

FATAL VENLAFAXINE AND ESCITALOPRAM TOXICITY

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ABSTRACT

Venlafaxine is a serotonin-norepinephrine reuptake inhibitor (SNRI), used in the treatment of depression. Venlafaxine is associated with high risk of suicidal ideation and complete suicide. A 32 year old female, who was treated with venlafaxine, died following ingestion of large dose of venlafaxine and escitalopram. Cardiotoxicity and neurotoxicity following ingestion of venlafaxine is known, however post-mortem studies are very few in literature. This case highlights the toxicity of venlafaxine and escitalopram with its histopathological findings of tissue and various drug interactions.

Keywords: venlafaxine; escitalopram; suicide; cardiotoxicity; hepatic necrosis

INTRODUCTION

Anti-depressants are associated with suicidal tendencies in adults with two-fold increase in suicidality and aggression in children and adolescents.^[1] Venlafaxine is associated with higher suicidal tendencies compared to citalopram, fluoxetine, and dothiepin.^[2] Suicidal tendencies are common in the first week of starting the drug hence it should be administered cautiously. All of the above mentioned studies are done in abroad and there are few Indian studies that reflect the same prevalence in Indian population.^[3] Cardio and neurotoxicity are the common features following fatal ingestion of venlafaxine and large clinical data are available in literature. Features of fatal dose of venlafaxine on liver, kidney and other organs are not fully available due very less cases subjected to autopsy examination.^[4] Largest ever postmortem study was done on focussing femoral blood concentration of venlafaxine and its various drug interactions.^[4] This case highlights the effects of venlafaxine and escitalopram when consumed in fatal dose and difficulty in toxicology analysis of these least known drugs and the role of forensic experts in reporting adverse drug reactions.

CASE REPORT

A 32 year old female, suffering from depression attempted suicide by consuming 10 tablets of Venlafaxine (37.5 mg) and 10 tablets of Nexito (combination of Clonazepam

and Escitalopram). She was found unconscious at home and was taken to a local hospital where stomach wash was done, later referred to the tertiary care centre where she was declared brought dead. On autopsy, 500 ml of straw coloured fluid was found in the pleural and abdominal cavity. Multiple sub-pleural haemorrhages were found over the lungs and on cut section the lungs were oedematous. Rest all organs were unremarkable. Since quantitative analysis was not available in RFSL, only qualitative test was done. To our surprise after extensive analysis it was reported that viscera showed traces of benzodiazepines rather than the expected anti-depressant drugs. Histopathology of lungs showed intra alveolar oedema and inter alveolar septal oedema. Liver showed sinusoidal congestion with focal necrosis and kidney showed acute tubular necrosis. The final cause of death was opined as combined effects of cerebral oedema, pulmonary oedema and acute tubular necrosis due to benzodiazepine poisoning.

DISCUSSION

Venlafaxine is a serotonin-norepinephrine reuptake inhibitor (SNRI) used as an antidepressant drug. From 1998 to 2000, Venlafaxine has caused death at the rate of 12.7 deaths per million prescriptions compared to other (Selective Serotonin Reuptake Inhibitor) SSRI, in England and Wales. ^[5] Venlafaxine not only has an effect on the central nervous system (CNS) but also on the cardio

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vascular system (CVS) like QRS and QTc prolongation and ventricular fibrillation. Tachycardia and prolonged QTc are mainly dose dependent and are noted following ingestion of large doses. (7) Fatal doses may cause acute Left ventricular failure and myocardial infarction. [8,9] Venlafaxine fatality is associated with severe drug interaction to tricyclic anti depressants and citalopram. [5] Central nervous system toxicity is mainly depressions and seizures. [10] Rhabdomyolysis and myopathy are associated with venlafaxine toxicity in adults. [11] In our case Tab. Nexito (Clonazepam and escitalopram) was co ingested along with venlafaxine. Escitalopram is an SSRI, would have augmented the toxicity of venlafaxine in our case, because both these drugs are proconvulsants. This case typically features serotonin toxicity due to venlafaxine and citalopram; hence death would have been more due to cardiac toxicity. [12] The setback in this case report is an obscure toxicology report, in which venlafaxine and escitalopram was negative but a benzodiazepine derivative was detected. Detection of benzodiazepine derivative was probably due to presence of clonazepam in the Nexito tab, co-ingested along with venlafaxine. Lack of quantitative test is also a major setback in toxicology analysis done in our labs, due to which fatal doses of drug cannot be substantiated. Focussing on the histopathology feature of this case, liver demonstrated focal hepatic necrosis, which is a feature of venlafaxine toxicity. [4] Demonstrating of acute tubular necrosis in venlafaxine toxicity is unknown in the literature. Further autopsy based tissue sampling studies are needed to widen the knowledge of venlafaxine toxicity.

CONCLUSION

There is wide source of literature on venlafaxine toxicity globally but very few or no statistical data regarding venlafaxine toxicity in India. In this case the patient had previous history of suicidal attempts unfortunately both venlafaxine and citalopram was given, which are potent suicide ideation drugs. The grounds on which the patient was put on these drugs, by the treating physician, this in spite of the danger of suicidal attempts is beyond the scope of this paper. However treating physicians should be more cautious in prescribing these drugs in patients with suicidal ideation and attempts. Role of the forensic expert is far more important in retrospectively alerting the physicians on fatality due to such kind of dangerous drug effects, thereby ensuring the cautious use of these drugs.

Conflict of Interest:

Declared none.

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