

Safety concerns related to antiseizure medication use in breastfeeding women with epilepsy

Review of questions to the Norwegian drug information and pharmacovigilance centres

Sunniva Reitan Riibe¹, Kristine Heitmann², Jan Schjøtt^{1,2}, Bettina Riedel^{1,2,3}

¹Department of Clinical Science, University of Bergen, ²Department of Medical Biochemistry and Pharmacology and Regional Medicines Information and Pharmacovigilance Centre, Haukeland University Hospital, ³Bergen Epilepsy Research Group, Department of Clinical Medicine, University of Bergen, Bergen, Norway

Background and Aim

Breastfeeding has well-established health benefits for both child and mother. Women with epilepsy (WWE) have lower breastfeeding rates compared to healthy women (1). Safety information of medication during breastfeeding is scarce and conflicting (2,3). We aimed to identify characteristic traits of safety concerns among healthcare professionals related to antiseizure medication (ASM) during breastfeeding in WWE by reviewing questions to the Norwegian drug information and pharmacovigilance centres (RELIS).

Method

Question-answer pairs (QAPs) related to breastfeeding, epilepsy, and ASM identified by the drugs' ATC-numbers were retrieved from a searchable database containing over 55 000 QAPs using a combination of indexed and Boolean database searches and manual inspection. The QAPs were analyzed retrospectively using descriptive statistics.

Results

In total, 112 QAPs were included. Most enquiries (n=60) were from physicians and 52 were from nurses/midwives and other healthcare workers. Enquiries related to monotherapy with either lamotrigine or levetiracetam were most prevalent, 33% (n=37) and 13,4% (n=15), respectively. When co-medication with other drugs than ASM was addressed (15,2 %, n=17) antidepressants (7%, n=8) were the most prevalent mentioned. Most enquirers called for general information about the compatibility of a specific ASM with breastfeeding. Some questions, predominantly posed by physicians, were related to ambiguous drug information advice. Other questions were raised due to concerns about polytherapy or adverse events in breastfed infants. Half of the enquiries were posed after the women had given birth, of which more than half were asked after initiation of breastfeeding, 12 of these motivated by suspected adverse drug reactions in the infants. In most cases RELIS recommended continued breastfeeding, but with drug-specific precautions.

TABLE 1 Topics of enquiries

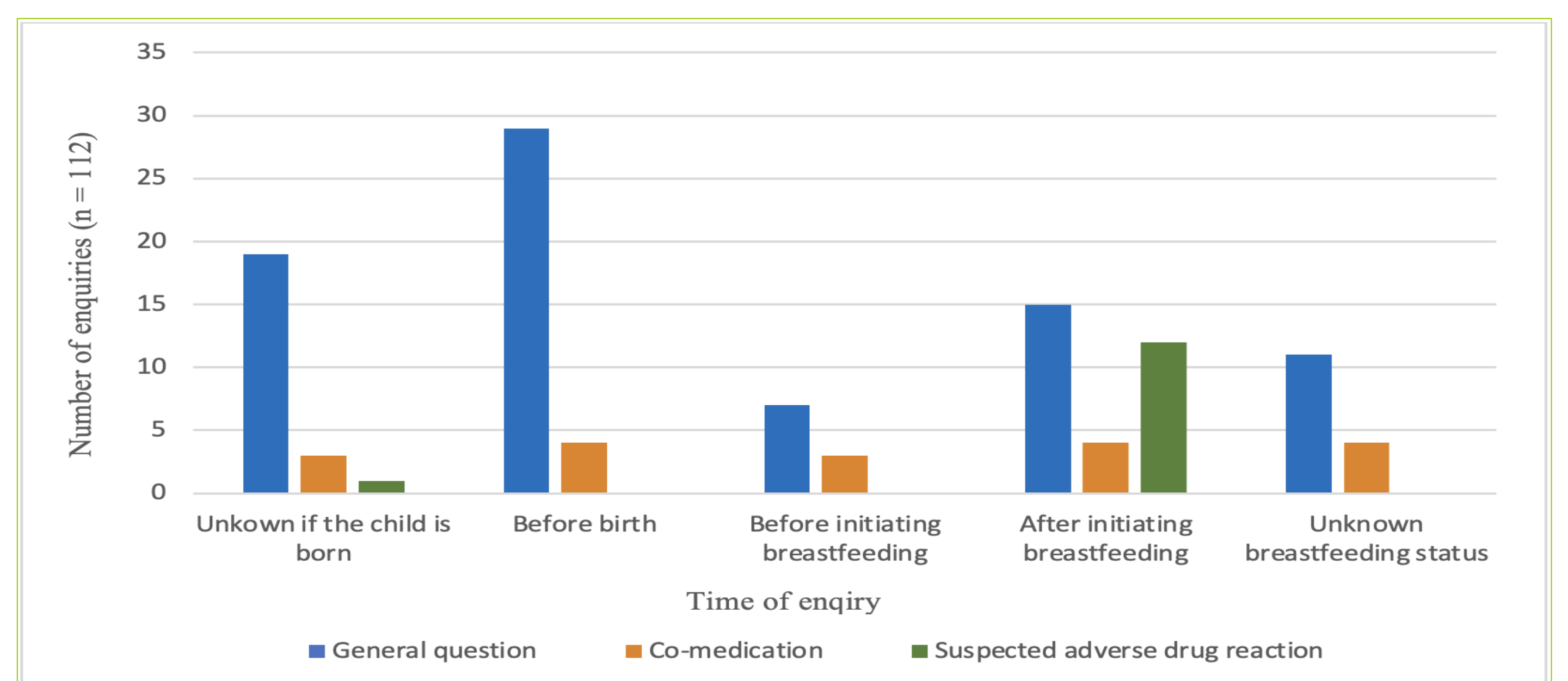
Topics	Example ¹	N	% ²
General question			
Requests general information regarding specific ASMs ³	Is the use of lamotrigine compatible with breastfeeding?	59	52.7
Requests updated assessment from RELIS	Is there more updated information, other than a RELIS article from 2007, on malformation risk and breastfeeding with ethosuximide treatment?	6	5.4
Not recommended or ambiguous product information advise ⁴	Is there any literature on whether perampanel is compatible with breastfeeding, as manufacturer writes that there is a lack of experience, and that risk cannot be ruled out?	12	10.7
Other	Can lamotrigine affect milk production?	4	3.6
Co-medication			
Uncertain due to treatment with several ASMs	Is the combined use of levetiracetam and carbamazepine compatible with breastfeeding?	9	8.0
Uncertain due to treatment with ASM in combination with other medication	Is it safe to breastfeed while using levetiracetam and escitalopram?	9	8.0
Suspected adverse drug reaction in breastfed infant	Could the mother's use of lamotrigine cause the child's twitching?	13	11.6

¹details about mother, child and dose omitted
²percent of 112 QAPs
³antiseizure medication
⁴The Norwegian Pharmaceutical Product Compendium or The Summary of Product Characteristics

TABLE 2 Topics of enquiries¹ in relation to different occupational groups of health care professionals

	Occupation			
	Physician		Other healthcare professionals ²	
	N	%	N	%
General question	35	31.3	34	30.4
Not recommended or ambiguous product information advise²	11	9.8	1	0.9
Co-medication	8	7.1	10	8.9
Suspected adverse effects in breastfed infant	6	5.4	7	6.3

¹percent of 112 QAPs
²nurses, pharmacists, other health care professionals
³Norwegian Pharmaceutical Product Compendium or The Summary of Product Characteristics



Take home message

Healthcare professionals with acknowledged high competence and skills in the topic were uncertain about the prevailing safety information of ASM during breastfeeding. The fear to harm the infant may lead to the decision not to recommend breastfeeding in lactating ASM-using WWE. Future information strategies should aim to reach these professions, encourage planning medication use before birth and support the professions' information need on this topic.

Literature

- Veiby G, Engelsen BA, Gilhus NE. Early child development and exposure to antiepileptic drugs prenatally and through breastfeeding: a prospective cohort study on children of women with epilepsy. *JAMA Neurol.* 2013;70(11):1367-74.
- Den norske legeforening. Retningslinjer for behandling av kvinner med epilepsi [Internet]. Oslo: Den norske legeforening; 2018 [cited 2022 8 August]. Available from: <https://www.legeforeningen.no/om-oss/publikasjoner/retningslinjer/retningslinjer-for-behandling-av-kvinner-med-epilepsi-2018/>
- Nørby U, Noël-Cuppers B, Hristoskova S, Desai M, Härmark L, Steel M, et al. Online information discrepancies regarding safety of medicine use during pregnancy and lactation: an IMI ConcePTION study. *Expert Opinion on Drug Safety.* 2021;20(9):1117-24.

