NSAIDs and Pregnancy: new elements to prefer paracetamol.

Two studies suggest an increased risk of miscarriage after nonsteroidal anti-inflammatory drugs (NSAID) use during the first trimester of pregnancy. The NSAID exposure during the first trimester of pregnancy could also be related to an increased risk in congenital anomalies (specifically cardiac defects). However, this teratogenic potential remains uncertain. In practice, a benefit/risk evaluation on a case-by-case basis should always be undertaken before prescribing NSAIDs during the first trimester of pregnancy and paracetamol should, whenever possible, be used instead.

A cohort study evaluating the risk factors associated with miscarriages highlighted an increase in the events after the use of NSAID during the first trimester of pregnancy (1' 055 pregnant women identified in a medical care program in the United States, 53 of them had taken NSAID). After adjustment for potential confounders (maternal age, gestity, parity, tobacco, alcohol, fever, diabetes, hypertension, acid folic), the relative risk (RR) for miscarriage was 1,8 (95% confidence interval (IC95%) 1 to 3.2). Statistical association was stronger if the use of AINS lasted more than a week (RR: 8.1; IC95% 2.8 to 23.4) or if the initial NSAID use occurred around the time of conception (RR: 5.6; IC95% 2.3 to 13.7). No association was found after Paracetamol used by 172 women [1]. A Danish case control study also highlighted an increased risk in miscarriage associated with the dispensation of NSAIDS (1599 women who had miscarriage of whom 45 had received a NSAID prescription; controls: 15' 990 women who had a live birth). The association was reinforced when the prescriptions occurred in the week before the date of miscarriage [2].

Four studies looking for a possible teratogen potential after NSAID use in early pregnancy didn't allow a precise evaluation of the risks [3]. A cohort study conducted by the same Danish group didn't highlight any increase in congenital malformations in newborn of mothers having used AINS (RR: 1.0; IC95% 0.8 to 1.7) [4]. A Swedish cohort study including 279'734 pregnancy of whom 2' 557 used NSAID in early pregnancy did not show any increase for any congenital anomaly (RR: 1.0; IC95% 0.8 to 1.3). However, the relative risk for cardiac defects was increased (RR: 1.9; IC95% 1.3 to 2.6) as well as for cleft palate (RR: 2.61; IC95% 1.01 to 6.78; only 6 cases) [5]. A Swedish case control study evaluated the maternal drug use of 5' 015 infant with cardiovascular defect in comparison with 577' 730 controls. The list of the 10 maternal used drugs, which were more often associated with cardiac defect in the newborn contained naproxene [6]. Another case control study conducted in Canada included 93 new-born babies having a congenital malformation who were born from 1' 056 women who received a prescription of NAISD

during the first trimester and 2 ' 478 new-born without anomaly and whom mother didn’t received a prescription of NAIDS. The relative risk for any anomalies was among 2.2 (IC95% 1.7-2.9), and rose to 3.3 (IC95% 1.9-6.0) for anomalies related to cardiac septum defect, and 9.6 (IC95% 3.1-29.6) for anomalies of the respiratory system [7].

At the moment, data are still missing to formally confirm an increased risk of miscarriage associated with the use of NSAIDS during the first trimester of pregnancy or before conception. The results should however be considered as a signal. The possible increased risk in cardiac defects associated to the NAIDS remains difficult to evaluate, as the number of cases observed is too low, and potential confounders couldn’t be excluded. However, while waiting for a confirmation or an invalidation of these results with new observations, a benefit/risk evaluation on a case-by-case basis before prescribing NAIDS to pregnant women in the first trimester of pregnancy is recommended. When an antalgic effect is required, paracetamol should, whenever possible, be used instead. At present, this molecule suffers from no limitation during the three trimesters of pregnancy. Finally, it seems not necessary to worry patients that have accidentally been exposed to NAIDS during the first trimester of pregnancy.

References

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