Exposure to potentially teratogenic drugs in pregnancy and perinatal outcomes: observational study on deliveries occurred in Emilia Romagna region between 2009 and 2011

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Background. External causes are responsible for 10% of congenital defects and, out of these, drugs represent about 1%. Since a large part of women take drugs during pregnancy, the specific gestational period (and even childbearing age), the dosage and the clinical condition of the women should be carefully considered before prescribing any potentially teratogenic substance.
Objective. The purpose of this study was to analyse the exposure to potentially teratogenic drugs during pregnancy in Emilia Romagna region between 2009 and 2011. Moreover, this study aimed to estimate the rate of some specific adverse perinatal outcomes and their differences between women exposed and not-exposed to potentially teratogenic substances.
Methods. The delivery (CeDAP) and prescription (AFT and FED) databases of Emilia Romagna region (about 4,400,000 of inhabitants) were searched to detect all deliveries occurred between January 2009 and December 2011 and their exposure to substances categorized as D and X by FDA (i.e. drugs with a potential embryo-foetal risks). Delivery date represented the index date of the study and 12 months pre-index date were analysed by dividing this time-window in preconception trimester and in 3 trimesters of pregnancy. Drug exposure was categorised accordingly. The following adverse perinatal outcomes were considered: Apgar index < 7, gestational age < 37 weeks, birth weight < 2,500 g, stillbirth and operative delivery. The rates of each outcome were estimated both for births exposed to D/X drugs and those not exposed. Differences between these two groups were analysed by the chi-square test ($p<0.05$). Analyses were performed for the whole period and for each trimester.
Results. Between 2009 and 2011, 111,284 deliveries occurred in Emilia Romagna; 11.1% of these were exposed during pregnancy to D and X drugs. Within D category, the most prescribed drug classes were NSAIDs, corticosteroids, antiplatelets and antidepressants; whereas within X category, oral contraceptives (especially during pre-conceptional trimester) and statins were mainly found. Out of 113,117 newborns recorded, 0.9% had an Apgar index <7, 8.2% were born before the 37th week, 6.9% had a birth weight <2,500 grams, 0.25% were stillbirth and 34.0% were born by operative delivery. Newborns exposed during pregnancy to D/X drugs, in comparison with those not exposed, showed a higher rate of all studied adverse perinatal outcomes: low Apgar index (1.3% vs. 0.8 %), preterm deliveries (15.1% vs. 7.3%; $p<0.01$), low birth weight (12.7% vs. 6.1%; $p<0.01$), stillbirth (0.34% vs. 0.23% $p<0.05$) and operative deliveries (45.5% vs. 32.5% $p<0.01$). Similar results were found analysing every single trimester.
Conclusions. The amount of women exposed during pregnancy to a potentially teratogenic therapy was not negligible and a raw analysis of adverse perinatal outcomes suggested possible association to actual adverse effects. Therefore, the choice to use these substances during pregnancy should be carefully evaluated, in order to reduce perinatal adverse outcomes both for newborn and for mothers. To enhance the appropriate use of drugs, health care professionals (physicians and midwives) should inform women about the benefit/risk profile of each therapy administered during pregnancy.

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