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Paternal exposure to immunosuppressive drugs: possible influence on pregnancy outcome and infant’s health, a systematic review

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Introduction: Although there are theoretical concerns about the possible influence on fertility, pregnancy outcome or complications and health of the offspring, preconceptional paternal drug exposure has not been studied significantly. This applies to immunosuppressive drugs like methotrexate and mycophenolic acid. As start of a research project on paternal immunosuppressive drugs and/or autoimmune diseases and their possible influence on fertility, pregnancy outcomes and child health we performed two systematic reviews, one on drugs and one on diseases. Here we give an overview of the pregnancy and infant outcomes of immunosuppressive drugs from the initial search.

Methods: The protocol for this systematic review is written according to the PRISMA-P statement and registered in PROSPERO. A systematic literature search was performed in Embase and MEDLINE. Additional sources included Cochrane Central register of Controlled Trials, Web of Science and Google Scholar. The initial search was done in April 2018. For each database a search profile was developed including keywords regarding male fertility, paternal exposure, pregnancy outcomes and complications and infant’s health. This was combined with immunosuppressive drugs. The literature search was limited to the English language and human subjects. The following type of studies were included: case control studies, cohort studies, cross-sectional studies, case reports and case series. The methodological quality of the studies was assessed with the Newcastle Ottawa Scale.

Results: After deduplication 3720 publications were eligible for title and abstract screening. Full text reading was done for 260 publications, which resulted in inclusion of 41 references on pregnancy and infant related outcomes. Since 2016, 7 population-based cohort studies were published based on the Danish registries, with potential overlap in included pregnancies. The Norwegian registries were used in 2 population-based cohort studies. Other cohort studies used data from Teratology Information Services, the USA National Transplant Pregnancy Registry or hospitals. Case series were mostly based on hospital records. Most studies looked at azathioprine and/or 6-mercaptopurine (n = 8) or methotrexate (n = 5). Other drugs in studies were TNA-alpha blockers, calcineurin inhibitors, mycophenolic acid or colchicine. The most frequently reported outcomes were pregnancy outcome (e.g. miscarriage, live birth), preterm birth (gestational age), low birthweight (birth weight) and congenital abnormalities, in general no major differences between exposed and the comparison group were reported.

Conclusions: Paternal use of immunosuppressive drugs preconceptionally has received more attention in the last years. Preliminary data of the systematic review implies that the reported outcomes after immunosuppressive drug use do not differ significantly from the comparison group. The numbers in the different publications, and also the total number of pregnancies included, are still low. The quality of the publications ranges between high and low.

Gadolinium-based contrast agents in pregnant women

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Introduction: Gadolinium-based contrast agents are commonly used for magnetic resonance imaging. Iodinated contrast media can be classified as either ionic or non-ionic and high-osmolar or low-osmolar. Iohexol which is one of iodinated non-ionic, low-osmolar contrast medium is used for visualization during angiography and