Clinical guidelines from the Priority Epilepsy Program of the public health sector in Mexico

Juan C. Reséndiz-Aparicio

Hospital Psiquiátrico Infantil Dr. Juan N. Navarro y P.P.E, Instituto Nacional de Neurología y Neurocirugía Dr. Manuel Velasco Suárez. Mexico City, Mexico

The Programa Prioritario de Epilepsia (PPE - Priority Epilepsy Program) was created based on the accord published in the Mexican Official Gazette of the Federation on October 24th, 1984. This program has labored in an uninterrupted manner to regulate, coordinate, methodize, and optimize the strategies in favor of patients with epilepsy, as well as their families and society. There are currently 78 centers of integral treatment for epilepsy in Mexico, located in various hospitals belonging to Mexico’s health sector.

The headquarters for the national coordination is in the Instituto Nacional de Neurología y Neurocirugía (National Institute of Neurology and Neurosurgery) “Dr. Manuel Velasco Suarez” (INNN due to its acronym in Spanish) in Mexico City, from where all actions are planned for this task. The national coordination is led by its creator and founder Francisco Rubio Donnadieu, MD and by the author.

The development of the first Clinical Guidelines (CGs) has been a laborious effort, one that has been finished due to the work of all the coordinators of the PPE, who are neurologists and pediatric neurologists certified by the Mexican Board of Neurology and who work in one of the many institutions of the health sector in Mexico. To elaborate the CG, all the coordinators of the PPE met in person in two meetings, the first in the city of Leon and the second in the city of Puebla, where we formed workgroups for each CG. These meetings were possible due to the support of the federal government and the contributions of the...
J. C. Reséndiz-Aparicio: Clinical Guidelines of the Priority Epilepsy Program

pharmaceutical laboratories that aid in training primary health-care physicians. These CGs are designed to aid the primary health-care physicians and the specialists in making adequate decisions when approaching epileptic patients of different age groups and genders. These are the culmination of the experience of their authors, who have followed the necessary steps for proper and updated scientific research, using the criterion of the American Epilepsy Society 2016 to analyze the levels of evidence and recommendations including the benefit for the patients. To evaluate the quality of the CG, two experts coordinated each table and applied the Spanish version of the AGREE instrument of 2001.

Due to the advances in the knowledge of epilepsy, the PPE group aims to update the CG every 5 years. These CGs constitute a series of recommendations developed by a group of medical physicians that have a particular interest in the field of epilepsy and work throughout the various institutions of the health sector; however, it is understood that the application of said recommendations depends on many factors. It is important to state that there are no conflicts of interest in these CGs due to the fact that they are editorially independent of any external funding.

Finally, I would like to thank the INNN for their hospitality and support in the coordination of the Program, the Mexican Academy of Neurology for the publication in their magazine, the Mexican Society of Pediatric Neurology who supported the process of translating the CG to English, and the authorities of the Hospital Psiquiátrico Infantil (Children’s Psychiatric Hospital) of Mexico City who have allowed me to work as the adjunct executive member of the Priority Epilepsy Program and above all, thank you to the coordinators of the Priority Epilepsy Program who worked on this project; this work is dedicated to them and their families and to which I express my most ample recognition.

Juan Carlos Reséndiz Aparicio, MD, Adjunct Executive Member

American Epilepsy Society 2016

**Article Classification: Evidence**

**Class I:** A randomized, prospective and controlled clinical trial with masked outcome assessment, in a representative population. The following are required:

a. No more than two specified primary results.

b. Blind allocation of subjects.

c. Exclusion/inclusion criteria are clearly defined.

d. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

e. Adequate accounting for dropouts with numbers sufficiently low to have a minimal potential for bias. (study was completed with at least 80% of the enrolled subjects).

f. Demonstration of superior design of the studies or demonstration of non-inferiority with a 10% non-inferior design margin.

**Class II:** A randomized, prospective and controlled clinical trial with masked outcome assessment that lacks one or two criteria of Class I a-e above, or a prospective matched cohort study with masked objective outcome assessment in a representative population that meets a-e.

**Class III:** All other control trials in a representative population, where outcome was independently assessed by objective outcome measurement.

**Class IV:** Evidence from non-controlled trials, including series reports, case reports, consensus, or expert opinion.
Evidence for the Recommendation

| Level A | One or more Class I trials or two or more Class II trials. |
| Level B | One or more Class II trials or three or more Class III trials. |
| Level C | Two or more Class III trials. |
| Level U | Absence of trials that complement levels A, B, or C. |

Level R-PPE

Conclusion and Recommendation

| Conclusion, Level A | Established as effective, ineffective, or harmful for the given condition in the specified population. |
| Recommendation: | Must be done or must not be done. |
| Conclusion, Level B | Probably effective, ineffective, or harmful for the given condition in the specified population. |
| Recommendation: | It must be considered or must not be considered. |
| Conclusion, Level C | Possibly effective, ineffective, or harmful for the given condition in the specified population. |
| Recommendation: | It could be considered or should not be considered. |
| Conclusion, Level U | Data is insufficient or inadequate given current knowledge, treatment is unproven |
| Recommendation: | Should not be performed |

Seizure

ES: epileptic seizure
GS: generalized seizure
GTCS: generalized tonic-clonic seizure
FS: focal seizure
FIAS: focal impaired awareness seizures (or disconnection from medium)
FAS: focal aware seizure/simple partial seizure
FBTCS: focal to bilateral tonic-clonic seizure
SE: status epilepticus
FeS: febrile seizure

Electrolytes and neurotransmitters

Ca++: calcium
Cl−: chlorine
K+: potassium
Mg++: magnesium
Na+: sodium
GABA: gamma-aminobutyric acid
NMDA: N-methyl-D-aspartate
AMPA: a-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

In all of the CGs of the Priority Epilepsy Program (PPE), the abbreviations we published are the same as the book “Epilepsia” by authors Rubio, Reséndiz, Alonso, and Sentíes, by the editorial Alfil in 2016, page numbers IX, X y XI; ISBN 978-607-741-168-0.

Glossary and Abbreviations

Channelopathies

SCN4A, SCN2A, SCN1B
KCNA1, KCNQ2, KCNQ3
CACNA1A
CHRNA4, CHRNB2
GLRA1
GABRG2

Ion: NA: sodium; K: potassium; CA: calcium; CH: acetylcholine; GL: glycine; GABA: gamma-aminobutyric acid
Channel or receptor: CN: channel; R: receptor; N: nicotinic
Subunit: A: α; B: β; Q: M; G: γ

No part of this publication may be reproduced or photocopying without the prior written permission of the publisher. © Permanyer 2019
Neurologic structures
BBB: blood–brain barrier
CSF: cerebrospinal fluid
CNS: central nervous system

Diagnostic tests
fMRI: functional magnetic resonance imaging
MRI: magnetic resonance imaging
PET: positron emission tomography
SPECT: single-photon emission computed tomography
CT: computed tomography scan
ECoG: electrocorticography/intracranial electroencephalography
EEG: electroencephalogram
MEG: magnetoelectroencephalogram
Video-EEG: video electroencephalogram
PSG: polysomnogram
EKG: electrocardiogram
LP: lumbar puncture/spinal tap

Genetics
AD: autosomal dominant
AR: autosomal recessive.
p: short arm of a chromosome
q: long arm of a chromosome
DNA: deoxyribonucleic acid
RNA: ribonucleic acid
NB: newborn/neonate

Organizations
AAN: American Academy of Neurology
AES: American Epilepsy Society
AAP: American Academy of Pediatrics
CAIE: Centros de Atención Integral para la Epilepsia or Comprehensive Care Centers for Epilepsy
FDA: Food and Drug Administration
IBE: International Bureau for Epilepsy
ILAE: International League Against Epilepsy
INNN: Instituto Nacional de Neurología y Neurocirugía or National Institute for Neurology and Neurosurgery.
WHO: World Health Organization
PAHO: Pan American Health Organization
PPE: Programa Prioritario de Epilepsia or Priority Epilepsy Program
SAdE: Sociedad Andaluza de Epilepsia or Andalusian Epilepsy Society

Additional neurological disorders
CVD: cerebrovascular disease
TBI: traumatic brain injury

Drug administration routes
IM: intramuscular
IV: intravenous
PO: oral
S/C: subcutaneous
S/L: sublingual

Syndromes and types of epilepsy
BECTS: benign epilepsy with centrotemporal spikes (Rolandic Epilepsy)
IGE: idiopathic generalized epilepsy
PME: progressive myoclonus epilepsy
JME: juvenile myoclonus epilepsy
MTS: mesial temporal sclerosis
LGS: Lennox-Gastaut syndrome
DRE: difficult to treat seizures/drug-resistant epilepsy

Miscellaneous
AED: antiepileptic drugs/anti-seizure medications
BZD: benzodiazepines

Antiepileptic drugs
ACZ: acetazolamide
ACTH: adrenocorticotropic hormone
NE: barbexaclone
NE: beclamide
CBZ: carbamazepine
CLB: clobazam
CZP: clonazepam
CLP: clorazepate
DZP: diazepam
ESM: ethosuximide
FBM: felbamate
GBP: gabapentin
LTG: lamotrigine
LEV: levetiracetam
LZP: lorazepam
MDL: midazolam
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Name</th>
<th>Abbreviation</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPH</td>
<td>methylphenidate</td>
<td>CBT</td>
<td>carabersat (SB-204269)</td>
</tr>
<tr>
<td>MPB</td>
<td>methylphenobarbital</td>
<td>TBT</td>
<td>tonabersat (SB-220453)</td>
</tr>
<tr>
<td>MSM</td>
<td>mesuximide/methsuximide</td>
<td>SFM</td>
<td>safinamide (PNU-151774E)</td>
</tr>
<tr>
<td>NTZ</td>
<td>nitrazepam</td>
<td>RUF</td>
<td>rufinamide (SGP33101)</td>
</tr>
<tr>
<td>OXC</td>
<td>oxcarbazepine</td>
<td>STL</td>
<td>soretolide (D-2916)</td>
</tr>
<tr>
<td>PAC</td>
<td>phenacemide</td>
<td>TLP</td>
<td>talampanel (GYKI 53773)</td>
</tr>
<tr>
<td>PTR</td>
<td>pheneturide</td>
<td>HUP</td>
<td>huperzine A</td>
</tr>
<tr>
<td>PB</td>
<td>phenobarbital</td>
<td>ATM</td>
<td>atipamezole</td>
</tr>
<tr>
<td>PSM</td>
<td>phensuximide</td>
<td>VLR</td>
<td>valroceamide (TV1901)</td>
</tr>
<tr>
<td>PHT</td>
<td>phenytoin</td>
<td>IVR</td>
<td>isovaleramide</td>
</tr>
<tr>
<td>NE</td>
<td>fosphenytoin</td>
<td>VPG</td>
<td>valproyl glycinamide</td>
</tr>
<tr>
<td>PGB</td>
<td>pregabalin</td>
<td>VLT</td>
<td>valnoctamide</td>
</tr>
<tr>
<td>PRM</td>
<td>primidone</td>
<td>VPD</td>
<td>valpromide</td>
</tr>
<tr>
<td>PRO</td>
<td>progabide</td>
<td>VCD</td>
<td>valroceamide</td>
</tr>
<tr>
<td>STM</td>
<td>sultiam/sulthiame</td>
<td>PID</td>
<td>propylisopropylacetamide</td>
</tr>
<tr>
<td>TGB</td>
<td>tiagabine</td>
<td>LiCBZ</td>
<td>licarbazepine</td>
</tr>
<tr>
<td>TPM</td>
<td>topiramate</td>
<td>EslCBZ</td>
<td>eslicarbazepine (BIA 2-093)</td>
</tr>
<tr>
<td>NE</td>
<td>trimethadione</td>
<td>FI-FBM</td>
<td>fluoroelbamate</td>
</tr>
<tr>
<td>VPA</td>
<td>valproic acid</td>
<td>NA</td>
<td>ganaxolone</td>
</tr>
<tr>
<td>VGB</td>
<td>vigabatrin</td>
<td>carisbamate</td>
<td>carisbamate (RWJ-333369)</td>
</tr>
<tr>
<td>ZNS</td>
<td>zonisamide</td>
<td>perampanel</td>
<td></td>
</tr>
<tr>
<td>NE</td>
<td>4-amino-3-hydroxibutiric Acid</td>
<td>ELB-139</td>
<td></td>
</tr>
<tr>
<td>FLN</td>
<td>flunarizine</td>
<td>JZP-4</td>
<td></td>
</tr>
<tr>
<td>LSG</td>
<td>losigamone</td>
<td>NS-1209</td>
<td></td>
</tr>
<tr>
<td>RLT</td>
<td>ralitoline (Cl-946)</td>
<td>CGX-1007</td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td>remacemide</td>
<td>SPD-421</td>
<td></td>
</tr>
<tr>
<td>STP</td>
<td>stiripentol</td>
<td>ICA27243</td>
<td></td>
</tr>
<tr>
<td>HRK</td>
<td>harkoseride</td>
<td>T2000</td>
<td></td>
</tr>
<tr>
<td>LCM</td>
<td>lacosamide</td>
<td>XP-13512*</td>
<td></td>
</tr>
<tr>
<td>RET</td>
<td>retigabine (D-23129)</td>
<td>YKP3089</td>
<td></td>
</tr>
<tr>
<td>BRV</td>
<td>brivaracetam</td>
<td>NE: not established</td>
<td></td>
</tr>
<tr>
<td>STM</td>
<td>seletracetam (ucb 44212)</td>
<td>NA: not applicable</td>
<td></td>
</tr>
</tbody>
</table>
Centers of integral care for epilepsy “CAIE” in Mexico

www.epilepsiamexico.gob.mx

No part of this publication may be reproduced or photocopying without the prior written permission of the publisher. © Permanyer 2019
Thanks to Jetzabel Fragoso and Dr. Francisco López for their support in all the activities of the Priority Epilepsy Program.