

optimal management of asthma during pregnancy is important for both mother and baby inhalation therapy with salmeterol may be continued.

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### Tramadol exposure in the first trimester of pregnancy: A case series

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**Introduction:** Tramadol is an opioid-like analgesic used for treatment of acute and chronic moderate to severe pains. It is a synthetic analogue of codeine. During late pregnancy tramadol is transferred over the placenta. Following use in the third trimester the neonate has a risk of the neonatal abstinence syndrome. There is scarce data on the use of tramadol in early pregnancy. In France, one prospective study was performed on 146 exposures to tramadol in the first trimester [1]. They found no increased risk of malformations. Here, in this case series the occurrence of malformations after exposure to tramadol in early pregnancy is described.

**Methods:** We analyzed prospectively collected data from the follow-up database of The Dutch Teratology Information Service (TIS). Health care professionals can consult TIS for the risk assessment of an exposure during pregnancy. Cases were women who were exposed to tramadol in the first trimester of their pregnancy defined as week 0 until week 13.

**Results:** Between 1989 and 2014 a total number of 64 women were included in the Dutch database after exposure to tramadol. Eleven pregnancies were lost to follow-up. In three cases the time of exposure was unclear, and in three cases exposure took place after the first trimester starting around week 20. Forty seven cases with known outcome were available for analysis. Forty three pregnancies were exposed in the first trimester after week 4, twelve of them continued exposure the entire pregnancy. In four cases tramadol was stopped before week 4. The doses used ranged from 50 to 400 mg/day. Pregnancy loss occurred in five cases: four spontaneous abortions and one terminated pregnancy (at eight weeks of pregnancy). Four newborns of the 47 pregnancies had a congenital malformation. Two newborns had a syndactyly (one a syndactyly of toes, exposed from week 0 until week 4; and one a syndactyly of fingers; exposed from week 0 until week 5), one a congenital ovarian cyst (exposed from week 0 until 4+3) and one a hemangioma on the leg (exposed entire pregnancy). No further details were provided on these congenital malformations, but probably only the syndactyly of the hand can be classified as a major malformation according to the EUROCAT guidelines. One newborn died after caesarean section at 34 weeks of pregnancy, probably caused by an intra-uterine infection. No congenital malformations were seen in this case. Exposure in this pregnancy was from week 0 until week 13.

**Conclusion:** One major congenital malformation (syndactyly of the hand) was seen in this case series of 47 live born babies exposed to tramadol in the first trimester of pregnancy. Although there were two cases of syndactyly, causal relation is not plausible. In both cases there was no exposure of tramadol after week 5, while separation of the digits starts in week 9 (7th embryonic week).

### Reference

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### Ultrastructural observations of adult and breastfeeding Balb/C mice lung tissues after exposure to airborne pollutants at heavy traffic sites (poster)

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**Introduction:** Air pollution has become a major threat to public health, with the problem being more urgent in urban areas. The particulate matter (PM) of the ambient air has been associated with an increase on the mortality and morbidity of respiratory diseases [1,2]. Many epidemiological studies have demonstrated association between fine particles, lung cancer and different cardiopulmonary diseases [3]. This study aims to investigate the effects of the PM on lungs of adults and neonate breastfeeding mice, exposed at the center of Thessaloniki, a Northern Creek heavy traffic city.

**Methods:** 30 adult female 12-week-old Balb/c mice were obtained from our Laboratory Animal Center. Animal procedures were carried out in accordance with Directive 2010/63/EU for animal experiments. The two adult experimental groups consisted of 10 treated mice and 5 control. For the breastfeeding experimental groups neonates were obtained from 10 pregnant treated and 5 control mice. All animals were placed in the Municipality's of Thessaloniki Air Quality Monitoring Station, located at the city center, where the treated groups were exposed to atmospheric air and the control groups to filtered air. Exposure of groups was within winter period. During exposure, animals had access to food and water *ad libitum*. 30 days after exposure, adults and neonates were sacrificed using a lethal dose of ether. Lung tissue samples from all groups were collected and processed for Transmission Electron Microscope observations.

**Results:** The ultrastructural study of lung tissues, taken from exposed adult animals, revealed intra-alveolar hemorrhage and infiltrated inflammatory cells such as neutrophilic leukocytes and reactive macrophages and type II alveolar cells, with irregular shape of nuclei and reduced number of lamellar bodies. The ultrastructural study of lung tissues from exposed neonatal breastfeeding animals also revealed lymphocytes' infiltration of the interstitial pulmonary tissue while sparse type II pneumocytes also presented degenerative alterations. In control animal groups, the ultrastructural appearance of lung tissues were quite normal.

**Conclusions:** The results of our study suggest that the particulate matters exposure, can cause degenerative and inflammatory alterations on adult and neonatal breastfeeding mice lungs.