Assessment of Side Effects of Most Commonly used Antiepileptic Drugs in Pediatrics

Thesis

Submitted for Partial Fulfilment
of Master Degree in ***Pediatrics***

By

Wafaa Lotfy Soliman Mohammed
M.B.B.Ch.,
Faculty of Medicine, Ain Shams University (2014)

Under Supervision of

Prof. Iman Ali Elagouza
Professor of Pediatrics
Faculty of Medicine, Ain Shams University

Prof. Dr. Maha Mohamed El Gaafary
Professor of Community Medicine and Public Health
Faculty of Medicine, Ain Shams University

Dr. Maha Zakariya Ramadan Mohammed
Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

Faculty of Medicine - Ain Shams University
2020

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to ***Allah*** *the Most Beneficent and Merciful.*

I wish to express my deepest thanks, gratitude and appreciation to ***Prof. Iman Ali Elagouza****, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance, valuable instructions and generous help.*

Special thanks are due to ***Prof. Dr. Maha Mohamed El Gaafary****, Professor of Community Medicine and Public Health, Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, for her sincere efforts, fruitful encouragement.*

I am deeply thankful to ***Dr. Maha Zakariya Ramadan Mohammed****, Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her great help, outstanding support, active participation and guidance.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Wafaa Lotfy Soliman Mohammed

List of Contents

List of Tables

List of Tables cont...

List of Tables cont...

List of Tables cont...

List of Tables cont...

List of Figures

List of Abbreviations

Abb.	Full term
AEDs	*Anti epileptic drugs*
BAEs	*Behavioral adverse effects*
CBZ	*Carbamazepine*
CLB	*Clobazam*
CZP	*Clonazepam*
ESL	*Eslicabazine*
ETS	*Ethosuximide*
FBM	*Flbamate*
FS	*Focal seizure*
GIT	*Gastro-intestinal tract*
GPT	*Gabapentin*
GTCS	*Genaralized tonic clonic seizure*
GVG	*Vigabatrin*
LCS	*Lacosamide*
LEV	*Levetiracetam*
LGS	*Lennox gastaut syndrome*
LTG	*Lamotrigine*
OXC	*Oxcarbazepine*
PB	*Phenobarbital*
PER	*Perampanel*
PGB	*Pregabalin*
PHT	*Phenytion*
RTG	*Retigabine*
RUF	*Rufinamid*

List of Abbreviations cont...

Abb.	Full term

SJS .....*Steven johnessen syndrome*

STM .....*Sulthiame*

STP .....*Stiripentol*

TEN .....*Toxic epidermal necrolysis*

TGB .....*Tiagabine*

TPM .....*Topiramate*

VPA .....*Valproic acid*

ZNS .....*Zonisamide*

INTRODUCTION

Epilepsy is the most common serious neurological disorder worldwide. It affects all age groups and crosses all geographic boundaries; although this distressing condition remits in some people, many will have epilepsy throughout their lives, About 50 million people worldwide have epilepsy, and nearly 90% of epilepsy occurs in developing countries mainly due to poor medical services ***(Ba-Diop et al., 2014).***

In Egypt, the prevalence was 6.98 / 1000; it became clearer that people with epilepsy are socially discriminated against on the ground of wide-spread lack of knowledge, negative public attitudes, and misconceptions about the disease ***(El-Tallawy et al., 2012)***. The social problems met by students with epilepsy as a result of negative attitudes and beliefs are enormous and the attitude and knowledge of teachers on adulthood epilepsy where that is likely to influence the educational performance of students with the disease ***(Al-Hashemi et al., 2016).***

Antiepileptic drugs (AEDs) have both negative and positive effects on cognition and behavior. AEDs are able to improve cognition and behavior, which has been attributed to reduction of seizure activity, and modulating effect on neurotransmitters and their psychotrophic effect. AEDs reduce neuronal irritability and increase postsynaptic inhibition or alter synchronization of neural networks to decrease excessive

neuronal excitability associated with seizure development and secondary spread of epileptic activity to the surrounding normal brain ***(Meador et al., 2005)***. However, excessive reduction of neuronal excitability may result in slowed motor and psychomotor speeds, and poor attention and memory processing, which are common side effects of sodium channel blockade and increasing GABAergic inhibitory activity, It is not surprising that patients with epilepsy are more susceptible to the adverse behavioral effects of AEDs than other populations, possibly due to the disease associated structural or functional changes that increase their risk of psychiatric disorders ***(Beltramini et al., 2015).***

The primary goals of AED treatment are to achieve complete seizure freedom, ideally without adverse events, reduce morbidity, mortality, and seizure-related accidents, and improve quality of life ***(Lee et al., 2014).*** In two-thirds of the patients with epilepsy these goals are feasible with optimum AED therapy ***(Luciano and Shorvon, 2007).***

Adverse effects of AEDs are common and result in treatment discontinuation in up to 25 % of patients. The profile of adverse effects varies greatly among AEDs and markedly affects drug selection for individual patients. The most common adverse effects like cognitive impairment, coordination difficulties, and other CNS-related adverse effects are predictable, dose dependent, and reversible. They are of particular concern in patients who work or study. Idiosyncratic

adverse reactions are unexpected events that cannot be explained by known mechanisms of action. Typically, they are not related to dose and they are associated with high risk of morbidity or even mortality. Some of them, like weight gain, can negatively affect treatment adherence ***(Perruca and Gilliam, 2012).***

The incidence of adverse effects is an important issue when prescribing AEDs, as some of the most effective medications for seizures are associated with a considerable degree of toxicity. Studies indicate that drug tolerability is a significant limiting factor in treatment maintenance, and drug retention rates are often determined by side-effect profiles ***(Bootsma et al., 2009).***