EFFECT OF VIGABATRIN ON CENTRAL NERVOUS SYSTEM OF ALBINO RATS

Thesis submitted to HIHT University

for award of

DOCTOR OF MEDICINE
IN
ANATOMY

2011

HIHT UNIVERSITY
SWAMI RAM NAGAR
DEHRADUN
UTTARAKHAND

Dr. DEEPA SINGH

CONTENTS

Conclusion and Summary

CONCLUSION AND SUMMARY

Vigabatrin is an antiepileptic drug that has demonstrated significant efficacy as adjunctive therapy for patients with poorly controlled partial epilepsy, refractory to other antiepileptic drugs. It is the drug of choice for infantile spasms.

In the present study, Vigabatrin was administered to albino rats in mild, moderate and high doses. Vacuolation was a significant finding in all treated groups and in all regions of the central nervous system that were studied, with severity increasing with increasing doses. IME secondary to elevated levels of GABA may underlie the pathogenesis. Demyelination was found at a few selected sites suggesting that different parts of the brain have different affinity for this feature after treatment with Vigabatrin. In the cerebellum and retina, significant degenerative and atrophic changes were seen even in mild dose treated group. Focal neuronal and neuroglial loss was mainly evident in these two parts suggesting that they are the main targets of toxic damage by Vigabatrin. Congested blood vessels and dilated perivascular spaces, found in all regions under study, were signs of edema. The involvement of retina explains the high incidence of visual field defects associated with the use of this drug. Present study has also demonstrated histopathological involvement

of the cerebellum which suggests that further extended studies should be done and should be correlated with the cerebellar functions.

Previous studies show that Vigabatrin's neuropathology is confined to the brain. Intramyelinic edema has not been found in the spinal cord and other remaining parts of the central nervous system (36, 40, 53). Keeping in view the results of the previous studies and considering the limited resources and time constraints, we have limited our study to only a few areas in the brain where histopathological changes were expected like cerebellum, retina, optic nerve, optic chiasma, cerebral cortex, internal capsule with basal nuclei, columns of the fornix and hippocampus. However, studies are going on in other areas of the central nervous system like spinal cord and brainstem, which can be future research prospects.

Although Vigabatrin is well tolerated and has the most favourable improvement rates in epilepsy as compared with other newer AEDs, it is associated with a risk of developing visual field defects and IME. Therefore, its use should be limited to patients who have failed treatment with other available AEDs, who have poor quality of life due to frequent complex partial seizures and who are not appropriate candidates for other therapies such as epilepsy surgery. Patients must have a baseline visual field examination before starting treatment. Vigabatrin should not be used in those with restricted visual fields at

baseline. VGB-treated adults and infants should have a follow-up visual field examination every 6 months. Tests for assessing cerebellar function should be done at the beginning of treatment and thereafter at regular intervals as this can help in determining the onset of toxicity. Early assessment of efficacy and ongoing evaluation of the benefits and risks of Vigabatrin therapy should be done. The potential for seizure reduction must be weighed against safety risks.

A cautious strategy of targeted patient selection and careful monitoring for visual field defects and cerebellar functions should optimize the risk-benefit ratio of Vigabatrin in the clinical setting.