An overview of Teratogenic effects of venlafaxine

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Abstract: Antidepressant therapy of venlafaxine in humans believed to be associated with its inhibitory activity of 5-HT and NE re-uptake. Venlafaxine also targeted to the dopamine re-uptake recognized as a significant advance in the treatment of depression as well as in generalized anxiety disorder. The other most frequent effects of venlafaxine are tremor, nausea and blurred vision. Abnormal ejaculation or orgasm is some dose related side effects of venlafaxine. In the present paper several teratogenic effects related issues has been reviewed and summarized during pregnancy, breast-feeding and in infants.

Key words: Teratogenic effect, venlafaxine, antidepressant therapy, Oxy-des methyl venlafaxine.


Introduction

Teratogenic effects belong to adverse effects category. It can be defined as the capacity of a drug to cause foetal abnormalities, when administered to the pregnant mother. Placenta not strictly constitutes a barrier and any drug can cross it to a greater or lesser extent. One of the most dynamic system is embryo and in contrast to adults, drug effects are often irreversible. In the present paper an attempt has been made to consider all these effects before prescribe. Because of the teratogenic effect of the “phthalimide” thousands of babies born with “phocomelia” in which limb become seal like. There are three stages in which drugs can affect foetus. First one is Fertilization and implantation: Conception of 17 days failure of pregnancy, which often goes unnoticed. Second is Organ genesis: 18-55 days of gestation, most vulnerable period, and deformalities are produced. Third Growth and development: 56 days onwards, development and functional abnormalities can occur. List of drugs is very long which cause teratogenic effects in humans and advicely should be avoided during pregnancy. There are no controlled studies in women. According to U.S.FDA drugs should be given only if the potential benefit justifies the potential risk to the foetus1. According to Australian Drug Evaluation Committee (ADEC) drugs which have been taken by only a limited number of pregnant women and women of child bearing age2. Without an increase in frequency of malfunction or other direct or indirect harmful effects on the human foetus have been observed. There is lack of studies in animal and information is also very inadequate. In the present review teratogenic effects during pregnancy and in breastfeeding is covered separately with their literature.

Teratogenic effects during pregnancy: Because of unavailability of human data no report is there to show that venlafaxine increase the rate of major malfunctions. In some exposed neonates adverse serotonergic like effects have been reported. Suggestion about tapering the venlafaxine during third trimester has been given by manufacturer. In the support of that one report is there according to which neonates exposed to venlafaxine or other serotonine and nor-epinephrin re-uptake inhibitors (SNRI) or selective serotonergic re-uptake inhibitors (SSRI) during this time have developed complications. Some were extended to hospitalization, respiratory support and tube feeding. Reported effects are respiratory distress. Cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hyperreflexia, tremor, jitteriness, irritability and constant crying have also been reported. These effects could be due to serotonin syndrome or drug discontinuation syndrome. In case of opposing of rats or rabbits subjected to exposure for 11-12 times more than recommended human daily dose.In Recommended human daily dose there were no malfunctions.Venlafaxine when started during pregnancy and continued until weaving a decrease in weight and increase in stillbirth and death have been showed by pups3.

Teratogenic effects during breastfeeding: In breastfeeding according to Thomson Lactation Rating the
risk is minimal. Venlafaxine is excreted in human breast milk in very low concentration. In nursing infants drug related adverse effects have not been reported. Infants exposed to venlafaxine via breast milk should be monitored closely for agitation, insomnia, poor feeding and failure to thrive. One case report describes that three lactating women treated with venlafaxine and their nursing infants found infant mean serum drug concentration to be 10.2% (5.3-19 range) for the sum of venlafaxine and oxy-des methyl venlafaxine of maternal serum drug concentration. Maternal drug dose was 75-225 mg/day. There was no evidence of adverse effects in infants as reported by mothers. As a result of this case report author suggested not to discourage breastfeeding while treated with serotonin re-uptake antidepressant. Another report shows teratogenic effect study of breastfeeding mothers treating with antidepressant (some mother took venlafaxine at a dose of 162.5 mg/day). Results of this study showed normal weight gain pattern in 6-month old infants exposed to venlafaxine. The mean weight of all infants exposed to antidepressant in the study were 7.26±0.71 kg for girls and 7.93±0.75 kg for boys.

Some human teratogenic drugs with their abnormalities are entitled as:

Methotrexate – anticancer drug shows multiple effects and foetus death. Androgens-cause virilization, esophageal defects, cardiac defects. Iso-tratinoin-cause cranio-facial defect and shows heart and CNS defects. Anti-thyroid drugs-foetal goiter, hypothyroidism. All the results not significantly differ from the normal growth data. Amount of venlafaxine and oxy-desmethyl venlafaxine have been detected in some infant’s blood samples collected at a mean of 7 hrs after normal maternal dosing at steady state. In one infant some amount about 5 mcg/L was detected and in four infants oxy-desmethyl venlafaxine was detected around 3-38 mcg/L.2.5.7.4 was the respective amount of venlafaxine and oxydesmethyl venlafaxine as milk to plasma ratio. No adverse effects have been noted in infants. Venlafaxine and oxy-desmethyl venlafaxine were concentrated in milk with 4:1.3:1 as milk to plasma ratio. In nursing infants no adverse effects have been selected. Total infant exposure was 7.6% of the weight adjusted maternal dose. The active drug levels in breast milk around 7.6% of %adult dose. The active drug metabolite venlafaxine: oxy-desmethyl venlafaxine ratio with plasma was about to 3.06±0.08.

Conclusion:

In a short review it is not possible to justify the literature surrounding the teratogenic effects of venlafaxine. In short it is to say that understanding the teratogenic effects in recent years have increased exponentially as the complexity has been uncovered and also the awareness has been explored. All these information gives significant insight into the understanding of critical role of venlafaxine- a novel antidepressant. This would also make major contribution in the field of clinical pharmacology by highlighting the advantages and teratogenic unwanted effects of venlafaxine. This review has paved the way for development of more selective approach towards teratogenic effects.

References:


