



Topiramate and risk of cleft lip or cleft palate.

FDA issues a warning about the risk of cleft lip or cleft palate after exposure to topiramate (Topamax® and generics) during early pregnancy.

Data from different sources (preclinical studies, pregnancy registries, case series) reviewed by the USA Food and Drug Administration (FDA) indicate an increased risk of cleft lip and cleft palate in newborns of mothers having received topiramate during their pregnancy. A North American survey found a frequency of cleft lip or palate of 1.4% in children of mothers treated with topiramate during the first trimester of pregnancy. This incidence was higher than the frequency of 0.38 to 0.55% observed in children exposed to other antiepileptic drugs, and of 0.07% in children not exposed to any such drugs. However, the size of the populations examined has not been disclosed, leaving the strength of this statistical association still unclear.

Data previously available in the literature already suggested that topiramate increased the risk of malformations, including cleft lip and palate [1]. In animal experiments, topiramate was shown to be both teratogenic and embryotoxic (craniofacial and skeletal deformities, growth retardation, loss of embryos). However, other antiepileptic drugs are known as well to increase the risk of birth defects, including cleft palate. This definite, though limited risk of cleft lip and palate after foetal exposure to topiramate should be weighed against the benefit of the treatment for the mother, with consideration to available therapeutic alternatives and seizure risk. Alternative antiepileptic treatments may also increase the risk of malformations, which deserves thorough evaluation. Actually, the dangers associated with seizures in pregnant women are generally considered to be more serious than the risk of malformations associated with antiepileptic drugs. Regarding therapeutic uses of topiramate outside the indication of epilepsy (migraine prevention, other unofficial uses), safer treatment alternatives should be generally recommended during pregnancy.

References:

1. Hunt S, Russell A, Smithson WH, Parsons L, Robertson I, Waddell R, Irwin B, Morrison PJ, Morrow J, Craig J. Topiramate in pregnancy: preliminary experience from the UK Epilepsy and Pregnancy Register. *Neurology* 2008 ;71:272-6.

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