UMKC
School of Pharmacy
Drug Information Center

UMKC Drug Information Center
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Dr. ,

Thank you for your questions regarding the use of Xyrem® during pregnancy and lactation. The 2021 American Academy of Sleep Medicine clinical practice guideline does not provide a specific recommendation regarding the use of sodium oxybate in pregnancy or lactation.[1]

Animal data suggests that the use of oral sodium oxybate during pregnancy may cause fetal harm.[2] Our current knowledge of this medication in pregnancy is limited to several case reports.

- Kuczkowski[3] reports a pregnant gamma-hydroxybutyrate (GHB) abusing patient – the ionized form of sodium oxybate – who developed mild respiratory depression and delivered a healthy newborn with a good Apgar score.
- Gashlin and colleagues[4] report a 27-year-old patient whose medication regimen included sodium oxybate 4 grams twice nightly (2200 and 0200), fluoxetine 20 mg daily, and cetirizine 5 mg daily taken throughout pregnancy and delivered a full-term, healthy newborn.
- Busardò and colleagues[5] report a 32-year-old patient whose medication regimen included sodium oxybate 4.5 grams taken throughout pregnancy. This patient gained 19 kg throughout pregnancy and delivered a newborn with a weight of 3.9 kg and Apgar score of 9.
- van Mechelen and colleagues[6] report a 29-week pregnant female who was treated with diazepam and sodium oxybate for illicit GHB, temazepam and baclofen-induced withdrawal symptoms. An initial dose of 1050 mg was titrated to 1950 mg every 2 hours and tapered off after 5 days. The patient gave birth to a healthy newborn at 37-weeks. The team concluded that sodium oxybate is safe to administer during the third term of pregnancy to treat severe illicit GHB withdrawal symptoms if initial treatment fails.

The overall quality and quantity of evidence for sodium oxybate in lactation is quite low and limited to case reports. GHB is excreted in human milk after oral administration of sodium oxybate and there is insufficient information on the risk to the breastfed infant and on milk production in nursing mothers.[2]

- Gashlin and colleagues[4] report also follows the patient and infant for 6 months while the infant was exclusively breastfed. The patient was recommended to breastfeed or pump prior to administering the 2200 and 0200 doses and use previously expressed breastmilk or formula for any feeding occurring within 4 hours after a dose. After 0600, breastfeeding or expression ad libitum was considered safe to resume. Through 6 months the infant was stable, showed no adverse effects of the medication, and grew and developed appropriately.
    - Growth charts showed 50th percentile for height, weight, and weight/height
    - At birth the head circumference was at the 50th percentile followed by the 75th percentile at 2 months and onward
    - The infant scored high normal for all categories of development in the Ages and Stages Questionnaires at 2, 4, and 6 months
- Busardò and colleagues[5] continued report determines endogenous GHB blood and breast milk concentrations, measured by analyzing GHB levels in 20 breastfeeding women and the 32-year-old

patient. Results show that 5 hours after administration of sodium oxybate 4.5 grams, the level of GHB returns to endogenous levels, supporting waiting until 5 hours after a dose to breastfeed.

- 20 breastfeeding women
  - Endogenous blood GHB levels: 0.57 mg/L, 95% Reference Interval [0.21 to 1.52 mg/L]
  - Endogenous breast milk GHB levels: 0.36 mg/L, 95% RI [0.13 to 1.03 mg/L]
- 32-year-old patient taking sodium oxybate

Time after dose (hours)	GHB Blood concentration (mg/L)	GHB Breast Milk Concentration (mg/L)
0.5	80.10	16.22
1	108.34	23.19
3	35.00	10.15
4	6.50	3.13
5	1.75	0.99

- Barker and colleagues[7] followed two patients who resumed taking sodium oxybate while lactating; however, these patients refrained from breastfeeding their infants during the study period and the breastmilk was only used for analysis of GHB levels. Based on the results of their analysis, they recommend waiting to nurse until 6 hours after a dose of sodium oxybate.
  - Patient 1 was a 37-year-old female, 5 months postpartum, using a dose of 6 grams on night one (3 grams twice nightly) and 9 grams (4.5 grams twice nightly). Concentrations were measured at 1 hour prior to first dose, 4 hours post first dose, 4 hours post second dose, and 6 or 7 hours post second dose.

Patient 1					
Dose	**GHB level 1-hour prior to first dose (µM)**	**GHB level 4-hours post first dose (µM)**	**GHB level 4-hours post second dose (µM)**	**GHB level 6-hours post second dose (µM)**	**GHB level 7-hours post second dose (µM)**
3 grams twice nightly	6.30	10.44	16.51	5.82	-
4.5 grams twice nightly	5.82	23.58	27.50	-	5.93

  - Patient 2 was a 27-year-old female, 10 months postpartum after her first and second pregnancy using a dose of 5 grams (2.25 grams twice nightly) and 6 grams (3 grams twice nightly). Concentrations were measured at 4, 10, and 16 hours post second dose.

Patient 2			
Dose	**GHB level 4-hours post to first dose (µM)**	**GHB level 10-hours post first dose (µM)**	**GHB level 16-hours post second dose (µM)**
2.25 grams twice nightly	14.96	15.41	11.22
3 grams twice nightly	34.01	9.52	8.11

Overall, there is not high-quality evidence about the use of Xyrem® (sodium oxybate) during pregnancy and lactation; therefore, we must rely on the information provided from the package insert and case reports discussed. Clinicians should consider the risks and benefits of use in pregnancy or lactation prior to initiating therapy with Xyrem®. Please let us know if we can help you with anything else.

Sincerely,

Vance Howerton, PharmD Candidate 2022
UMKC Drug Information Center

References:

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