase pathways, formation of reactive oxygen species and mitochondrial function disruption, eventually leading to cell death [18, 33-37].

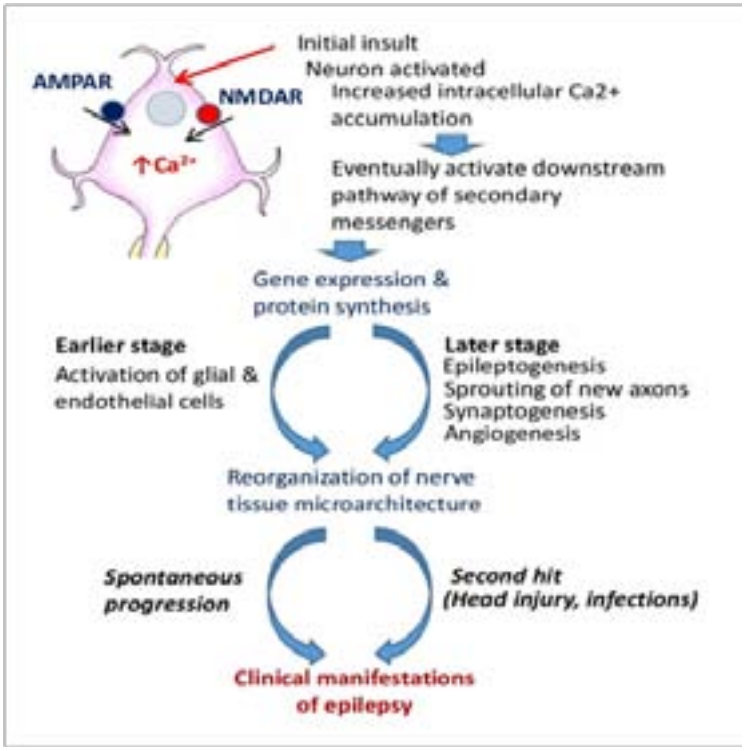

Figure 2: Pathophysiology of hippocampal sclerosis.

Synaptic plasticity is the biological process by which specific patterns of synaptic activity result in changes in the synaptic strength and it is believed to be one of the important pathophysiological factors responsible for generation of post traumatic epilepsy. Synaptic plasticity occurs due to the reorganisation of the structure and function of neuronal membrane receptors [38, 39]. Altered expression of the structural protein subunits of GABA (gamma amino butyuric acid) receptors, their assembly and distribution have been seen in experimental studies [40] as well as in surgically resected hippocampus from TLE patients. Abnormalities in the synaptic neurotransmission are not confined to the membrane receptors but also include changes in the synthesis and release of neurotransmitters. Extracellular GABA concentration depends upon its rate of uptake and altered levels of GABA transporters (GAT-1 and GAT3) have been shown in TLE [41, 42]. Altered expression of neuronal cation chloride cotransporters (NKCC1 and KCC2) is seen in epilepsy which switches the inhibitory action of GABA to excitatory (Figure 3A) [43-45].

Neuropeptides are small proteinaceous substances produced and released by neurons through the regulated secretory route and acting on neural substrates [46]. Their half-lives are longer than that of neurotransmitters and hence can modulate neuronal activity over longer periods of time [47]. NPY (neuropeptide Y) is the most studied of all the neuropeptides in epilepsy. Normally, it has anti convulsant properties. NPY expressing cells are seen in the CA4 region of hippocampus, whose axons pass through the outer molecular layer to synapse with the dendrites of the granule cells in the dentate gyrus (Figure 3B) [48]. In HS, loss of NPY neurons along with extensive sprouting and beading of NPY axons is seen [49-51]. Gene therapy studies have been conducted recently in which induction of NPY overexpression by using viral vectors has resulted in decreased seizure frequency [52].

Hippocampus contains mainly 2 types of neurons - principal neurons and interneurons. Principal neurons or the pyra-

midal neurons generally form excitatory synapses on other neurons of brain while interneurons usually form inhibitory synapses on the principal neurons or other interneurons [12]. Structural and biochemical changes in HS are seen not only in the principal neurons but in the interneurons as well. Loss of protein expression, reduction in number, cell hypertrophy, abnormal dendritic projections with altered distribution of spines and axonal sprouting are some of the changes reported in the interneurons in HS [42, 53-58]. These changes in the interneurons are likely to represent compensatory responses to the seizures but they may also be responsible for excitatory/ inhibitory imbalances leading to sustained epileptogenesis [42].

Gliosis is an important histopathological finding seen in the hippocampus of TLE patients and biochemical and structural changes in the astrocytes have been described in epilepsy. Dysfunction of kir4.11 potassium channels and aquaporin-4 channels [59] which normally maintain ion and water homeostasis in the brain, was implicated in the pathogenesis of epilepsy (Figure 3C). Excitatory amino acid transporters are present normally on glial cells which capture excess excitatory neurotransmitters from synaptic cleft [60] and hence impaired clearance of glutamate by astrocytes could cause seizures. Astrocytes also release gliotransmitters upon activation, which then act on the synapse to modulate pre- and post-synaptic responses [61]. Increased gliotransmitter release, including glutamate in gliosis may play a significant role (for HS) in pathological hypersynchronia of neuronal firing [62].

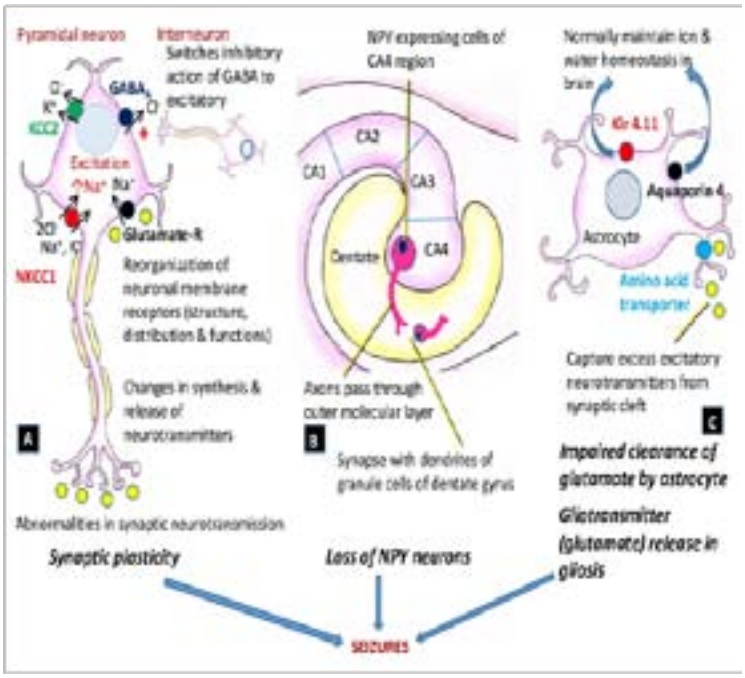

Figure 3: Altered expression of neuronal cation chloride cotransporters (NKCC1 and KCC2).

In epilepsy switches the inhibitory action of GABA to excitatory (Figure 3A). Loss of NPY (neuropeptide Y) neurons of CA4 region in hippocampal sclerosis results in seizure (Figure 3B). Role of astrocytes (gliosis) in hippocampal sclerosis (Figure 3C).

Immune mechanisms and inflammatory responses have been increasingly implicated as a potential pathophysiologic mechanism in MTLE-HS [63]. Epileptogenic brain injuries and convulsive events cause activation of glial cells and extravasation of macrophages and granulocytes in the area of injury [63-65]. The activated glial cells release a number of pro-inflammatory cytokines, for example, interleukin (IL)-1β, high-mobility group box 1 (HMGB1), tumour necrosis factor (TNF)-α, and related molecules. These inflammatory molecules act on their receptors present on the glial cells, neurons and endothelial cells. The IL-1 receptor/TLR (Toll-like receptor) pathway is one of the most important pathways implicated [66-68]. Signaling activation in glia generates tissue inflammation via NF-κβ (nuclear factor- κβ) dependent transcriptional up-regulation of various inflammatory genes. Adhesion molecules are upregulated in endothelial cells of the BBB (blood brain barrier), contributing to the recruitment of circulating leukocytes and breakdown of tight junctions, eventually causing BBB damage. Activation of this pathway in neurons increases neuronal excitability and reduces seizure threshold [69-72].

Recently, miRNAs have also been implicated in the pathogenesis. Increased expression of miR146, which regulates the IL-1 receptor/TLR signaling pathways, has been shown in the reactive astrocytes in both animal models and human TLE [73]. Miller-Delaney SF et al identified a panel of 13, methylation-sensitive microRNA in temporal lobe epilepsy including MIR27A, miR-193a-5p (MIR193A) and miR-876-3p (MIR876). They also documented the differential methylation of long non-coding RNA [74]. Genome wide expression profiling have shown altered expression of coding transcripts in epilepsy, for example, genes coding for ion channels and genes involved in synaptic remodelling, inflammation, gliosis and neuronal death [75]. Epigenetic mechanisms have also been studied in epilepsy. Promoter methylation of reelin was seen in temporal lobe epilepsy and it correlated with granule cell dispersion [76]. Increased levels of DNA methyltransferases 1 and 3a have been seen in the hippocampus in human temporal lobe epilepsy [77]. In a recent study, 146 protein-coding genes exhibited altered DNA methylation, mainly in the promoter region, in temporal lobe epilepsy hippocampus. The genes involved were associated with neuronal, neurotransmitter/synaptic transmission and cell death functions. Differential hypermethylation of genes associated with transcriptional regulation was also seen. However, how these alterations influence the pathomechanisms in epilepsy was not clear [74].

Recent studies have evaluated the role of autophagy in epilepsy. Autophagy mediates the turnover of cytoplasmic constituents via lysosomal degradation and its activity is negatively regulated by the mammalian target of rapamycin (mTOR). Since (mTOR) pathway regulates a number of physiological processes, such as synaptic plasticity and ion channel expression, its abberant hyperactivation is said to result in epileptogenesis under pathological conditions [78]. Tuberous sclerosis complex (TSC) is the prototypic disorder in which dysregulated mTOR signaling is seen and refractory epilepsy constitutes it's one of the important neurological manifestations [79]. Studies have shown occurrence of epilepsy due to direct failure of autophagy depending on mTOR pathway overactivation [80]. At the same time, impaired autophagy causing epilepsy due to mechanisms independent of mTOR pathway have also been described. These include lack of ATG18 and ATG7, both of which are autophagy regulators [81]. So, it might be speculated that

impaired autophagy can trigger epileptogenesis.

Neuropathology:

On histopathological examination, HS is characterized by degeneration and selective loss of pyramidal neurons, pathological proliferation of interneuronal networks, and severe glial reaction. Cytoskeletal abnormalities in residual hilar neurons in the form of enlargement or ballooning of the cell body and processes, intense Nissl and silver staining and cytoplasmic accumulation of neurofilaments have been seen (Figure 4) [25].

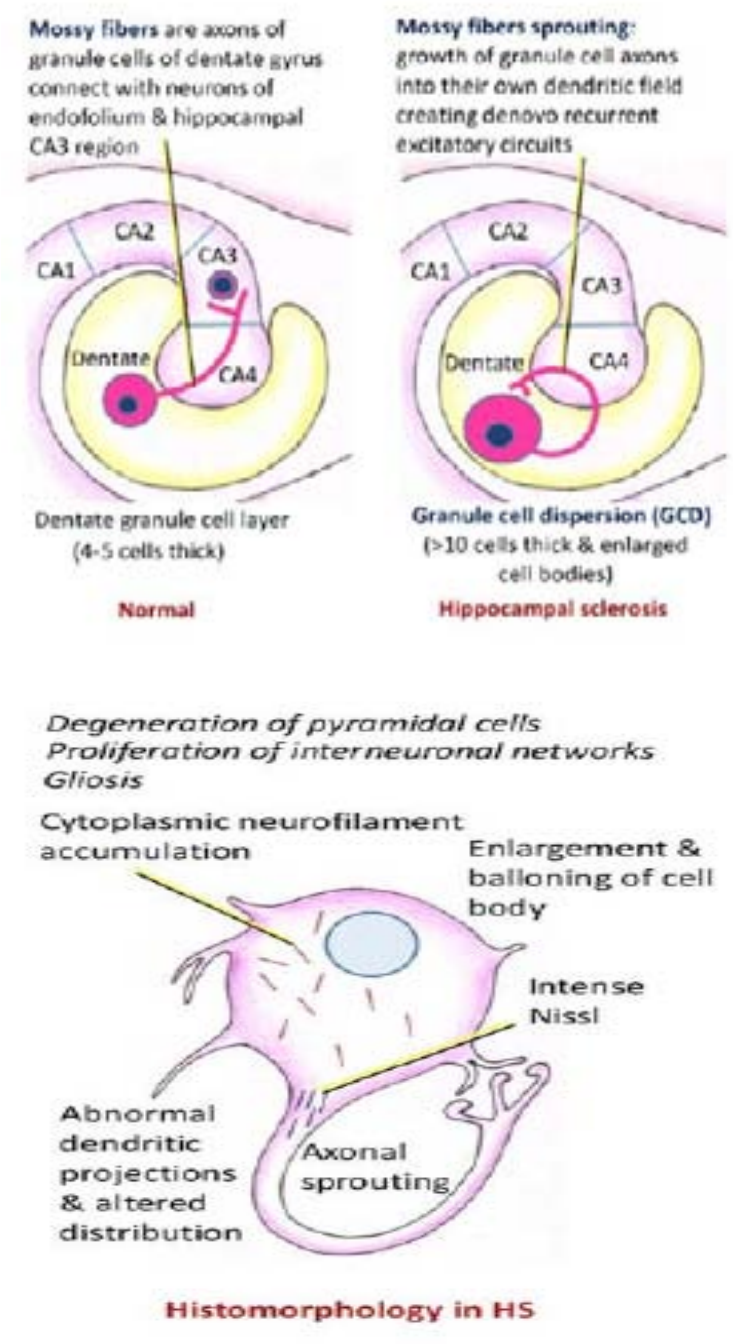

Figure 4: Schematic representations of Mossy fibres in normal brain; Mossy fiber sprouting and morphological changes in hippocampal sclerosis.

In addition to neuronal degeneration and gliosis, the mossy fiber sprouting and the dentate gyrus granule cell dispersion are also characteristic of HS. Normally, dentate granule cell layer is 4-5 cells thick and granule cell dispersion (GCD) is defined as greater than 10 cells thick, enlarged granule cell bodies, bilaminar layer, and diffuse upper granule cell boundary. It is seen in 40-50% cases of HS [63]. The degree of GCD is related to the extent of hippocampal damage [25]. Various theories have been proposed for GCD, e.g., neurotropin overexpression during seizures [64, 65] role of Cajal-Retzius cells and reelin due to their abnormal persistence seen in HS [66, 67]. Seizures have been seen to influence neurogenesis in hippocampus. GCD can occur either because of neuronal heterotopia of newly generated neurons following aberrant neurogenesis or because of abnormal migration of mature neurons. These migrated neurons then integrate with the existing network and acquire pro-epileptogenic physiological properties [42].

Mossy fibres are axons of granule cells of dentate gyrus, which connect with the neurons of the endfolium and hippocampal CA3 region (Figure 4). When CA3 neurons and end-folium neurons are lost during the process of HS, their feedback projection to granule cells is also lost. Such deinnervation leads to mossy fibre sprouting [12], which is defined as growth of granule cell axons into their own dendritic field in the inner molecular layer and thus creating denovo recurrent excitatory circuits. It has, however, been seen in the studies that mossy fiber sprouting is not required for epileptogenesis and sprouting can be blocked without reducing the occurrence of seizures. But with the extensive mossy fiber sprouting seen in patients with epilepsy, it is possible that they impact other brain functions like cognitive disruption or other comorbidities [17].

Conclusion:

Despite being the topic of research for decades, whether hippocampal sclerosis is a cause or a result of epilepsy has remained an enigmatic question. Studies have shown both the concepts to be true. The pathology in HS is not just confined to neuronal death. Changes are seen in the neuronal network as well, like synaptic plasticity and structural and biochemical alterations in interneurons, which are eventually responsible for development of seizures. More studies, especially dedicated towards the molecular abnormalities are needed to further shed light on the causes, pathogenesis and prevention of HS.

Abbreviations:

HS-Hippocampal sclerosis; EEG- Electroencephalography; NMDA -N-methyl-D-aspartate; AMPA -α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; CA- cornu Ammon; TLE-temporal lobe epilepsy; ILAE -International League Against Epilepsy; MTLE-Mesial temporal lobe epilepsy; H&E- hematoxylin & eosin; IHC –immunohistochemistry; GFAP -glial fibrillary acidic protein; NeuN-neuronal nuclei; ApoEƐ4 -apolipoprotein E Ɛ4; NKCC1- neuronal cation chloride cotransporters; GABA -gamma amino butyuric acid; GAT- GABA transporters; NPY -neuropeptide Y; (IL)-1β-interleukin-1β; HMGB1-high-mobility group box 1; TNF-α-tumour necrosis factor-α; TLR- Toll-like receptor; NF-κβ -nuclear factor- κβ; BBB -blood brain barrier; mTOR-mammalian target of rapamycin; GCD- granule cell dispersion.

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Conflict of interest: None

Abstract:

This paper elaborates the various innovative strategies used in Kenya to demystify epilepsy and engage the communities in understanding the right facts on this condition. Stakeholders in epilepsy care in Kenya came together 8 years ago to try to understand why despite efforts to treat epilepsy there still existed a treatment gap of 70%. Youth on the Move a nongovernmental organization based in Nairobi City took the lead to mobilize partners who later joined and formed the National Epilepsy coordination Committee. The biggest gap in epilepsy management was found to be lack of knowledge on the condition; what epilepsy is, its cause, prevention, treatment, first aid and lifestyle issues pertaining to epilepsy. With one voice all members under the umbrella body NECC agreed to embark on a thorough awareness creation that started off under the slogan 'Kifafa ina tiba, muone daktari" (epilepsy is treatable, visit a doctor) and later on changed to 'Angaza Kifafa' (Shine light on epilepsy.)
Since inception several epilepsy awareness campaigns have been used including training of community health volunteers, epilepsy road caravans, epilepsy awareness through local music, hiking, cycling, epilepsy afro fashion fairs, and awareness programs on media and in learning institutions, epilepsy health centers and among organized groups. The results continue to improve tremendously
For the last 10 years, Youth on the Move as an organization has reached out and sensitized 500,000 people in communities, trained 750 community health volunteers and welfare officers, trained 150 youth living with epilepsy who later are involved in awareness creation, trained 300 caregivers of persons living with epilepsy and 60 prisoners and 130 prison wardens. Through NECC 750 medical officers (doctors, clinical officers and nurses) have been trained on the proper diagnosis and treatment of epilepsy. The Angaza Kifafa road caravan has since reached to 4 million
people in 18 Countries in Kenya.

Key words: Epilepsy- Awareness- Strategies- Sensitized - Kenya.

Résumé:

Ce document expose les différentes stratégies innovantes utilisées au Kenya pour démystifier l'épilepsie et amener les communautés à comprendre les faits relatifs à cette maladie. Les acteurs de la prise en charge de l'épilepsie au Kenya se sont réunis il y a 8 ans pour essayer de comprendre pourquoi, malgré les efforts déployés pour traiter l'épilepsie, il existait encore un écart de traitement de 70 %. Youth on the Move, une organisation non gouvernementale basée à Nairobi, a pris l'initiative de mobiliser des partenaires qui ont ensuite rejoint et formé le comité national de coordination de l'épilepsie. La plus grande lacune dans la gestion de l'épilepsie a été constatée dans le manque de connaissances sur cette maladie ; ce qu'est l'épilepsie, sa cause, la prévention contre cette maladie, son traitement, les premiers secours et les questions de style de vie qui lui sont liées. D'une seule voix, tous les membres du NECC ont accepté de se lancer dans une campagne de sensibilisation approfondie qui a débuté sous le slogan "Kifafa ina tiba, muone daktari" (l'épilepsie peut être traitée, il suffit de consulter un médecin) et qui s'est transformée en "Angaza Kifafa" (Lumière sur l'épilepsie).
Depuis le début, plusieurs campagnes de sensibilisation à l'épilepsie ont été effectuées, notamment la formation de volontaires de santé communautaire, les caravanes routières pour l'épilepsie, la sensibilisation à l'épilepsie par le biais de la musique locale, la randonnée, le cyclisme, les salons de mode afro pour l'épilepsie et les programmes de sensibilisation dans les médias, les établissements d'enseignement, les centres de santé pour l'épilepsie et parmi les groupes organisés. Les résultats continuent de s'améliorer considérablement
Au cours des dix dernières années, l'organisation "Youth on the Move" a sensibilisé 500 000 personnes dans les communautés, a formé 750 bénévoles de la santé communautaire et des agents sociaux, a formé 150 jeunes vivant avec l'épilepsie qui participent ensuite à la sensibilisation et a formé 300 soignants de personnes vivant avec
l'épilepsie, 60 prisonniers et 130 gardiens de prison. Grâce au NECC, 750 agents médicaux (médecins, agents cliniques

et infirmières) ont été formés au diagnostic et au traitement appropriés de l'épilepsie. Depuis, la caravane routière Angaza Kifafa a atteint 4 millions de personnes dans 18 regionne du Kenya.

Mots-clefs: Epilepsie - Conscience - Stratégies - Sensibilisation - Kenya.

Background:

Epilepsy is a neurological brain disorder that makes one prone to seizures. According to the World Health Organization (WHO), worldwide, an estimated 50 million people are faced with this condition, 80% of these are from developing countries because the capability to identify people with epilepsy and provide cost-effective care is compromised by the wide spread poverty, illiteracy, inefficient and unevenly distributed health systems, social stigma and misconception surrounding the disease. Globally, the estimated proportion of the general population with active epilepsy at a given time is between 4 and 10 per 1000 people. It is also estimated that five million people are diagnosed with epilepsy each year. In high-income countries, there are estimated to be 49 per 100,000 people diagnosed with epilepsy each year. In low- and middle-income countries, this figure can be as high as 139 per 100,000. (India Journal of Medical Research).

In Kenya, epilepsy is the most common chronic neurological disorder (2/100 people affected) and the 4th in the World. Approximately 1,000,000 people live with epilepsy and about 77 new cases in every 100,000 are diagnosed every year. Persons living with epilepsy in Kenya face a lot of stigma. This is due to lots of myths and misconceptions attached to this neurological condition. Combined with lack of knowledge on the condition, there exists a treatment gap of 70% as only 30% seek treatment. The rest seek alternative care like visit to witch doctors, performing rituals and prayers as the condition is associated with witchcraft, demon possession or curses.

About Kenya and its healthcare system

Figure1: Afrique,Kenya.

Kenya is one of the Countries in East Africa. Its capital is Nairobi. According to the world meter elaboration of the latest United Nations Data, the current population of the country is 54,263,910 as on December 3, 2020. This population is equivalent to 0.69% of the world total population. The population density in Kenya is 94 per km2.

Kenya's Health System

There are three major healthcare providers in Kenya:- Public (government service), private and missionary hospitals with public hospitals being the major health care providers to the majority of the Kenyan population (Amayo, 2006). Kenyatta National Hospital is the largest public hospital, with 7.5 percent of all medical cases seen in this hospital being neurological illnesses (Kwasa 1992).

Kenya's government health sector is one of the 14 devolved functions managed by the 47 county governments as provided in the Fourth Schedule of the 2010 Constitution. There are six different levels of public health care facilities namely:

1. Community facilities run by certified medical clinical officers
2. Health dispensaries run by clinical officers
3. Health centers – these are small hospitals with minimal facilities
4. County hospitals which provide holistic services
5. Country referral hospitals and
6. National referral hospital.

The first five are managed on the county level, the sixth level by the national government. In this system the patients may move from one level to the next by using a referral letter.

There are 4 major major university hospitals namely Nairobi, Kenyatta, Moi and Aga Khan. The Country has approximately 27 neurologists who are concentrated in the major cities (Nairobi, Mombasa and Kisumu)

The World Epilepsy atlas gives four factors (the four A's) as the treatment gap: Available, Accessible, Affordable health care and lack of Awareness. In Kenya awareness is given high priority upon realization by stakeholders that despite several treatment centers for epilepsy coming up; not many people seek their services. It is for this reason that stakeholders in epilepsy care formed the umbrella body National Epilepsy Coordination Committee (NECC), in order to unite efforts for epilepsy campaigns. Since inception 10 years ago, various public engagement strategies have been employed. NECC actively engages its members to come up with innovative strategies that can help create awareness by engaging the public at the grassroots. Youth on the Move, (YotM) Empower Talents with Epilepsy is one of the non-governmental organizations that has actively empowered youth living with epilepsy and reached out to communities and has contributed a lot to NECC activities.

In the year 2020 in celebrating the international days the following strategies were used.

1.International Epilepsy Day February 10, 2020:

1.1: National Epilepsy Coordination Committee - Angaza Kifafa (shed light) Caravan:

During the International Epilepsy Day, NECC partnered with Bank of Africa Kenya (BOA), Kenya Medical Research Institute (KEMRI Welcome Trust) and the County government of Kilifi in Coast region to celebrate this day.

Figure 2,3: Celebration of world epilepsy Day in Kenya, Kilifi County in Coast province.

An epilepsy road caravan was organized equipped with trained community health volunteers, medical professionals and civil activists and an entertainment crew. There were printed epilepsy information flyers, t shirts and caps. The caravan crossed through the Kilifi County making stop overs in populated market centers where the team alighted to train the masses and share facts on epilepsy. Those affected were recorded and referred for treatment. This strategy has proved effective as the entertainment attracts the crowd and through that the public is engaged and questions on what epilepsy is and where to seek help is shared.

Figure 4,5 : Celebration of World Epilepsy day through educative songs on epilepsy in Nairobi.

1.2: Epilepsy walks:

Figure 6,7: Community members join the youth in matching for epilepsy in Mathare slums Nairobi, Kenya.

Epilepsy walks have proved to be effective to alert the community of conditions that have been treated as sacred or special. During the international Epilepsy day youth living with epilepsy and their caregivers armed with placards made walks through one of the informal settlements in Nairobi called Mathare. They also sang songs, passed information that epilepsy is not witchcraft or curses but rather a medical condition. Through this they attracted the attention of the onlookers who in the process followed the crowd to where they were headed in order to learn more. The walk ended at one of the most known epilepsy health center in Mathare slums that attends to more than 500 epilepsy patients and other n on-communicable diseases.

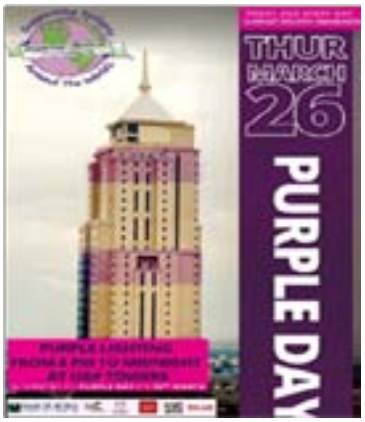

Figure 8,9: UAP towers one of the tallest building in Nairobi City was lit purple to celebrate purple day on 26yh March 2020.

At the health center the patients at the hospital and the crowd that followed the youth were educated on epilepsy and provided with epilepsy flyers and manuals so that they could go read more. Youth with epilepsy shared their experiences, challenges and successes. Drink and snacks were later shared to commemorate the day.

2.Purple Day:

This is another internationally recognized day commemorated worldwide. Purple Day is an international grassroots effort dedicated to increasing awareness about epilepsy.

On March 26th annually, people in countries around the world are invited to wear purple and host events in support of epilepsy awareness.

In Kenya, the COVID-19 outbreak did not stop the celebration of this day. Though public meetings were not allowed, NECC mobilized its members and partnered with other stakeholders and approached the UAP/Old Mutual company to light their building which is the tallest in Nairobi City purple. At night, the building could be seen from far estates which prompted people to find out through social media why the building was lighting purple. This was reinforced by media engagements and shows about epilepsy.

3.St. Valentine's Day.

Figure 10,11 : Youth on the Move beneficiaries dressed in red celebrating St. Valentine's day on February 14 2020

February 14th, Valentine's Day, is traditionally known as a day for lovers with cards, chocolates and red roses exchanged. Not so many people know that St Valentine is also the patron saint of epilepsy sufferers among the Christians. Just as it is today in most African cultures, so it was in ancient times when there was very little medical knowledge, epilepsy was regarded with a lot of myths, misconceptions, fear and suspicion and was thought to be caused by supernatural forces, retribution by the gods or evidence of being possessed by evil spirits and curses for wrong doing. St. Valentine was a priest as well as a physician who was known to help epilepsy sufferers. The link between Valentine and epilepsy, which was also known as the falling sickness, could be due as well to the similarity between the German verb 'fallen' and the first part of the saint's name.

In Kenya, Youth on the Move, an organization for and by youth living with epilepsy use this day to share words of hope, encouragement and gifts with their peers living with epilepsy. They also extend their love to children homes of children living with various disabilities including epilepsy. This year youth gathered at their training center, exchanged flowers, shared stories and reminiscenced about St, Valentine.

This strategy has worked quite well in boosting the self-esteem of persons living with epilepsy as the topic on epilepsy, love, dating, courtship and marriage is usually well discussed. The day provides a good socialization forum where questions pertaining matters love and friendship are shared by professionals.

4.November Epilepsy Awareness Month:

4.1 Media engagement

Figure 12 : Social media to alert audience to listed to the talk show

Figure 13: Sorry of a lady who now lives positiely with epilepsy

Stakeholders in epilepsy care took the month of November with a lot of weight and used the month to engage the media to educate the community. Participants range from medical professionals, social workers, counseling psychologists, social workers, community health volunteer, caregivers and persons living with epilepsy. The aim is to have an all-round approach to epilepsy awareness. National, international and local media stations – television, radio and print were utilized.

4.2Community Health Volunteers Engagement:

Figure 14: Experience sharing among youth with epilepsy

Figure 15: Trained Community Health Volunteers in Nyanza region

Figure 16: One of the most active Community Health Volunteers and musician trained by Youth on the Move Taita Taveta County

Community Health Volunteers (CHVs) play a key role in epilepsy awareness. Youth on the Move partners with NECC and Bank of Africa to training CHVs in all Counties in Kenya. The CHVs are then used as a link between the affected, health facilities and epilepsy organisations. The CHVs have made great impact because they live within the community and they pass on epilepsy facts in mother tongue. They are also in constant touch with the affected and their caregivers. For this reason, they are well placed in monitoring progress of the patients and directly assist in reporting to the facilities where .the patients are attached for treatment

Photo and narrative on the left is by one of the CHVs (Rhoda Soko from Taita Taveta County at the Coast) trained and who now shares how the knowledge she gained has impacted the community she serves

4.3 Epilepsy Expeditions

Figure 17: Hiking and cycling expeditions in preparation of Fred Beuch's Kilimanjaro challenge for epilepsy awareness in Kenya

Other innovative activities are also sought. This year the stakeholders joined hands and partnered with one epilepsy activist named Fred Beuchi in hiking and cycling activities in Kenya and ultimately in climbing the tallest mountain in Africa – Mount Kilimanjaro with one voice that epilepsy is manageable.

Conclusion:

From observation and follow up phone calls and inquiries from the community, a lot need to be done in epilepsy awareness. The strategies used have shown that there is still a huge knowledge gap on epilepsy in Kenya. On a positive note however, the larger population is willing to learn and seek more information on epilepsy as well as the proper treatment and management of the condition.

More pictorials for activities of epilepsy public engage ment in Kenya

More pictorials for activities of epilepsy public engagement in Kenya

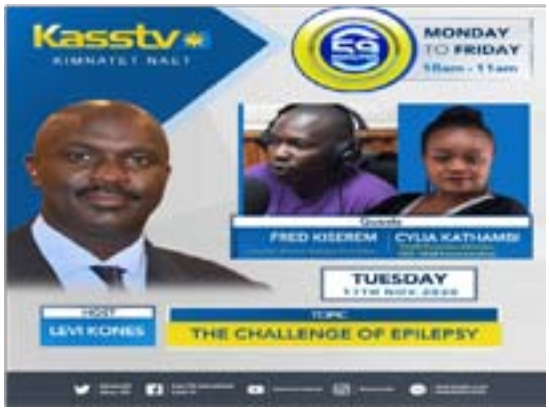

Figure 18: Televison talk

Figure 19: Epilepsy awareness through music

Figure 20: Epilepsy sensitization in a local church

Figure 21:Epilepsy webinars

Figure 22:Epilepsy training for community health volunteers

Figure 23: St. Valentine celebration

Figure 24: Epilepsy education in schools

Figure 25 : Epilepsy awareness in market places

Figure 26: Pictures of activities the youth engage in to build their self-esteem, create awareness and for lobby and advocacy and awareness creation

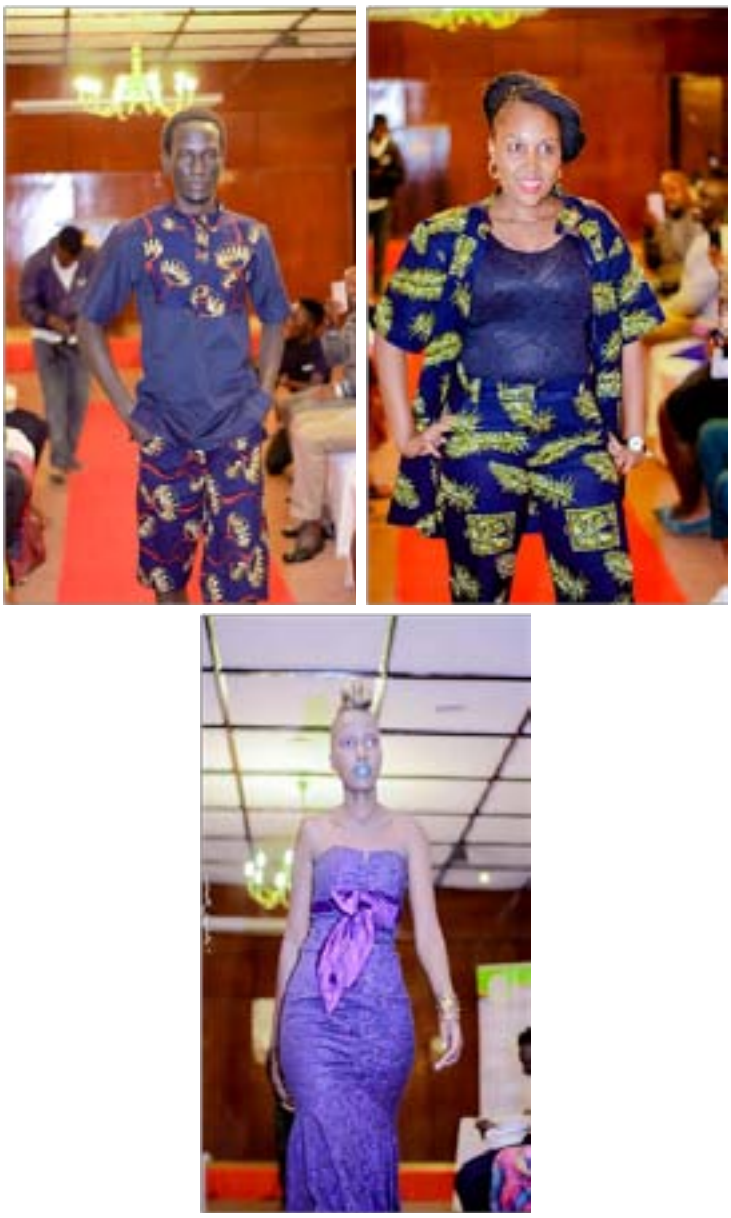

Figure 27: Youth with epilepsy show case their talents through fashion and cat walking

About Youth on the Move

Youth on the Move, Empower Talents with Epilepsy is a non-governmental organization based registered under the NGO ACT in Kenya. The organization started in 2008. It depends on donor and well-wishers support but also run an internet café where the youth gain computer literacy skills as it generates some income from the public. It is guided by the following vision and mission

Vision: An understanding and responsive society that ensures equal participation of persons with epilepsy in developing countries in all aspects of life.

Mission: To empower persons with epilepsy and ensure equal participation in society through lobby and awareness creation in partnership with stakeholders

Physical:Nairobi West, along Birongo Square, New Life Church Building 1st floor, P.O. Box 20689 - 00100

Location:Email:Epillose@yotmkenya.com/epillose@yahoo.com, Phone +254 712 623 681

Website:www.yotmkenya.com and www.epilepsykenya.org

Appeal: The organisation appeals to any organisation, company, corporate or individual to support our activities. Feel free to reach us on the contacts provided

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Logos.

1.Logo 1 is for Youth on the Move, a non governmental organization epowering youth with epilepsy and creating awareness based in Nairobi Kenya

2.Is the slogan adopted by the National Epilepsy Coordination Committee (an Umbrellla society in Kenya) that brings all stakeholders working in epilepsy care in Kenya to engage the public on epilepsy education.

3.Logo 3 is the logo of the National Epilepsy Coordination Committee where Youth is a member

4.The photos depict various events a explained under each subheading.

Acknowledgment

I will to sincerely thank Dr. Najib Kissani for motivating me to write this paper. His guidance and support is quite immense. My appreciation too goes to Dr. Nafia Sanaa for translating part of the text to French language. I am grateful to the Epilepsy Alliance Africa through which I got connected to Dr. Najib who linked me up to the Africa and Middle East Journal for the publication of this paper. Forever grateful for Youth on The Move Kenya where I work and to my colleague Beckham Leonard Ouma who contributed in the writing of this paper.

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Conflicts of interest: None

ABSTRACT:
This is my personal account of how the consoling of peers and encouragement from them is just as important to the well-being of persons with epilepsy as medical treatments. The financial, educational, and medical benefits that were provided to me as a person with epilepsy, were the fruits that were laboriously sewn by epilepsy advocates years ahead of when I needed them. However, those advocates' efforts still weren't the relief I needed to avoid an emotional collapse.
Because of the physiological and emotional impairments suffered by people with epilepsy, they must find out what opportunities are open to them and just as importantly, get a steady flow of encouragement if they are to succeed.
Having once been on the brink of suicide, to the point where my life blossoms with opportunity, it has become my goal to be a source of encouragement to individuals who live with epilepsy.

Key words: Advocate – Consoling – Epilepsy – Medication - Productive - Support group.

RESUME :
C'est mon témoignage personnel sur la façon dont la consolation des pairs et leurs encouragements sont tout aussi importants pour le bien-être des personnes épileptiques que les traitements médicaux. Les avantages financiers, éducatifs et médicaux qui m'ont été fournis en tant que personne épileptique ont été les fruits du travail laborieux des militants de l'épilepsie, des années avant que j'en aie besoin. Cependant, les efforts de ces derniers n'étaient pas toujours suffisants pour éviter un effondrement émotionnel.
En raison des déficiences physiologiques et émotionnelles dont souffrent les épileptiques, ils doivent découvrir les possibilités qui s'offrent à eux et, ce qui est tout aussi important, recevoir un flux constant d'encouragements s'ils veulent réussir.
Ayant été autrefois au bord du suicide, je suis arrivé au point d'épanouissement avec les opportunités qui m'ont été offerte. Ainsi, mon objectif est devenu d'être une source d'encouragement pour les personnes qui vivent avec l'épilepsie.

Mots clés : Avocat - Consoler - Épilepsie - Médicaments - Productif - Groupe de soutien.

Photo:Tim Ulmer

Wanting to be "Normal":
My heart's often broken when I see many people peeking into a conference room's doorway, not because they are uncertain about whether that is where an epilepsy group support is meeting, but rather because they are hesitant about being identified with a group of people who have epilepsy. I have led support group meetings in Chicago, Los Angeles, and currently in Atlanta. Once people are welcomed to step inside, they walk as cautiously as they would walk over broken glass because they still are not sure whether they belong there. Many have droopy shoulders and sunken expressions, and clearly need some support. It appears that either they aren't getting the care they need for their conditions, the education they need to properly treat it, or any persuasive encouragement from others.
If you ask most people with epilepsy what they would like most, they say that they want to be "normal" people. The word "normal" has become despicable to me. People with many other disabilities also say that they want to be "normal". What does "normal" mean? A person with epilepsy might describe "normal" as someone who is: employed, healthy, happy, has a family, and is able to drive. If they only knew the truth! Only one person in 20 worldwide (4.3%) had no health problems in 2013, while ONE-THIRD of the world's population (2-3 billion individuals) having more than five ailments at once! [1]. Very few people fit into that category of "normal."
While trying to get them to see things differently, I point out that it is possible that some of their despair may simply be a side-effect of a medication they are taking to control their seizures, and it troubles me how few are aware of that possibility. I have suffered those side-effects and know what an impact common medication can have on people's moods.

Epilepsy's Effect on My Life

Even though I've had seizures since I was injured at the age of two, and it ruined my dreams for a career in military aviation and aerospace, I was still fighting to do something monumental for others. My biggest effort until 1991 was being on the Epilepsy Foundation of Chicago's board of directors that oversaw support groups. Not long after joining the board, an economic recession started blowing dark clouds over my career in investments until they formed a personal hurricane! Consequently, the frequency with which I was having complex-partial seizures accelerated from having one monthly to one every 36-hours. The auras that preceded those seizures terrified me because in addition to the typical tingling and deja'vu, I began seeing hallucinations of myself as a homeless person, which was a strong possibility during that recession. The hallucination even included a wretched stink that would be characteristic to a homeless vagrant! My seizures while driving caused

five multiple-vehicle accidents on Chicago expressways, but miraculously no one was injured. I lost my job, my apartment, and had to move to a tiny farm community and live with my parents.

Psychiatric help wasn't available to me then (my age was 28). However, based on my current understanding of psychology, and a family history of emotional disturbances, I'll wager that all those events plunged me into having an emotional breakdown which should have been treated immediately, but was ignored.

There was no future in that town available to me with my college degree and work experience, particularly since I was unknown to the town's residents. Being unable to drive to a larger community nearly an hour away, where employment opportunities might have been available, and that my seizures had not yet been controlled, was depressing. No friends were nearby to offer support. There were no gyms where I could exercise, nor did a support group exist. Computers that could access the Internet were not yet available in homes, and smart phones had yet to be invented. Watching television and eating were my only activities. Once TV stations ended their broadcasts playing the American National Anthem at midnight, I remained awake with nothing else to do except take a walk.

Without having had any psychiatric diagnosis or treatment, I took long walks on the gravel roads that exited the town. Since it was wintertime and the cornfields had been harvested, the severity of the wind increased with the number of miles it blew without anything blocking it. That wind and my depression created tears that stung my face because they froze on my cheeks.

I gazed at the stars overhead, and shouted at the top of my lungs, "God! Why are you doing this to me? You always said, 'Do unto others as you'd have them do unto you'. I did all that, but you put me in this place!"

I searched the sky in vain for something like a shooting star that might indicate that my call had been heard. After hours of watching, I would shuffle home and try to get some sleep.

Now, years later, whenever broken people wander into my support group meetings, I restrain myself from hugging and soothing them by confessing, "I've been there. I've done that."

Discovering My Pride in Being Epileptic

My parents were teachers with excellent counseling skills. There was also one friend who telephoned me every night to remind me that since no one was ever injured in those car wrecks, it meant that it had not been my time to die; therefore, God had a mission for me. I was oblivious to the improvements in my condition in the following months, but found programs that paid for me to return to college and earn a degree in Television Production. I had a wonderful internship at a world-renowned TV drama-series until the morning I had a seizure: producers told me to leave the studio by lunchtime. A producer at another popular TV series rescinded his job offer when it became necessary for me to explain to him that my epilepsy was the reason I couldn't drive. Repugnantly, he was willing to overlook my inability to drive if it was because of alcoholism or substance abuse.

Then I became a TV news producer. My time at work had to be limited, because if my income was too much, I would lose the government assistance that was essential to pay for my medications.

As time went on, my experiences did get better. Eventually, I took a job teaching English in China. When I was explaining my epilepsy to my graduate students, I saw--for the first time in my life--that I had epilepsy for a reason! Most of those students had never heard of epilepsy, so I became proud to be the one to educate those Chinese and others about it!

Newer Epilepsy Diagnoses Than During My Day and Age

My belief is that, today, people who are suffering the losses that I incurred 30-years ago are at an even bigger risk. While my only impediment was watching too much television, people are telling me today about dividing their time between television, social media, or playing games on their computers or smart phones. Research shows that the over-use of computer games and computer displays causes a person to experience lower self-worth, and have no confidence, and turning to suicidal and criminal behavior. Some video games can exacerbate certain seizures called reflex epilepsy that were non-existent during my period of misfortune [2]. During those years, I had suicidal thoughts and was ashamed of my plight in comparison to my friends' achievements in business and romance, expounded by my only ability being to watch television.

The improvement from the frequency or severity of my seizures was insignificant then—and would be until I moved away from my parents to college and began the schedule of a more typical workweek. Because food was available to me anytime I wanted it, my eating was irregular, and I gained weight. Good grief! I was taking walks in the middle of the night, so I was deprived of sleep! Finally, because of my interest in writing, my mother got me a primitive computer with a green glowing display on which my eyes were fixated for hours. It would be years until epilepsy research discovered that computer screens are often a seizure trigger. Nowadays, that epileptic trigger is called electronic stress, since people's vision and minds are fixated on the tiny screens of their smart phones and tablets [3]. If the effect on one's vision is not hazardous enough, the act of typing on a computer keyboard can cause in some people's praxis-induced seizures [4]. It is no wonder that I found little relief from my seizures even if my employment at a stressful company had ceased.

Being an Advocate Versus Being an Example

I've never been one to let things happen to me, rather, preferring to make things happen, like helping other people with epilepsy. Helping others is therapeutic to me. It is reasonable to identify me as being an "advocate" about epilepsy, since I fight for quality healthcare, against illegal job discrimination, and to promote new research and therapies. However, I choose to spend most of my time working with epilepsy support groups and producing a television series that makes people with epilepsy aware of how others have overcome it. There are thousands of "advocates", but quite frankly, their efforts do not affect people's lifestyles fast enough to be significant to their immediate daily needs. It can take years, maybe decades, for a meaningful law prohibiting job discrimination against people with epilepsy to be established and effectively be enforcedif ever! That makes it more satisfying to me to help people who are floundering and need to be rescued immediately from self-destruction.

Those people must recognize what their talents and resources are rather than wait for the government or charitable organizations to handle their fights for them.

Advocates previously lobbied government and health institutions for the kind of assistance that did raise me from a pitiful existence, but others were available who made me aware of those blessings. Most people being treated for epilepsy are not "at their best" because of the side-effects of their medications—

grogginess, slow speech, short memories, etc.—so they do not make the best advocates to motivate impatient government and business decision-makers to quickly change things. Besides, busy people do not like listening to others complain about their lives.

My Own Answer

Being experienced at creating and leading several epilepsy support groups, I never put pressure on anyone to speak or reveal what their personal disorder is. It took courage for them to just come to a meeting! I follow the protocol of the famous support organization, Alcoholics Anonymous, and do not make people speak about themselves other than to give us their first name. They must first be assured that they are among friendly people. The meetings are monthly, and that might be about the right pace for people who are still ashamed and dejected by their epilepsy. Once their attendance becomes regular, I try to bring them into the conversations more often. I might use my own stories as a means to start conversations. In doing that, they learn that I survived the suffering that epilepsy caused by prohibiting me from a military career flying fast jets, making me a business failure, and threatening me with car-wrecks. Not to sound arrogant, but I chuckle inside when they learn that I was active in national politics, worked for a famous TV show, and have travelled by myself to work for years in a foreign nation. Many of them get excited by learning that I published a book about the experience, Involuntary MISSION, In China with a Thorn in the Flesh, am producing an awareness TV series that will be streamed internationally called Epilepsy Gangster all while I am taking 6,000mg of medications for my epilepsy! Most of those medications affect a person's mood, but people see me as being charismatic, confident, and caring!

For me, in addition to needing a good family, I needed examples of famous people who weren't hindered by epilepsy. Realizing that epilepsy didn't stop such great people as Julius Caesar, Alexander the Great, Albert Einstein, Sir Isaac Newton, Pablo Picasso, Elton John, Napoleon, Mohammed, or St. Paul from shaping mankind—so why should epilepsy stop me from having a comfortable home, a dear family, and being a productive member in my community?

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Conflits d'intérêt : Aucun

Abstract:

African & Middle East Epilepsy Journal (AMEEJ) is a bilingual (English and French) journal specializing in epilepsy. It is published in Marrakech from 2012 and printed at the rate of 6 issues per year. Professor N. Kissani took care to develop this journal by inviting a committee of renowned readers. It started off as an epilepsy journal in North Africa and the Middle East, but after 2015 it has been indexed in CAMES (High African and Madagascar Council of education) and expanded across all Africa and became an African epilepsy journal. The geographical distribution of the AMEEJ is international and diversified, focusing on Africa and the Middle East. We analyzed all the published volume over the past 8 years. Of the 232 published papers from 36 different countries, the majority comes from Africa while the rest is distributed on all the other continents. Through our study we ranked into 3 categories the 36 countries according to their number of articles appeared in the AMEEJ. All over these 8 years, AMEEJ facilitate the health research for all medical and paramedical staff, in order to advance the research level on epilepsy in Africa.

Keywords: Epilepsy – African and Middle East Epilepsy Journal - Publications

Résumé:

Journal de l'épilepsie en Afrique et au Moyen-Orient est une revue bilingue (anglais et français) spécialisée dans l'épilepsie. Il est publié à Marrakech à partir de 2012 et imprimé au rythme de 6 numéros par an. Professeur N. Kissani a pris soin de développer cette revue en invitant un comité de lecteurs de renom. Il a commencé comme un journal sur l'épilepsie en Afrique du Nord et au Moyen-Orient, mais en 2015, il s'est étendu à toute l'Afrique et devient un journal africain sur l'épilepsie. La répartition géographique du Journal de l'épilepsie en Afrique et au Moyen-Orient est internationale et diversifiée, centrée sur l'Afrique et le Moyen-Orient. Nous avons analysé tous les volumes publiés au cours des 8 dernières années. Sur les 232 articles publiés de 36 pays différents, la majorité vient d'Afrique tandis que le reste est distribué sur tous les autres continents. Grâce à notre étude, nous avons classé en 3 catégories les 36 pays en fonction de leur nombre d'articles parus dans le Journal de l'épilepsie en Afrique et au Moyen-Orient. Tout au long de ces 8 années, le Journal de l'épilepsie en Afrique et au Moyen-Orient a facilité la recherche en santé pour l'ensemble du personnel médical et paramédical, afin de faire progresser le niveau de la recherche sur l'épilepsie en Afrique.

Mots-clés: Epilepsie - Journal de l'épilepsie en Afrique et au Moyen-Orient - Publications.

Introduction:

African & Middle East epilepsy journal is one of the rare African journals specialized in epilepsy. As we know epilepsy represents a huge health problem for the African countries, with a social dimension that goes beyond the etiological and nosographic representations of this disease. Also, the lack of qualified personnel and the need of contextualized medical information on epilepsy, forced the creation of a journal interested to epilepsy in Africa. Moreover Africa's research capacity remains feeble [1]. The reasons for this are varied, including low funding, inadequate research infrastructure, the relatively low number of active scientists and scientific journals [1]. Consequently the AMEEJ was created in 2012 by Professor Najib Kissani, to fill the gap of specialized journals in epilepsy in Africa. Add to that the higher number of patients with epilepsy, and the social dimension of epilepsy which is clearly further than the etiological and nosographic representations. The main journal mission is to make scientific information on epilepsy more available for health professionals in Africa, and to give a chance to senior and junior neurologists to publish their works concerning epilepsy. Furthermore, this journal has increased the number of publications on epilepsy in the continent. The aim of this paper is to describes the number and the origins of publication during eight years from 2012-2019, to make a rank of the countries in terms of publication and to look for limitations and difficulties faced to sustain this product. These results will help bringing to light the experience of the AMEEJ, developing a medium and long term vision for empowering the journal and index it in Scopus then in Pubmed and to encourage the expansion of knowledge in the African scientific community.

Methods:

We reviewed retrospectively all the publication of AMEEJ between January 2012 and December 2019, at the neurology department, Mohamed VI university hospital of Marrakech; where we established our editorial AMEEJ office.

We consult the archives at the journal website. We analyze the numbers, type, and origin of publications from all the published volume. Each volume corresponds to one year, it contains 6 issues numbers, each issues number includes one editorial and 4 articles. The country classification was based on the number of publications. All data were stored and analyzed by Microsoft Excel software for Windows (version 2007).

Results:

Of a total of 232 published papers, over eight years from January 2012 to December 2019. The number of published articles is variable, with a high rate in 2013 with 46 articles and a low rate in 2019 with only 12 articles **(Figure1).**

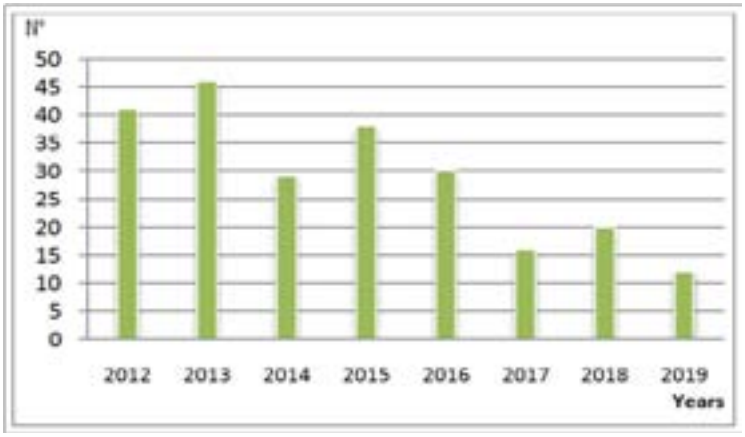

Figure 1: Number of AMEEJ papers by years

The average number of publications was around 29 articles per year, which makes 5 articles per issue. The articles came from 36 different countries, distributed on all continents. The majority of the articles published came from Africa with 195 articles, followed by Europe with 17 articles and North America with 12 articles. Unfortunately, the Middle East is in fourth place with less than 5 articles; Latin America has the lowest publication rates of all 5 continents **(Figure 2)**.

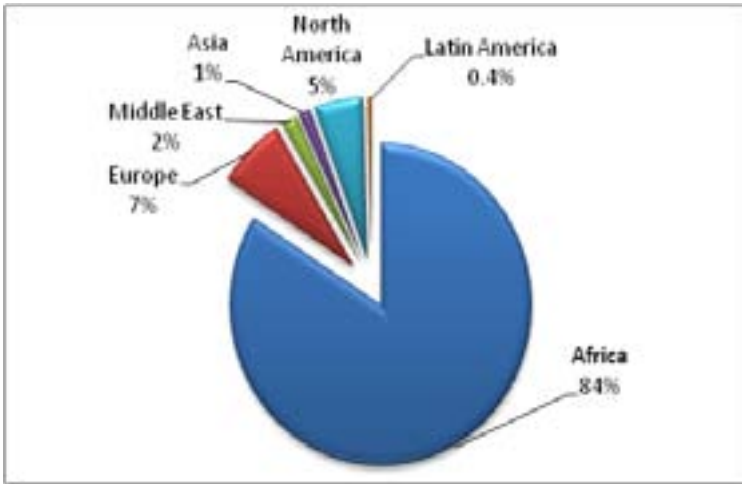

Figure 2: Percentage of AMEEJ papers by continents.

Morocco, Senegal and Mali represent 70% of all the African publications, while France and USA comes first in their continents. Through our study we ranked the 36 countries according to their number of articles appeared in the AMEEJ (Figure 3). Three categories were proposed, the first one regroup countries with a publication rates more than 6% (> 13 articles) of the all papers in AMEEJ, the second one countries with a publication rates between 2% and 5% (4 to 11 articles) then the third category with a publication rates of 0% to 1% (0 to 2 articles).

All the publications are free to access and download from the website AMEEJ, which allow the share and citation of papers. During the review, we found an article from Mali 'Epilepsy genetics in Africa challenges and future perspectives' published in Pubmed Central 'North Afr Middle East Epilepsy J. Sep-Oct 2014;3(5):5-7. PMID: 26413584'.

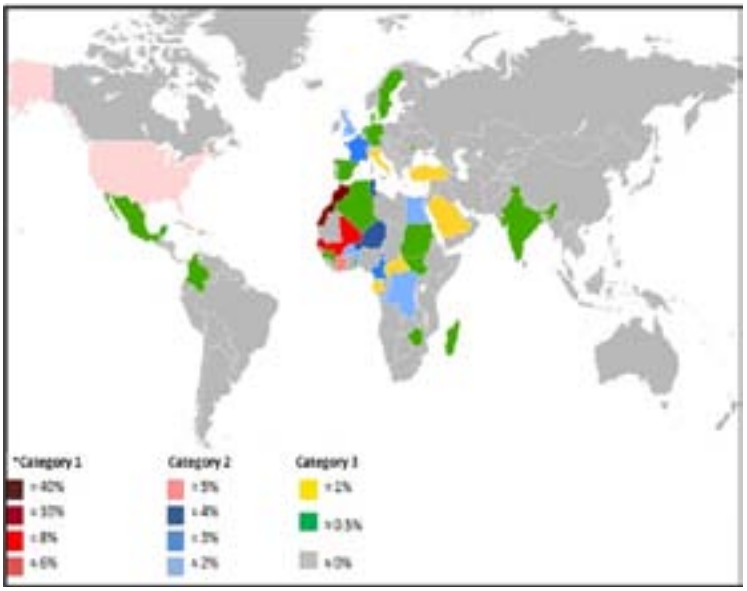

Figure 3: Rank and origins of published papers in AMEEJ from different geographical locations

Discussion:

AMEEJ provides an international forum for the publication of papers on topics related to epilepsy, including the natural history, epidemiology, differential diagnosis and practical management of epilepsy. Our dataset highlights that the productivity of epilepsy articles in Africa is at an all time high, while the number of neurologist on the continent remains feeble compared to total African population.

Epilepsy in Africa is not always viewed as a neurological disease. Instead, patients suffering from epilepsy may be thought possessed by evil spirits. Consequently they may not seek medical treatment but may instead turn to a traditional healer [2]. The important thing is to change people's attitudes and recognize that epilepsy is a chronic disease like any other disease [2]. For these reasons the AMEEJ was created to spread the current information available on different aspects of seizures and epilepsy.

AMEEJ represents an example of rare journals specializing in epilepsy in Africa, since its creation in 2012; growing interest is increasing regarding the number of presented manuscripts, the upgrade of scientific spectrum and volume of the journal. It provides an opportunity for all African practitioners to share their experiences, to present the current

situation of epilepsy in each African country and to discuss effective strategies to improve the overall management of epilepsy patients.

Scientific collaboration represent a bright side of AMEEJ, on national and international level, the possibilities of expansion and of internationalization of research underway in Africa will increase. The creation of African journals would have major implications for the capacities of scientific leadership in all different areas especially medical field.

Limitations:

The limitations of the study are the lack of number in some volume.

Perspectives:

Through this paper we traced the evolution of such a specialized journal with the aim to index AMEEJ in Scopus subsequently in Pubmed.

Conclusion:

African and Middle East Epilepsy Journal count up eight-year of a rich editorial path. Such journal increases the motivation to undertaking epilepsy research. So AMEEJ facilitate the health research for all medical and paramedical staff, in order to advance the research level on epilepsy in Africa.

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https://doi.org/10.1016/S0001-706X(03)00038-X

History of publication in the Ameej

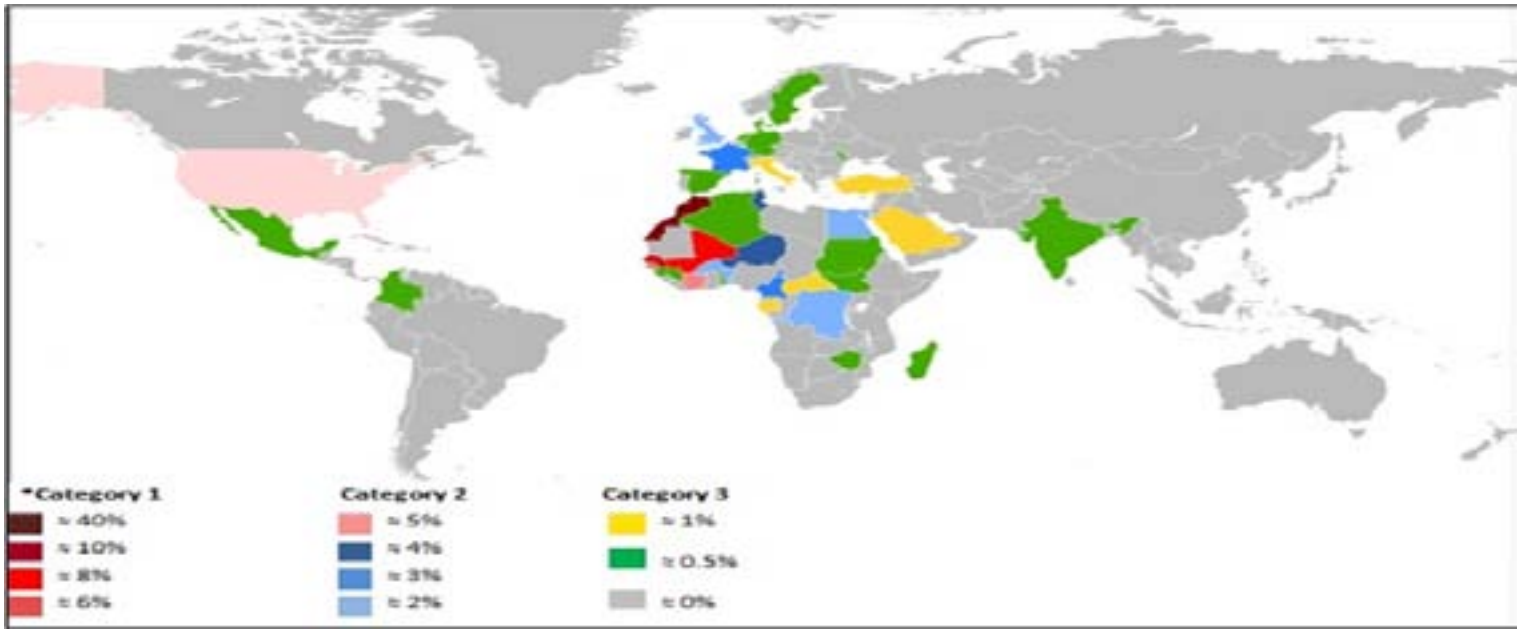
and origin of the papers

Since its creation in January 2012, Nameej received more than 300 papers, 90 have

been published in the different volumes

This map is summarizing all the origins of these papers published

Africa is leading all the continents with 70,16%,
Followed by Europe 10, than North America 7,46%
Asia and latine America are still missing up to August,2020.



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