Original Research Paper

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Histopathological changes induced by Desvenlafaxine in cerebral cortex of Swiss albino mice.

Anatomy

KEYWORDS:

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ABSTRACT

Introduction. As a dual reuptake inhibitor of serotonin and nor-adrenaline, Desvenlafaxine is designated as newer antidepressant drug used for treatment of various depressive disorders.

Methods. Swiss albino mice were given Desvenlafaxine in the dose of 80mg per kg body wt for first 6 days of gestation (group 2) and from gestation days 1-18(group 3).controls were treated with equivalent amount of tap water respectively(Group 1).

Result. Cerebral cortex of group 2, showed mild alteration in the laminar pattern of frontal cortex. Group 3 cortex, showed marked oedematous space with cellular necrosis.

Conclusion. Above changes suggest probable role of desvenlafaxine in causing oxidative damage to frontal cortex of swiss albino mice.

INTRODUCTION

Desvenlafaxine succinate is chemically bicyclic phenylethylamine compound known to act by reuptake inhibition of serotonin and nor-epinephrine. It also causes week interaction with dopamine transporter[1]. In contrast to other antidepressants like selective serotonin reuptake inhibitors (SSRI) it showed modulatory effect on nerve terminals and neuronal plasticity[2].In vitro studies suggest that it is more potent for blockade of norepinephrine transporter and succinate salt was added to enhance its bioavailability[2]. It is treatment of choice for the various depressive disorders like major depressive disorder, panic disorder, social anxiety disorder etc[3].Although it has different mode of action & lesser side effects than the typical antidepressant it has been put under pregnancy category "C",due to lack of studies showing its safety in pregnant female[4]. Being a neurotropic drug which is rampantly used even in pregnancy there is a need of this study. So this study was undertaken to study effect of desvenlafaxine on fetal brain tissue.

MATERIAL AND METHODS.

The following study was undertaken in Department of Anatomy, Institute of Medical Sciences,BHU Varanasi after getting the institutional ethical committee clearance. Adult female Swiss albino mice were chosen for the study. After keeping the animals in plastic polypropylene cages at a room temperature of 25^0c and relative humidity around 50-60%, the mice were subjected to the experiment. The mice had adequate access to the pelleted diet and tap water. Female and male mice were kept for mating in the evening and the following morning females were examined for the presence of vaginal plugs which will indicate about positive pregnancy status of the female mice. The pregnant female mice were given drug in the dose of 80mg/kg body wt from day 1-6(group 2) and day 1-18 of gestation (group 3).The control female mice(group 1) received equivalent amount of tap water for the corresponding period via oral route. All the following group animals were reared and fetuses were delivered by uterotomy under deep ether anaesthesia. The fetuses were fixed in neutral formalin and brains were removed afterwards for the study. The fixed brain tissue were processed, sectioned and stained with haematoxylin and eosin to study effect of desvenlafaxine on microanatomy of the fetal brain.

RESULT.

Desvenlafaxine does not produce frank gross external abnormalities but the histological examination of treated group showed distortion in normal laminar pattern of cerebral cortex.

Cerebrum of the Group 2(Fig A)showed slight changes in comparison to Group 1(control Fig B)whereas significant changes were observed in group 3 in the form of enlarged trabecular edematous spaces giving it spongiform appearance.(Fig C).The enlarged spaces caused neuronal cell compression with aggregation of plenty of pyknotic or degenerated cells and nuclei. Hyalinization was seen in plexiform layer. In control group the different layer of cerebral cortex were well discernible, but in Group 3(treated group) all the different layers of cortex are intermixed and no details of cells were observed. The intercellular matrix was highly compressed and hyalinised due to plexiform edematous spaces. Cellular debris was wide spread. All these features indicate severe neuronal degeneration.

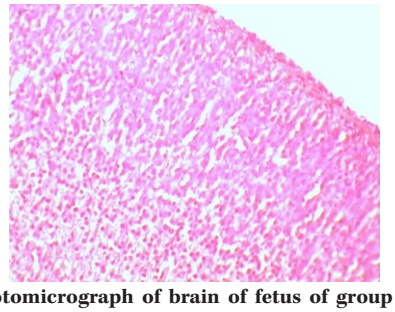

Fig. A Photomicrograph of brain of fetus of group 1(control H&Ex400)

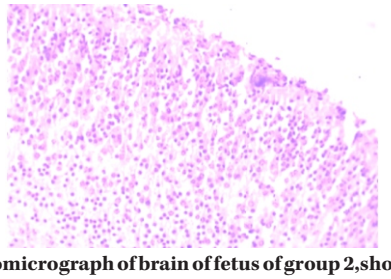

Fig B Photomicrograph of brain of fetus of group 2,showing mild alteration in the laminar pattern of frontal cortex(H&Ex400).

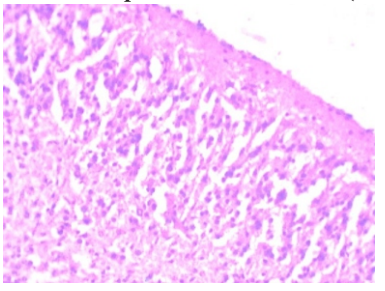

Fig C Photomicrograph of brain of fetus of group 3, showing marked edematous spaces (arrow head) with cellular necrosis (*), thus giving it spongiform appearance (H&Ex400)

DISCUSSION.

Depression is emerging as major epidemic in female of reproductive age group due to modern lifestyle and stress. A major number of

females not only experience depression in pregnancy but also in post-partum period as postpartum blues, so treatment is a must. Desvenlafaxine has been labelled as novel and relatively safer drug than other antidepressants but well controlled studies regarding its safety is missing. In our study, we observed histological changes in cerebral cortex as spongiform degeneration, hyalinization of layers, pyknotic nuclei etc. This can be explained on the basis of fact that this drug by inhibiting reuptake of serotonin & nor-epinephrine in synapse as well as in mice cortical and hypothalamic level causes decrease neuronal firing of their receptors. Activation of inhibitory cell body receptor helps in potentiating this action. The metabolism of desvenlafaxine in humans was similar to mice, rats and dog. O-glucuronidation is the major pathway while minor pathway involves N-methylation, hydroxylation and formation of N—oxide6. The uninhibited accumulation of these unconjugated products leads to oxidative and radical cell injury leading to tissue damage. Our study coincides with the other study in which authors say, acute administration of SNRI to rats produce modest increase in extracellular level of both 5HT and noradrenalin in forebrain sites7.

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