PLEASE NOTE: This trial has been registered retrospectively.

**Trial Description**

**Title**
Effects of NSAID and metamizole exposure in the 1st trimester of pregnancy - An observational cohort study series

**Trial Acronym**
NSAIDs and Metamizol during pregnancy

**URL of the trial**
[---]*

**Brief Summary in Lay Language**
Non-steroidal anti-inflammatory drugs (NSAID) are often used during 1st and 2nd trimester of pregnancy. Primary objectives of this study are risk estimation of major congenital birth defects and miscarriage (spontaneous abortion rate) after exposure to the study medication during 1st trimester. Data analysis will be based on cases which are prospectively ascertained and archived in the pharmacovigilance database of the German Embryotox Pharmacovigilance Centre.

**Brief Summary in Scientific Language**
Due to the high prevalence of pain symptoms, analgesics are commonly used and needed in pregnancy. Paracetamol (acetaminophen) is considered safe in terms of teratogenicity and recommended as the analgesic of choice throughout pregnancy. During 1st and 2nd trimester ibuprofen as a well proven non-steroidal anti-inflammatory drug (NSAID) is another analgesic of first choice. However, various situations and reasons may lead to the use of not sufficiently explored analgesics in pregnancy. Therefore, different NSAIDs, coxibes, acetylsalicylic acid (ASA) and also metamizole may be used intentionally or inadvertently during pregnancy although sufficient data on prenatal risk and safety are still lacking. Therefore, it is urgently needed to improve the risk profile of these analgesics in pregnancy. This would support adequate counselling of pregnant women and their health care providers.

Based on their different action mode the following analgesics will be studied separately: 1) NSAIDs, 2) selective cox inhibitors (coxibes), 3) acetylsalicylic acid (ASA) in analgesic doses (defined as > 300mg/d), 4) metamizole.

Objectives are to estimate the risk of major birth defects and miscarriage (spontaneous abortion) after exposure to the study medication during 1st trimester.

The Institute for Clinical Teratology and Drug Risk Assessment in Pregnancy counsels patients or their physicians about the risk of medication during pregnancy. This counselling mainly takes place in early pregnancy when outcome or prenatal diagnostic is not known. If the pregnant patient agrees, data are recorded by a structured questionnaire. Eight weeks after the estimated date of...
birth a further questionnaire is send to collect data about the pregnancy outcome. Analysis of those prospectively ascertained pregnancies can be used for risk assessment of pathologic pregnancy course including congenital malformations. Both exposed group and control group are recruited from the already collected and archived data.

Organizational Data

- DRKS-ID: DRKS00011140
- Date of Registration in DRKS: 2016/10/11
- Date of Registration in Partner Registry or other Primary Registry: [---]*
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: EA4/029/16, Ethik-Kommission der Charité - Universitätsmedizin Berlin-

Secondary IDs

- ICD10: Q89.9 - Congenital malformation, unspecified
- ICD10: O03 - Spontaneous abortion

Health condition or Problem studied

- ICD10: Q89.9 - Congenital malformation, unspecified
- ICD10: O03 - Spontaneous abortion

Interventions/Observational Groups

- Arm 1: Via questionnaire prospectively ascertained pregnancies with systemic NSAID/metamizole exposure during first trimester [1) NSAIDs, 2) selective cox inhibitors (coxibes), 3) acetylsalicylic acid (ASA) in analgesic doses (defined as > 300mg/d), 4) metamizole]. Exclusion criteria: exposure to a known teratogen or fetotoxicant; maternal malignancies. Data from our institute's patient registry.
- Arm 2: Control group: Via questionnaire prospectively ascertained pregnancies not exposed to a study medication [1) NSAIDs, 2) selective cox inhibitors (coxibes), 3) acetylsalicylic acid (ASA) in analgesic doses (defined as > 300mg/d), 4) metamizole], known teratogens or fetotoxicants; Exclusion criteria: maternal malignancies. Data from our institute's patient registry.

Characteristics

- Study Type: Non-interventional
- Study Type Non-Interventional: Observational study
Study Type: **Non-interventional**
Study Type Non-Interventional: **Observational study**
Allocation: **Non-randomized controlled trial**
- Blinding: [---]*
- Who is blinded: [---]*
- Control: **Other**
- Purpose: **Other**
- Assignment: **Other**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

### Primary Outcome

Is there an increased rate of major birth defects after systemic exposure to the study medication [1) NSAIDs, 2) selective cox inhibitors (coxibes), 3) acetylsalicylic acid (ASA) in analgesic doses (defined as > 300mg/d), 4) metamizole] during 1. trimester of pregnancy?

Is there an increased rate of spontaneous abortion after systemic exposure to the study medication 1)-4) during 1. trimester of pregnancy?

The Institute for Clinical Teratology and Drug Risk Assessment in Pregnancy counsels patients or their physicians about the risk of medication during pregnancy. This counselling mainly takes place in early pregnancy when outcome or prenatal diagnostic is not known. If the pregnant patient agrees, data are recorded by a structured questionnaire. Eight weeks after the estimated date of birth a further questionnaire is send to collect data about the pregnancy outcome.

### Secondary Outcome

Is the risk for preterm delivery or low birthweight increased after systemic exposure to study medication 1)-4) during 1. trimester of pregnancy?

Is there evidence of an exposure time-dependence spontaneous abortion rate during the 1st trimester?

### Countries of recruitment

- DE Germany

### Locations of Recruitment

- University Medical Center **Berlin**
Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2016/05/01**
- Target Sample Size: **8000**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Female**
- Minimum Age: **no minimum age**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Prospectively ascertained pregnancies, i.e. neither the outcome of pregnancy nor results of prenatal diagnostics are primarily known, but are ascertained at a later stage

Exclusion criteria

Exclusion of cases with maternal malignancies or maternal exposure considered as potent teratogens or fetotoxicants: i.e. acenocoumarol, ACE-inhibitors and ARBs (AT1-Antagonists), carbamazepine, lenalidomide, methotrexate, mycophenolate, phenobarbital, phenprocoumon, phenytoin, retinoids (acitretin, adapalen, isotretinoin, tazarotene, tretinoin), thalidomide, topimarat, valproic acid, warfarin.

Addresses

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Sources of Monetary or Material Support

Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)

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Status

Recruitment Status: Recruiting complete, follow-up complete
Study Closing (LPLV): 2017/10/09
## Trial Publications, Results and other documents


* This entry means the parameter is not applicable or has not been set.

*** This entry means that data is not displayed due to insufficient data privacy clearing.