



UNIVERSITY OF TORONTO
LESLIE DAN FACULTY OF PHARMACY

TOXICOLOGY GROUP TRAINEE SEMINAR PROGRAM

Wednesday, July 15, 2015, 2:10–3:30 pm

Room 850

Leslie Dan Faculty of Pharmacy

144 College Street

Title: [First Trimester Exposure to Topiramate and the Risk of Oral Clefts in the Offspring: A Systematic Review and Meta-analysis](#)

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Advisory Committee: Dr. B. Kapur, Dr. D. Colantonio, and Dr. L. Dupuis

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ABSTRACT

BACKGROUND: Topiramate (TPM) is an increasingly used drug during childbearing ages for treatment of epilepsy, migraine, and appetite suppression as well as for off-label indications such as sleep and psychiatric disorders. Presently, while there are published reports suggesting increased teratogenic risk, mainly for oral cleft (OC), these studies are balanced by studies that could not confirm such association and the current literature remains controversial. Our objectives were to conduct a systematic review and meta-analysis of all studies reporting on women treated with TPM in the first trimester of pregnancy and to estimate the overall rate of OC.

METHODS: Databases were searched using MEDLINE, EMBASE, and Web of Science from January 1 1996 to 30 October 2014. Studies were selected based on the following criteria: cohort or case-control studies that reported fetal outcome after exposure to any dose of TPM during the first trimester of pregnancy and compared the outcome with that of an unexposed control group. Two independent reviewers extracted and assessed the quality of the articles.

RESULTS: Of the 2327 publications reviewed, 6 papers met the inclusion criteria including 3420 patients and 1,204,981 controls. The meta-analysis of six controlled studies on pregnant women exposed to TPM in the first trimester detected that the rate of OC in this group was statistically increased compared with the unexposed group and that there was no heterogeneity among included studies. The OR of OC after TPM exposure was 6.26 (95% confidence interval: 3.13–12.51; P=0.00001).

CONCLUSIONS: This study provides strong evidence that TPM is associated with an increased risk of OC in infants exposed to TPM during embryogenesis and should lead to a careful review of TPM use in women of reproductive ages.