



## Unborn children still exposed to NSAIDs

● A study based on data from France's mandatory health insurance system estimates that about 5000 to 6000 women per year in France are prescribed nonsteroidal anti-inflammatory drugs from the 6<sup>th</sup> month of pregnancy, excluding self-medication.

The Clermont-Ferrand Regional Pharmacovigilance Centre and Centre for Evaluation and Information on Drug Dependence studied the analgesics prescribed for pregnant women (1). They used the "General Sample of Health Insurance Beneficiaries" (EGB), a database that contains data on prescription drugs dispensed in community pharmacies and then submitted for reimbursement to the French National Health Insurance Fund for Salaried Workers (CNAMTS). They selected women who had given birth to a live baby between 1<sup>st</sup> January 2011 and 30<sup>th</sup> December 2013 (1).

The study population consisted of 221 002 women with an average age of about 30 years (1). About two-thirds (131 535) of these women had received at least one reimbursement for an analgesic during their pregnancy: about 60% for *paracetamol*; 5.6% for a nonsteroidal anti-inflammatory drug (NSAID); 3.8% for a *paracetamol + codeine* fixed-dose combination, *tramadol* or *paracetamol + tramadol*, or *paracetamol + caffeine + opium*; 0.4% for a triptan and 0.06% for a strong opioid (1).

Women who received reimbursement for *aspirin* at the dose used for an antiplatelet effect, an antidepressant or an antiepileptic were excluded (1).

**5000 to 6000 pregnant women per year in France exposed to a prescribed NSAID from the 6<sup>th</sup> month of pregnancy.** During the 3 months before pregnancy, 24% of the women had claimed reimbursement for at least one prescription of *paracetamol*, 4.8% for a weak opioid such as *codeine* or *tramadol*, and 16.5% for an NSAID (1).

0.8% of the pregnant women studied received reimbursement for an NSAID from the 6<sup>th</sup> month of pregnancy. This corresponds to about 5000 to 6000 women per year in France. This is undoubtedly an underestimate of the true levels of exposure, because it excludes self-medication with over-the-counter and sometimes off-the-shelf NSAIDs, such as *ibuprofen* for oral or cutaneous administration, or *urbiprofen* lozenges (1,2). About 4% of the women studied claimed reimbursement for an NSAID during the first trimester of pregnancy.

Given their pharmacological properties, NSAIDs may increase the risk of spontaneous abortion during the first trimester of pregnancy. There are also concerns over a link with congenital heart defects. In the second and third trimesters of pregnancy, NSAIDs, including *aspirin* at anti-inflammatory doses, can provoke sometimes irre-

versible fetal renal failure, premature closure of the ductus arteriosus and persistent pulmonary hypertension of the newborn, even with topical use or brief oral exposure. Cases of necrotising enterocolitis and intracranial and gastrointestinal haemorrhage have been reported in children exposed in utero to certain NSAIDs. NSAIDs can also cause bleeding in the pregnant woman and the unborn child (3-5).

**In practice** This study shows that about 5% of unborn children in France are exposed to prescribed NSAIDs, including about 1% from the 6<sup>th</sup> month of pregnancy.

These percentages could probably be reduced if health authorities communicated and repeated the simpler, much stronger message: "NEVER USE NSAIDs DURING PREGNANCY"

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### Selected references from Prescrire's literature search

- 1- Delorme J et al. "Analgesic drug dispensation patterns before and during pregnancy: a retrospective cohort study in France" 37<sup>th</sup> Pharmacovigilance Meeting [conference], Nancy: 19-21 April 2016. *Fundam Clin Pharmacol* 2016; 30 (suppl.1): 30 (abstract PM1-025) (full version 1 fipage).
- 2- ANSM "RCP-Strefen" 26 June 2016: 6 fipages.
- 3- Prescrire Rédaction "À écarter en cas de grossesse: les anti-inflammatoires non stéroïdiens (AINS)" *Rev Prescrire* 2013; **33** (358): 604-605.
- 4- Prescrire Rédaction "Patientes enceintes souhaitant un antalgique non spécifique" *Rev Prescrire* 2013; **33** (358): 601-607.
- 5- Prescrire Editorial Staff "Six tablets of an NSAID: closure of the ductus arteriosus and emergency caesarean section" *Prescrire Int* 2016; **25** (174): 214.