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Sympathomimetic decongestants during pregnancy: risks for the unborn child

● **In addition to the risk of cardiovascular events and neurological disorders, sympathomimetic decongestants have teratogenic potential, albeit weak, when taken during the first trimester of pregnancy, probably through disruption of the vascular system of the embryo and the pregnant woman. In the second and third trimesters of pregnancy, the fetus is exposed to the same adverse effects as the mother.**

The decongestants that are sometimes proposed as a treatment for ear, nose and throat symptoms are sympathomimetic vasoconstrictors. The main ones are *ephedrine*, *naphazoline*, *oxymetazoline*, *phenylephrine* (*m-synephrine*), *pseudoephedrine* and *tuaminoheptane* (1).

Sympathomimetic decongestants have an unfavourable harm-benefit balance both during and outside of pregnancy: irrespective of the route of administration, their adverse effects are unacceptable for drugs indicated for such minor ailments as the common cold (2). They can provoke serious systemic adverse effects, even with intranasal use: cardiovascular disorders such as hypertensive crisis, stroke and cardiac arrhythmia (tachycardia, angina), and neuropsychiatric disorders (seizures, insomnia, anxiety, etc.) due to their central stimulant effects (1,2).

They pose various specific risks during pregnancy.

First trimester: gastroschisis, intestinal atresia, hemifacial microsomia. Sympathomimetic decongestants are teratogenic in animals. Cardiovascular anomalies were more frequent, especially with *ephedrine*. Impaired fertility appeared more common with *pseudoephedrine* and *oxymetazoline* than in the unexposed control groups (3).

Cohort studies and case-control studies, including nearly 10 000 pregnant women exposed to at least one decongestant during pregnancy, showed an increased risk of malformations related to disruption of the embryo's vascular system (3-7).

Several cohort studies found no increased risk of malformations with *pseudoephedrine*, *ephedrine*, *oxymetazoline* or *phenylephrine* (3-6).

Five case-control studies found an increased risk of certain malformations such as gastroschisis (defective closure of the abdominal wall), intestinal atresia and hemifacial microsomia with *pseudoephedrine* and *oxymetazoline* (3-7). Two case-control studies yielded conflicting results regarding a possible link between first-trimester exposure to *phenylephrine* and cardiovascular defects (3-6).

Our literature search identified no relevant data on *naphazoline* or *tuaminoheptane*.

Second and third trimesters: fetal hypoxia, bradycardia, etc. When decongestants are used during the second and third trimesters of pregnancy and close to birth, the fetus, the neonate and the pregnant woman are exposed to their sympathomimetic effects. The foreseeable effects are reduced uterine and fetal perfusion with impairment of fetal development and fetal hypoxia, and cardiovascular disorders, with elevated maternal blood pressure and fetal and neonatal bradycardia (1,3,6).

In animal studies, growth retardation, preterm birth, acidosis and hypoglycaemia were reported with *pseudoephedrine* at doses equivalent to those used in human therapy (3,4).

Neonatal acidosis and fetal heart rate decelerations have been reported when *ephedrine* was used during labour (3-6). Cyanosis and hypertension occurred in a neonate whose mother had used a nasal spray containing *naphazoline* throughout pregnancy.

In practice. Sympathomimetic decongestants provoke serious, albeit rare, adverse effects, that sometimes leave sequelae. These risks are unjustified given their minimal efficacy.

The risk of malformations associated with their use during the first trimester of pregnancy appears low. It is better to discuss this information with the patient or couple, to help make decisions about monitoring during pregnancy. In the second and third trimesters, the fetus is exposed to the same adverse effects as the mother. These drugs should quite simply never be used, including via the nasal route.

Selected references from Prescrire's literature search.

1- Prescrire Rédaction "Patientes enceintes ayant une infection ORL courante" *Rev Prescrire* 2013; **33** (358): 618-628.

2- Prescrire Rédaction "Sinusite aiguë infectieuse" Premiers Choix Prescrire, January 2015 update: 5 pages.

3- "Reprotox" Micromedex Healthcare Series. www.rightanswerknowledge.com accessed March 2015.

4- "TERIS Teratogen Information System". www.rightanswerknowledge.com accessed March 2015.

5- "Shepard's Catalog of Teratogenic Agents". www.rightanswerknowledge.com accessed March 2015.

6- "Briggs Drugs in Pregnancy and Lactation" Lippincott Williams and Wilkins, Philadelphia 2011.

7- Yau WP et al. "Use of decongestants during pregnancy and the risk of birth defects" *Am J Epidemiol* 2013; **178** (2): 198–208.