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Research paper

Impact of ambulatory EEG in the management of patients with epilepsy in resource-limited Latin American populations



Alioth Guerrero-Aranda^{a,b,*}, Francisco J. Taveras-Almonte^c, Fridha V. Villalpando-Vargas^{a,b}, Karla López-Jiménez^{a,b}, Gloria M. Sandoval-Sánchez^c, Julio Montes-Brown^d

^a Epilepsy Clinic, Hospital "Country 2000", Mexico

^b University Center "Los Valles", University of Guadalajara, Mexico

^c Professional Health Tower "Corazones Unidos", Dominican Republic

^d Medicine and Health Sciences Department. University of Sonora, Mexico

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ABSTRACT

Objective: Ambulatory electroencephalography (AEEG) monitoring allows for prolonged recordings in normal environments, such as patients' homes, and is recognized as a cost-effective alternative to inpatient long-term video-EEG primarily in resource-limited countries. We aim to describe the impact of AEEG on the assessment of patients with suspected or confirmed epilepsy in two independent Latin-American populations with limited resources.

Methods: We included 63 patients who had undergone an AEEG due to confirmed/suspected epilepsy. Clinical (demographic, current antiseizure medication and indication) and electroencephalographic (duration of the study, result, and impact on clinical decision-making) were reviewed and compared.

Results: The main indication for an AEEG was the differentiation of seizures from non-epileptic events with 57% of patients. It was categorized as positive in 36 patients and did have an impact on the clinical decision-making process in 57% of patients. AEEG captured clinical events in 35 patients (20 epileptic and 15 non-epileptic).

Conclusions: AEEG proves to be a valuable tool in resource-limited settings for assessing suspected or confirmed epilepsy cases, with a significant impact on clinical decisions.

Significance: Our study provides valuable insights into the use of AEEG in under-resourced regions, shedding light on the challenges and potential benefits of this tool in clinical practice.

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1. Introduction

Epilepsy is a neurological disorder characterized by recurrent, unprovoked seizures resulting from sudden, excessive electrical discharges in the brain (Fisher et al., 2017). It is a relatively common condition, affecting more than 50 million people worldwide, with 80 % of cases found in low- and middle-income countries (Fisher et al., 2014). The diagnosis of epilepsy typically involves a comprehensive medical evaluation that includes multiple tests. Electroencephalography (EEG) is the most commonly used test during the evaluation of patients suspected of having epilepsy. This non-invasive test measures the electrical activity of the brain through small electrodes placed on the scalp (Schomer and da Silva, 2012). The diagnosis of epilepsy remains clinical. However, the recording of the electroencephalographic correlate of a clinical seizure is of paramount importance. For example, the ictal EEG pattern could give a clue about the etiology (i.e., a focal ictal pattern in the appropriate clinical context could suggest a structural etiology). Inpatient long-term video-EEG is considered the gold standard for evaluating the electroclinical features of a seizure (Tatum et al., 2018). Typically, monitoring through video-EEG is performed in Epilepsy Monitoring Units (EMUs). However, the cost of special resources, personnel, and hospitalization poses a disadvantage, especially in resource-limited countries where EMUs are scarce (Tatum et al., 2022a,b).

Ambulatory electroencephalography (AEEG) monitoring is a modality that allows for prolonged recordings in normal environments, such as patients' homes (Hasan and Tatum, 2021). Although not a recent technology, it is currently underutilized in clinical practice. However, it has received a boost in popularity during the recent pandemic due to the need for remote monitoring and

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^{*} Corresponding author at: Epilepsy Clinic, Hospital "Country 2000", Av. Cvln. Jorge Álvarez del Castillo #1542, Colonia Chapultepec Country, CP 44620 Guadalajara, Jalisco, Mexico.

E-mail address: alioth.garanda@academicos.udg.mx (A. Guerrero-Aranda).

is now recognized as a cost-effective alternative to inpatient longterm video-EEG (Tatum et al., 2021). This alternative becomes increasingly important in resource-limited countries with a shortage of EMUs. Therefore, in this study, we aim to describe the impact of AEEG on the assessment of patients with suspected or confirmed epilepsy in two independent Latin-American populations with limited resources.

2. Methods

2.1. Patient inclusion

We enrolled all patients who underwent an AEEG between March 2021 and December 2022 at two distinct EEG labs in independent Latin American populations. The first lab is situated in the state of Jalisco, Mexico, while the second one is located in the state of Santo Domingo, Dominican Republic. At the time of conducting this study, patients from these regions did not have access to an EMU for inpatient long-term video-EEG. The study was approved by the local Ethics Committee of our centers.

2.2. Clinical evaluation and EEG assessment

Neurology clinical charts were reviewed for demographic data, current antiseizure medication (ASM), indication for an AEEG, number/results of previous Magnetic Resonance Imaging (MRI), and the number/results of previous routine EEGs. AEEG was reviewed for duration of the study, result, and impact on clinical decision-making.

The indication for an AEEG was categorized into one of four primary reasons for performing the study. The first reason was the *differentiation* of seizures from non-epileptic events. The second reason was the *quantification* of seizures and epileptiform discharges (ED), for example, to assess treatment efficacy. The third reason was the *characterization* of seizure type, which helps define possible etiology, and the final reason was the *localization* of epileptogenic focus during presurgical evaluation. All these patients had frequent events and that was the main factor influencing the decision to perform an AEEG.

In our study, previous MRIs and routine EEGs were deemed positive only when results were specific to epilepsy. For instance, if a patient with Functional Neurological Disorder (FND) had diffuse mild leukomalacia, the MRI was categorized as negative. However, if a patient had a focal lesion (i.e., tumoral, vascular, etc.), even if the localization was not consistent with clinical semiology, the MRI was categorized as positive. Similarly, for routine EEG, diffuse mild slowing was considered negative in a patient with focal epilepsy. However, an epileptiform EEG was always categorized as positive, regardless of the morphology and localization of the EDs.

The results of the AEEG were considered positive only if seizures or EDs were recorded, regardless of the indication for the study. For instance, if a patient with suspected FND had a normal AEEG (no seizure nor EDs), the study was considered negative, even though it helped to confirm the diagnosis (i.e., when recording the habitual non-epileptic event). The impact of AEEG on clinical decision-making was dichotomized as either "yes" or "no". A "yes" was recorded when the AEEG result led to a change in clinical management. In the case mentioned above, where the AEEG was negative, it still impacted clinical decision-making, and thus was categorized as "yes".

2.3. EEG recording/interpreting

The EEGs were recorded using 21 electrodes placed according to the International 10–20 System. A 32-Channel Clinical EEG

machine was used (Cadwell Arc Alterna in Jalisco, and a Natus Xltek Trex in Santo Domingo). Both systems had the same recording features including a high-pass filter of 0.53 Hz, a low-pass filter of 70 Hz, a sampling rate of 256 Hz, and impedances of less than 5 k Ω . Before leaving the clinics, every patient/relative received a diary and an indication of how to fulfill it, placing special emphasis on habitual events. Additional indications regarding the button event were also given.

To quantify seizures and EDs, the visual revision was complemented by a quantitative analysis using Persyst software (Persyst Inc. Germany) for all recordings. Two board-certified and experienced clinical epileptologists / electroencephalographers reviewed all EEG studies.

2.4. Statistical analysis

Descriptive analyses were performed to compare both populations. Quantitative variables were reported as mean \pm standard deviation and qualitative ones were reported as absolute and relative values. Statistical difference was evaluated using an independent samples *t*-test for quantitative variables and a chi-square for the qualitative ones. The significance threshold was set at *p* < 0.05. All analyses were performed using SPSS version 19.0 statistical software (SPSS, Chicago, IL, USA).

3. Results

Sixty-three patients were included in the present study (57 % females). There was no statistically significant difference between the gender distribution in both populations (X^2 [1, N = 63] = 0.3, p = .56). The mean age was 24.6 years old (range 3–71 years old) for the entire cohort, and both populations showed a similar distribution of patients' age (t [61] = 1.28, p = .48). Out of the 63 patients, 44 (70 %) were on ASM regardless of the indication for the AEEG. There was no statistical difference between populations (X^2 [1 N = 63] = 1.27, p = .26). Table 1 shows the main clinical and electroencephalographic characteristics of the populations.

The main indication for an AEEG in both populations was the differentiation of seizures from non-epileptic events with 35 patients (57 %). Fourteen patients (23 %) underwent an AEEG for the quantification of seizures and EDs, eight (13 %) for the characterization of their seizures, and six (7 %) for the localization of the epileptogenic focus during presurgical evaluation. There was a slight but non-significant difference between populations (X^2 [3, N = 63] = 7.64, *p* = .05). In the Mexican population the main indication was differentiation (55 %), followed by quantification (30 %), localization (12 %) and characterization (3 %). In the Dominican population, the main indication was differentiation (57 %), followed by characterization (23 %), quantification (13 %), and localization (7 %).

All patients had at least one previous routine EEG, and in 81 % of them, the EEGs were reported as negative. Regarding the neuroimaging study, all Dominican patients had an MRI. However, only 15 patients (45 %) from the Mexican population had a previous MRI. The duration of the AEEG was statistically different between populations (X^2 [1, N = 63] = 9.73, p < .05). Eighteen patients (55 %) in the Mexican population versus only five (7 %) in the Dominican population received a 24hrs AEEG. The rest of them received a 12hrs AEEG (45 % and 83 % in the Mexican and Dominican populations, respectively).

The AEEG was categorized as positive in 36 patients (57 %). Both populations showed a non-different results pattern (X^2 [1, N = 63] = 0.005, *p* = .94). Fifty-eight percent of patients showed a positive result and 42 % negative in the Mexican population, while 57 % showed a positive result and 43 % negative, in the Dominican pop-

Table 1

Clinical and electroencephalographic characteristics.

		Ambulatory EEG (n = 63)	Ambulatory EEG (n = 63)	
		Mexican population (n = 33)	Dominican population (n = 30)	
Mean age (SD) Gender, n(%)		22.2 (15.1)	27.3 (16.2)	p = .48 p = .56
	Male	27 (43 %)		*
		13 (39 %)	16 (53 %)	
	Female	36 (57 %)		
		20 (61 %)	14 (47 %)	
Indication, n(%)				p = .05
	Differentiation	35 (57 %)		
		18 (55 %)	17 (57 %)	
	Quantification	14 (23 %)		
		10 (30 %)	4 (13 %)	
	Characterization	8 (13 %)		
		1 (3 %)	7 (23 %)	
	Localization	6 (7%)	2 (5 %)	
ACD 4 (01)		4 (12%)	2 (7%)	26
ASM, $n(\%)$		44 (70%)		<i>p</i> = .26
D		21 (64%)	23 (77%)	
Duration	101	10 (63 %)		p < .05*
	12 h	40 (63 %)		
	24 h	15 (45 %)	25 (83 %)	
	24 11	23 (37 %)	F (7 %)	
Doculto		18 (55 %)	5 (7 %)	n = 0.01
Results	Positivo	26 (57 %)		p = .94
	FOSITIVE	10 (59 %)	17 (57 %)	
	Epiloptic ovent	13(30%)	11 (27 %)	
	Negative	14(42%)	11 (37 %)	
	Negative	$\frac{27}{43\%}$	13 (13 %)	
	Non-enileptic event	6(18%)	1 (13 %)	
Impact	Non-epilepile event	0(10%)	4 (15 %)	n - 20
IIIpact	Vec	36 (57 %)		p = .25
	103	20 (61 %)	16(54%)	
	No	17 (27 %)	10 (34 %)	
	110	10 (30 %)	7 (23 %)	
	Unknown	10 (16 %)	, (2370)	
	Charlown	3 (9%)	7 (23 %)	
		5 (5 %)	. (20.%)	

Percentages are calculated from specific subgroups. SD: standard deviation. ASM: antiseizure medication. Asterisks denote statistical differences.

ulation. In the Mexican population, 20 (60 %) patients presented clinical events during the recording (14 epileptic and six non-epileptic), while in the Dominican population, 15 (50 %) patients presented clinical events (11 epileptic and four non-epileptic). The results of the AEEG did have an impact on the clinical decision-making process in 36 patients (57 %). There was no statistical difference between populations (X^2 [2, N = 63] = 2.44, *p* = .29). We were unable to contact the treating physicians of ten patients (three from Mexico and seven from the Dominican Republic) to evaluate the impact of the AEEG results.

4. Discussion

To date, only one study has documented the utilization of AEEG for the evaluation of epilepsy in Latin America (Chicharro et al., 2020). This study focused on the presurgical assessment of patients with drug-resistant temporal epilepsy, despite having the facilities for conducting inpatient long-term video-EEG monitoring. In contrast, our research aimed to investigate the impact of AEEG in the evaluation of patients with suspected or confirmed epilepsy in two distinct resource-limited populations lacking access to inpatient long-term video-EEG monitoring.

The primary indication for an AEEG in both populations was the differentiation of seizures from non-epileptic events. However, it is important to note that comparing this finding with other studies can be challenging due to variations in categorization by different authors. The challenge of categorizing indications for ancillary tests is a complex matter that extends beyond just EEGs, as it is greatly influenced by the preferences and clinical judgment of the treating/ordering physicians. Specifically concerning AEEG, there lacks a universally standardized or rigorous defined classification for its indications. For instance, some authors include the capture and characterization of any clinical event, regardless of its nature, as a separate category from the detection of EDs (Dash et al., 2012).

Nonetheless, a recently published guideline by the American Clinical Neurophysiology Society (Tatum et al., 2022a,b) outlines various potential clinical indications, some of which align with those utilized in our study. While this categorization could potentially introduce bias to the results, it is important to note that our aim was to consolidate the primary indications as directed by the treating physician, irrespective of whether the AEEG also addressed other clinical questions.

For instance, capturing a seizure could potentially address both the question of whether the event is epileptic (differentiation) and the understanding of its electroclinical features (characterization). However, it is important to acknowledge that in certain instances, the inclusion of video data was not feasible due to suboptimal quality or absence, thereby the study served to differentiate but not to characterize. Conversely, recording a seizure along with accompanying video data can indeed provide insights into the electroclinical features (characterization); nevertheless, this might not invariably fulfill the requirements for presurgical assessment (localization). In some patients without evident MRI findings, the AEEG was indicated for recording as much as possible ictal and interictal activity for supplemental Electrical Source Imaging (ESI) during the presurgical evaluation (localization).

Despite this variation in the indication classification, our findings align with numerous studies where AEEG is primarily utilized for diagnostic purposes (Faulkner et al., 2012; Goodwin et al., 2014; Kandler et al., 2017; Primiani et al., 2021; Syed et al., 2019). AEEG offers a higher likelihood of capturing both clinical events and interictal EDs compared to routine EEGs (Hernández-Ronquillo et al., 2020). Many patients in both populations presented with clinical events characterized by inconclusive semiology and normal routine EEG findings. Consequently, AEEG emerged as a viable alternative to explore and determine the possible nature of the events.

Although not statistically significant, there was a slight variation in the order of the indications between the two populations. In the Mexican population, the second most common indication was quantification, whereas in the Dominican population, it was the characterization of seizures. This discrepancy could potentially be attributed to the geographic origin of the patients in the Mexican population, specifically from a region known as Los Altos de Jalisco (The Highlands of Jalisco). This region is recognized for its high prevalence of genetic disorders, primarily due to a significant proportion of consanguineous and endogamous marriages (Murrell et al., 2006; Yescas et al., 2006). Consequently, there has been a documented higher incidence of developmental and epileptic encephalopathy (DEE) with genetic etiology in this population (i.e., in our series, eight out of the ten patients evaluated for quantification). Therefore, it is likely that many patients in this population underwent an AEEG for assessment of treatment efficacy, specifically for the quantification of seizures and EDs. For instance, patients with DEE often experience events related to their movement disorders and cognitive impairment, which can be challenging to differentiate from seizures.

Another possible explanation for the difference in the indication of localization of the epileptogenic focus between the Mexican and Dominican populations could be attributed to the presence of a more mature epilepsy surgery program in Mexico. However, further investigations and comparative studies are needed to establish a definitive correlation between the maturity of epilepsy surgery programs and the choice of indications for AEEG in different populations.

An interesting finding in our study was the significant proportion of patients who were on ASM despite the main indication for AEEG being uncertainty in the diagnosis. Surprisingly, half of the patients who underwent an AEEG for differentiation were already taking at least one ASM. This finding is consistent across both populations, with no statistical difference observed. The prevalence of ASM use in these cases is not unexpected, as it aligns with the well-documented phenomenon of overdiagnosis and overtreatment of epilepsy in daily clinical practice (Benbadis, 2007; Chowdhury et al., 2008; Walker and Sander, 1994).

In the face of a paroxysmal event, physicians often feel compelled to provide a definitive diagnosis. Consequently, in case of diagnostic uncertainty, some physicians may opt to start medication rather than risk a missed diagnosis (erring on the side of caution). However, it is important to acknowledge that evidence has shown that delaying treatment in patients with epilepsy does not affect long-term prognosis (Marson et al., 2005). On the contrary, unnecessary exposure to ASM can pose significant risks and even be life-threatening.

In our series, it is notable that every patient from both populations had undergone at least one previous routine EEG, with the majority of them (eight out of ten) yielding normal results. The diagnostic yield of the first EEG in patients with epilepsy has been reported to vary widely, ranging from 32 % to 59 % in children and from 12 % to 44 % in adults (Baldin et al., 2014). The relatively lower sensitivity observed in our study can be attributed to the fact that many of our patients ultimately did not have epilepsy. Regarding neuroimaging, interestingly all Dominican patients had undergone a previous MRI, whereas only half of the Mexican patients had access to this imaging modality. MRI is an expensive diagnostic test that may not be easily accessible to many patients within the public health system of developing countries. However, in the Dominican Republic, private medical insurance coverage provided by employers is more prevalent, facilitating greater accessibility to expensive diagnostic tests. In contrast, in Mexico, private medical insurance coverage is primarily limited to larger companies, leaving the majority of the population reliant on the public health system with limited access to such resources.

The duration of AEEG recordings varied between populations, with a predominance of 24-hour recordings in Mexico and 12hour recordings in the Dominican Republic. The exact reason for this discrepancy is not entirely clear but could be attributed to local preferences. Further investigations and understanding of these variations would be beneficial. Another important question regarding the length of the recordings is whether it was related to event frequency or indication of the study. However, this was not formally assessed.

Although recognizing the significance of this aspect, we decided not to conduct this analysis due to the anticipated low statistical power. Additionally, we think it could be quite complex to interpret such results. For example, a preliminary overview of the data reveals that among the cohort of 40 patients who underwent 12hour AEEG recordings, 23 patients (58 %) presented one or more clinical events (epileptic or non-epileptic). Conversely, within the 23 patients subjected to 24-hour AEEG recordings, 13 (56 %) manifested one or more clinical events. Nonetheless, it is noteworthy that in the 24-hour group, there was a predominant indication for quantification, primarily among patients with epileptic encephalopathy characterized by heightened seizure frequency. This inherent difference could potentially introduce a bias into the outcomes and therefore, further interpretation complexities.

In our study, the AEEG was deemed positive in slightly over half of the patients. AEEG was considered positive whenever a seizure or EDs were captured. Considering that most patients had normal routine EEGs, this result demonstrates an increase in the diagnostic yield of AEEG. Moreover, as mentioned before, many patients in our series did not have epilepsy; therefore, our overall yield of AEEG in patients with confirmed epilepsy was 86 %, aligning with findings from previously published studies (Faulkner et al., 2012; Goodwin et al., 2014; Kandler et al., 2017; Primiani et al., 2021; Syed et al., 2019).

When physicians order a diagnostic test, their primary objective is to confirm or rule out their clinical suspicions. Consequently, the test results have the potential to significantly impact clinical decision-making. In our study, the utilization of AEEG led to a change in clinical management in nearly 60% of patients, regardless of the population they belonged to. This finding aligns with previous studies that have reported obtaining valuable information from AEEG in 52-84% of patients (Dash et al., 2012; Olson, 2001). Furthermore, AEEG proved to be effective in capturing the clinical events under investigation in 19 out of the 35 patients who underwent AEEG for differentiation purposes. Interestingly, among these 19 patients, ten were identified as having non-epileptic events, leading to a confirmed diagnosis of Psychogenic Non-Epileptic Seizures (PNES) in all cases. The diagnosis of PNES was only confirmed in patients with their habitual clinical events recorded and the absence of ictal correlate in the EEG (none of these patients exhibited any semiology characteristic of frontal mesial epilepsy).

Multiple studies have consistently shown a higher diagnostic yield of AEEG in the detection of PNES compared to routine EEG (Kandler et al., 2017; Mikhaeil-Demo et al., 2021; Tolchin et al., 2017). While inpatient long-term video-EEG monitoring remains the gold standard for diagnosing PNES, AEEG serves as a viable alternative in regions where access to an EMU is limited. It is important to mention that we could not evaluate the impact of the AEEG on a subgroup of patients, and this may have implications for the generalizability of our findings.

It is also important to mention that at the time of conducting this study, none of the enrolled patients had undergone a subsequent AEEG. It could be argued that a multi-day or repeated study, particularly in cases with negative results that did not influence clinical decision-making, might have yielded different results. Nonetheless, in regions with constrained resources, the financial implications of such additional studies are pivotal and frequently render their repetition infeasible.

Nowadays, advances in technology make it possible to record video along with AEEG and to make use of trending software to process long recordings. However, this progress introduces new challenges, particularly in resource-limited regions. For instance, a 32-channel 24-hour video EEG recording generates data files of substantial size, requiring costly computing infrastructure for storage. Furthermore, the interpretation of lengthy recordings is timeconsuming and requires special expertise. Consequently, there is an immediate necessity for the training of clinical neurophysiologists, particularly in the domain of quantitative analysis of prolonged EEG recordings using trending software. Meanwhile, telemetry emerges as a viable alternative to bring expertise to regions with limited human resources and constrained facilities.

Our study has several important limitations that should be acknowledged. Firstly, the small sample size limits the generalizability of our findings. However, it is important to note that our study primarily aims to provide a descriptive account of the experience of using AEEG in resource-limited regions. Secondly, the lack of video availability in some patients and the presence of unreliable video signals in others (i.e., patients out of the camera's field of view) represents another significant limitation. This may have impacted our ability to accurately assess and analyze the data, potentially affecting the diagnostic yield of the AEEG. Another limitation is the presence of selection bias in our study. As a real-life population-based study, there is a possibility of misdiagnosis and misindication of AEEG, which could introduce bias and influence our results.

Despite these limitations, our study provides valuable insights into the use of AEEG in under-resourced regions, shedding light on the challenges and potential benefits of this tool in clinical practice. Future research with larger sample sizes and improved methodology should be conducted to further validate our findings and address these limitations.

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Ethical policy

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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