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Reduction of retinal nerve fiber layer thickness in vigabatrin-exposed patients: A meta-analysis



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ABSTRACT

Objective: Vigabatrin (VGB) is currently served as an effective adjunctive therapy for patients with partial epilepsy worldwide. In this study, meta-analysis was conducted to comprehensively evaluate the changes in peripapillary retinal nerve fiber layer (RNFL) thickness assessed by optical coherence tomography (OCT) in epilepsy patients who were treated by VGB.

Material and methods: Publications on PubMed, Wiley Online Library and the Elsevier Science databases were searched by September 2016. The statistical analysis was performed by RevMan 5.3 software.

Results: Four studies were identified, and 202 eyes in VGB-exposed patients (VGB group) as well as 162 eyes in patients who never received VGB treatment (NON-VGB group) were included. The studies demonstrated that the total RNFL thickness is attenuated in VGB treated patients (weighted mean differences in μ m, WMD = -15.96, 95% CI: -23.69 to -8.23, P < 0.0001). RNFL thickness in 3 quadrants were significantly reduced in VGB group: superior (WMD = -18.15, 95% CI: -23.31 to -12.98, P < 0.00001), inferior (WMD = -23.19, 95% CI: -32.23 to -14.15, P < 0.00001) and nasal (WMD = -19.29, 95% CI: -35.57 to -3.02, P = 0.02). However, the temporal RNFL thickness in these two groups showed no significant difference: temporal (WMD = -2.41, 95% CI: -6.67 to 1.85, P = 0.27).

Conclusion: Based on the meta-analysis, RNFL thickness appears to reduce in epilepsy patients who received VGB treatment, and OCT could be a useful tool to help clinicians assessing its retinal toxicity and guiding its dosage.

1. Introduction

Epilepsy is considered as a group of neurological diseases, and characterized by epileptic seizures[1]. The prevalence of this disease is 0.5–1%, with an overall rate of complete seizure controlled by drug treatment in 40–50% of epileptic patients[2]. Vigabatrin (VGB), an inhibitor of γ -aminobutyric (GABA) transaminase, is currently served as an effective adjunctive therapy for epilepsy patients with partial onset seizures [3–5] and as a monotherapy for infantile spasm [6,7].Unfortunately, asymptomatic visual field defects were recognized as side effects caused by treatment of VGB, and many studies have shown that VGB can cause toxicity to eye in terms of visual field constrictions [8–11]. The incidence of visual field defects in patients treated with VGB is higher than 30%[12], thus damage to vision became a vital safety concern with the use of VGB, and for those patients who were taking this drug, periodic vision tests are required [13].

Optical coherence tomography (OCT) nowadays has been wi dely applied as a technique to show the cross-sectional images of the internal retinal structure. Since it is non-invasive[14], it can be used to observe and measure the thickness of peripapillary retinal nerve fiber layer (RNFL) easily and safely[15]. Recently, an increasing number of studies were found to focus on the RNFL thickness change caused by the toxicity of VGB to the eye [16–20]. Thus, other than vision field, OCT could be used as a helpful tool to evaluate the toxicity to the eye caused by VGB in epilepsy patients.

The intent of this study is to provide a comprehensive meta-analysis overview of the available results offered by the OCT technique. And by analyzing the RNFL thickness change after VGB treatment in epilepsy patients, we can evaluate the toxicity of this drug through the morphological change of the retina.

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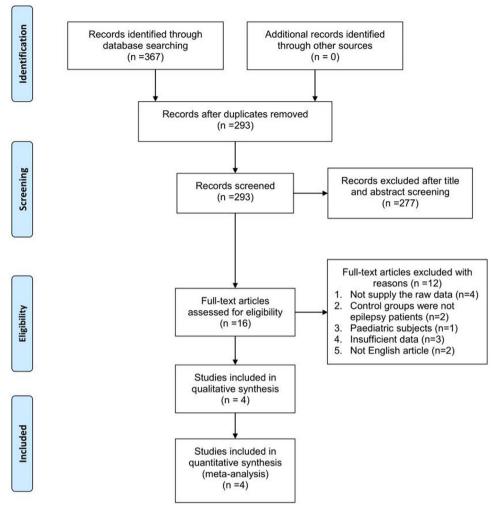


Fig. 1. Flowchart of study selection.

Table 1Characteristics of the included studies in the Meta-analysis.

Reference	Year	Area	OCT model	Еу	ves (No.)	Age (Years)		Gender (F/M)		NOS Score
				VGB	NON-VGB	VGB	NON-VGB	VGB	NON-VGB	
Lawthom	2009	UK	Carl Zeiss Meditec	27	13	39.6 ± 14.1	47.7 ± 14.2	20/7	9/4	7
Akcakaya	2010	Turkey	Carl Zeiss Meditec	28	24	38.6 ± 14.3	33.5 ± 16.28	10/4	16/8	8
Moseng	2011	Norway	Carl Zeiss Meditec	18	14	54.3 ± 9.5	48.1 ± 9.3	4/5	3/4	7
Clayton	2012	UK	Carl Zeiss Meditec	129	87	45.9 ± 11.4	36.4 ± 11.4	64/65	52/35	6

 $VGB = Vigabatrin-treated\ group;\ NON-VGB = Non-Vigabatrin-treated\ group;\ OCT = Optical\ Coherence\ Tomography;\ UK = United\ Kingdom;\ NOS = Newcastle-Ottawa\ Scale.$

	VGB			NON-VGB			Mean Difference		Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Akçakaya 2010	87.23	15.29	28	101.545	14.5	48	24.7%	-14.31 [-21.31, -7.32]	-		
Clayton 2012	78.9	12.4	129	88.8	10.9	87	29.5%	-9.90 [-13.03, -6.77]	*		
Lawthom 2009	80.06	16.98	27	93.2	11	13	22.2%	-13.14 [-21.90, -4.38]			
Moseng 2011	75.6	12.7	18	103.5	9.7	14	23.6%	-27.90 [-35.66, -20.14]	-		
Total (95% CI)			202			162	100.0%	-15.96 [-23.69, -8.23]	•		
Heterogeneity: Tau ² = 50.13; Chi ² = 18.01, df = 3 (P = 0.0004); I ² = 83%											
Test for overall effect: Z = 4.05 (P < 0.0001) VGB NON-VGB											

Fig. 2. Forest plots of weighted mean difference (WMD) in VGB group and NON-VGB group for total RNFL thickness. Horizontal lines are 95% confidence intervals.

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