NOWS and Developmental Vulnerabilities Following Maternal Buprenorphine Exposure

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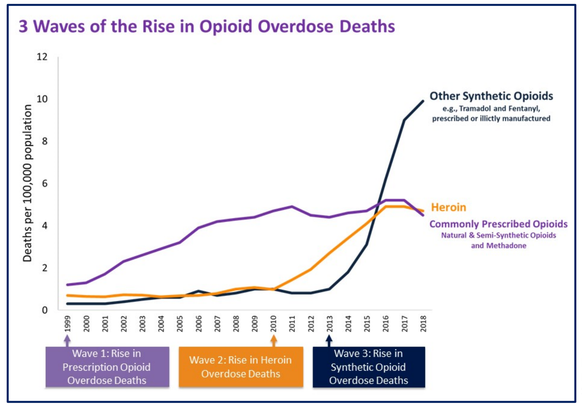
Introduction

- The opioid epidemic has remained a prominent health crisis in the United States [1].



[1] SOURCE: National Vital Statistics System

- Buprenorphine (BUP) medications were FDA-approved for treatment of opioid use disorder (OUD) in 2002 [2].
- Women struggling with OUD during pregnancy may be prescribed buprenorphine.
- There is an inherent vulnerability in the offspring of mothers exposed to opioids during pregnancy that has not yet been systematically characterized with behavioral and biochemical outcomes.
- **Objective:** Use the literature to examine current models and existing knowledge on maternal buprenorphine exposure and NOWS.

Methodology

- An in-depth review was performed on the available literature on preclinical studies of prenatal buprenorphine exposure in rodents.
- Literature ranged from years 1993 to 2019.
- All publications were accessed through PubMed.
- Criteria used: ”buprenorphine neonate rodent” and “buprenorphine NOWS in-utero neonate”

Results

Physical Metrics

- Resorptions and birthweight of offspring were unaffected. Observations suggest that BUP does not cause maternal or offspring toxicity, and that offspring did not experience behavioral or growth effects [3].
- The mortality index, number of stillbirths, and occurrence of resorptions increased in all BUP exposed groups [4].
- In guinea pigs, low doses of gestational BUP caused increased withdrawal symptoms [5].
- Low doses of BUP (0.3 mg/kg) were considered “therapeutic” and generally safe with only slight effects on rodent offspring (delayed development, decreased weight/survival/pain sensitivity). Overexposure (1.0 mg/kg) caused NOWS and reduced maternal care and offspring survival [6].

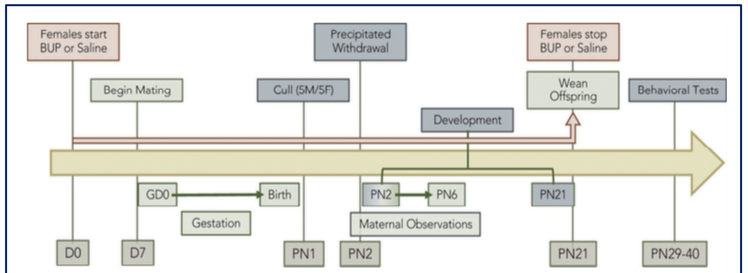


Fig. 1. Schematic of experimental timeline.

[6] SOURCE: Wallin 2019

Biochemical Metrics

- Rats exposed to at least 0.5 mg/kg of BUP experienced MOR reduction by 47-75%, with binding affinity unaffected [7].
- P1 rat brain membranes showed 64% down-regulation of MORs following in-utero BUP treatment [8].
- Exposure to 0.3, 0.6, 2.5 mg/kg doses showed down-regulation of brain opioid receptor density [9].

Drug Abuse Risk

- BUP + Naloxone treatment for maternal heroin abuse may be beneficial, as BUP was found to be favorable in preclinical studies against methadone [10].
- Rats exposed prenatally to 0.3 & 3.0 mg/kg/day doses had higher withdrawal scores (NLX challenge) compared to control groups, indicating the development of physical dependence [11].

Conclusions and Future Directions

- Preclinical rodent models provide varying insights into the effect of maternal buprenorphine exposure. Depending on things such as dose administered, period of exposure, and other experimental factors, different observations and results were found.
- This review focuses on the effects of buprenorphine on offspring in preclinical studies, working to summarize current understandings. An important next step is to investigate clinical studies in the same manner.

Acknowledgements

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