36th ENTIS Conference 11th – 14th Sept 2025
ARISTOTLE UNIVERSITY'S RESEARCH DISSEMINATION CENTER (KEDEA)
THESSALONIKI, GREECE
E-Poster 58

Is the use of mesalazine during pregnancy at concern for the fetal kidneys?

Corinne Simon [a], Aurélie Grandvuillemin [b], Isabelle Lacroix [c], Thierry Vial [d], Sophie Gautier [e*], Annie-Pierre Jonville-Bera [a].

[a] Pharmacovigilance Center - University Hospital Tours, France; [b] Pharmacovigilance Center - University Hospital Dijon, France; [c] Pharmacovigilance - University Hospital Toulouse, France; [d] Pharmacovigilance Center - University Hospital Lyon, France; [e] Pharmacovigilance Center - University Hospital Lille, France

Introduction

5-ASA s (5 – AminoSalicylic Acid) derivate from salicylic acid and are used in inflammatory bowel disease (IBD) since years. Although **considered as safe dring pregnancy**, in France, the dose during pregnancy **should not exceed 2 g/d as fetal kidney injury has been reported** with a 4 g/d exposure (1).

Recent prospective case : mother treated with mesalazine (1g/d) for IBD during pregnancy, whose fetus presented with an unilateral multicystic renal dysplasia, which secondary evolved into unilateral renal agenesis at birth.

Objective : analysis of the mesalazine safety for fetal kidneys.

Material et Methods

All cases of renal congenital anomalies associated with mesalazine exposure during pregnancy and reported to the French Pharmacovigilance network (FPVN) until November 2024 were examined as follows

i) major renal malformations
ii) fetal or neonatal adverse effects resulting from renal damage (oligohydramnios, anamnios, hyperechogenic kidney parenchyma, increased creatinine at birth).

References :
(1) Lancet 1994 ; 344(8922) : 620-1;(2) The FASEB Journal 2021, 35(7), e21718; (3) World J Nephrol. 2017 Jan 6;6(1):21-28; (4) *Official journal of the American College of Gastroenterology| ACG 2020; 95*(12), 3343-3345.

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Resultats

Among the **38 cases of malformations reported** with mesalazine to the FPVN until november 2024

- **8 (21 %) are major renal malformations** :
  - 6 renal agenesis (4 unilateral)
  - 2 multicystic dysplasias (1 unilateral)

- **9 (35 %) fetal/neonatal renal functional abnormalities without kidney malformation**
  - 6 oligohydramnios (4 isolated, 1 with hyperechogenic renal parenchyma, 1 with elevated creatinine at birth)
  - 2 isolated elevated creatinine at birth
  - 1 hyperechogenic parenchyma with neonatal insufficiency
    - Median dose at 2 g/d [1-4]; 5 cases < 2g/d
    - Exposure at least at trimester 2
    - 2 resolutions of oligoamnios after withdrawal (dose<2 g/d)

Vigibase (OMS) : Total pharmacovigilance reported cases (including French cases)

Signal of disproportionate reporting with mesalazine for renal aplasia (5 cases), renal dysplasia (3 cases), oligoamnios (8 cases) and renal cystic disease (4 cases).
(to date, also + with sulfasalazine for oligoamnios (7 cases))

Discussion - Conclusion

- **Transplacental transfer**
- **Major renal malformations: homogenous although low spontaneous prevalence rate**
  - Pharmacoepidemiological studies and meta analysis (4424 exposures): no increase in malformative risk.
  - Hypothesis from recent experimental studies (2-3): abnormal nephrogenesis induced by an effect on prostaglandins (PGs) in early pregnancy (demonstrated with ibuprofen) or an effect similar to that observed with acetylsalicylic acid on renal growth, independent of PGs.
- **Fetal and neonatal renal dysfunction : few cases but 2 reservible after withdrawal**
  - Systemic diffusion of 5-ASA ≈ 60%. Effects observed with dose < 2g/d.
  - Mesalazine reduces PG and leukotriene synthesis by regulating inducible COX2/ PG E2 signalling (4).
- Mesalazine induced renal toxicity : in animals (rat, dog: renal tubular and papillary necrosis) and in humans :
  - Acute = immuno-allergic, delay ≈ 6 months +/- fever, hepatitis, rash, ...
  - Chronic = insidious (median 3 years): risk of end-stage renal failure

- **Possible deleterious impact of mesalazine on the fetal kidney, even with weak dose (2g/d).**
- **Risk of major renal malformations: to be confirmed.**
- **Recommendation: fetal kidney and amniotic fluid ultrasound monitoring regardless the maternal dose during pregnancy.**