

# Pharmacological review of vigabatrin

## Editorial

Gamma-aminobutyric acid (GABA) is the most important inhibitory neurotransmitter in the brain which involves in many neurological diseases: Alzheimer's disease, epilepsy, schizophrenia and some other disorders.<sup>1</sup> It is anabolized by decarboxylation (GAD enzyme) of glutamic acid and catabolized by GABA-aminotranferase (GABA-T enzyme) into glutamic acid and succinic semialdehyde.<sup>2</sup> Then, GABA interacts with its receptors GABA<sub>A,B&C</sub> of which GABA<sub>A</sub> are the most significant in controlling the inhibitory function via chloride channel.<sup>2</sup> Drugs that inhibit GABA-T produce high brain GABA concentrations.<sup>1,2</sup> Vigabatrin is one of the most significantly studied GABA-T inhibitors. It produces about 10-fold increases in brain GABA levels.<sup>2</sup> Vigabatrin acts by selective irreversible inhibition of the enzyme GABA-T without changing other central neurotransmitter systems.<sup>2</sup>

Vigabatrin is well-known experimentally anti-convulsant agent for various models of convulsion and clinically potent anti-epileptic drug.<sup>3</sup> During 1990s, vigabatrin was progressively used in treatment of epilepsy in patients with resistance to anti-epileptic drugs.<sup>4</sup> It reduces seizures by more than 50% in children with Lennox-Gastaut syndrome who could not be controlled by valproate.<sup>5</sup> In the beginning of 2000, vigabatrin was used as an adjunctive therapy with other anti-epileptics in patients who are resistant to complex partial epilepsy, secondary generalized epilepsy and infantile spasms. Thereafter, FDA approved vigabatrin as monotherapy for pediatric patients with infantile spasms for whom the potential benefits outweigh the potential risk of vision loss and as an adjunctive (add-on) therapy for adult patients with refractory complex partial seizures. Recently, age was found to have no impact on vigabatrin effects once dosage was adjusted to body weight differences.<sup>6</sup> The anticonvulsant efficacy of vigabatrin for infantile spasms and for adjunctive use in the treatment of refractory complex partial epilepsy was considered but better response in partial seizures than in generalized seizures was obtained. Vigabatrin has a reliable anticonvulsant effect in patients with chronic drug-resistant epilepsy, especially patients with severe epilepsy and a history of psychosis.<sup>7</sup> Few patients suffer from headache, vertigo, confusion, depression, memory and speech disorders, aggression, vision abnormalities and insomnia.<sup>8</sup> The most common side effects are sedation, psychotic reactions and weight gain on chronic administration without showing microvacuoles.<sup>9</sup> Use of vigabatrin is limited by a high risk of retinopathy and peripheral visual field deficiencies.<sup>7</sup> Teratogenicity, use of vigabatrin in pregnant women with epilepsy produces congenital malformations. This was experimentally confirmed in rabbits, thus, low doses produce cleft palate and higher doses produce more profound effects in pups. No survive offspring's were found in rats. In pregnant mice, the high dose was lethal to all mice but the low dose did not produce maternal toxicity. Others, such as growth retardation, mandibular and maxillary hypoplasia were noted in the malformed pups. This may due to generate cortical and hippocampal abnormalities linked to cell migration defects.<sup>10</sup>

Behaviorally, low dose of vigabatrin produces an anxiolytic-like effect without any addiction aspect seen upon chronic intake.<sup>11</sup> Thus, vigabatrin protects against both tolerance and dependence

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development upon chronic diazepam intake.<sup>12</sup> It also reduces ethanol voluntary intake but it enhances both water and food intake.<sup>13</sup> This may be due to vigabatrin potentiates the effects of ethanol. Indeed, two-fold increase in brain GABA-T activity after ethanol acutely and chronically use in rats was found.<sup>14</sup> Further to this, no evidence was recently and clinically given for the use of vigabatrin in treatment of patients with cocaine dependence.<sup>15</sup>

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## Conflict of interest

Author declares that there is no conflict of interest.

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