

Rosuvastatin Is Transferred into Human Breast Milk: A Case Report

To the Editor:

Controversy exists on whether lactating women with familial hypercholesterolemia should resume statin treatment. This is partly due to the unavailability of data in humans regarding the transfer of statins into breast milk. Statin manufacturers advise against statin use for nursing mothers, referring to a study on rats indicating the transfer of atorvastatin via breast milk.¹ It is generally accepted that statin levels of animal breast milk may not accurately reflect human breast milk levels. To our best knowledge, no published data are available on the transfer of 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors via breast milk in humans.

CASE SUMMARY

We present a case of a 31-year-old white woman with familial hypercholesterolemia. Before pregnancy, her serum low-density lipoprotein cholesterol (LDL-C) level was 3.6 mmol/L with chronic daily treatment of 40 mg rosuvastatin (Crestor; AstraZeneca, Wilmington, DE) (Table). Statin use was stopped during pregnancy. It is known that LDL-C levels increase during pregnancy, and in this patient the LDL-C was 12.6 mmol/L 9 days postpartum. Thirty-three days postpartum, a daily dose of 40 mg rosuvastatin treatment was resumed.

Panel A in the Figure demonstrates the hourly increases in rosuvastatin concentrations in breast milk after oral ingestion, whereas panel B shows the breast milk concentrations on various days after initiation of

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Table Serum Cholesterol Profile

	Treatment	TC (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)
1 month before pregnancy	40 mg rosuvastatin	5.8	3.6	1.6
9 days postpartum	None	14.6	12.6	1.4

HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol.

treatment. Rosuvastatin concentrations in breast milk increased steeply from hour 1 to 7 (ie, 15.2 to 29.4 ng/mL) after oral intake, with a peak expected after approximately 10 hours. We obtained predominantly hindmilk samples on the days indicated in the Figure, panel B, but the foremilk-to-hindmilk ratio may be different for the hourly samples in panel A. Whether there are differences between fore- and hindmilk statin concentrations is unknown.

The breast milk concentrations ranged between 21.9 and 22.8 ng/mL over 3 test days (Figure, panel B) with sampling done 3, 3.8, or 21 hours after intake. Serum rosuvastatin concentration 23 hours after dose intake was lower than overall breast milk concentrations, namely, 18 ng/mL.

DISCUSSION

Our case report presents the first human evidence for transferal of rosuvastatin into breast milk, confirming a study in rats.¹ Breast milk rosuvastatin concentrations were higher than in serum (22.4 vs 18 ng/mL) at 21-23 hours after intake. We found clear dose-related hourly fluctuations in breast milk rosuvastatin concentrations, but further studies are needed to demonstrate 24-hour concentration curves.

Although these data add to our knowledge regarding statin transfer into breast milk, it does not provide information on the safety of statins for infants. Controversy exists on when statin treatment should be initiated in children of families with familial hypercholesterolemia. Rodenburg et al² suggest the earlier the better, in line with the American Heart Association recommendation of ≥ 10 years in males and at the onset of menses in females.³ Elahi et al⁴ found reduced cardiovascular risk in offspring of mice exposed to a high-fat diet and pravastatin during pregnancy and lactation.

Consequently, physicians are uncertain whether, when, and how to treat children with familial hypercholesterolemia. Potential benefits of early statin treatment are evident, but unless indicated otherwise, the possibility exists that

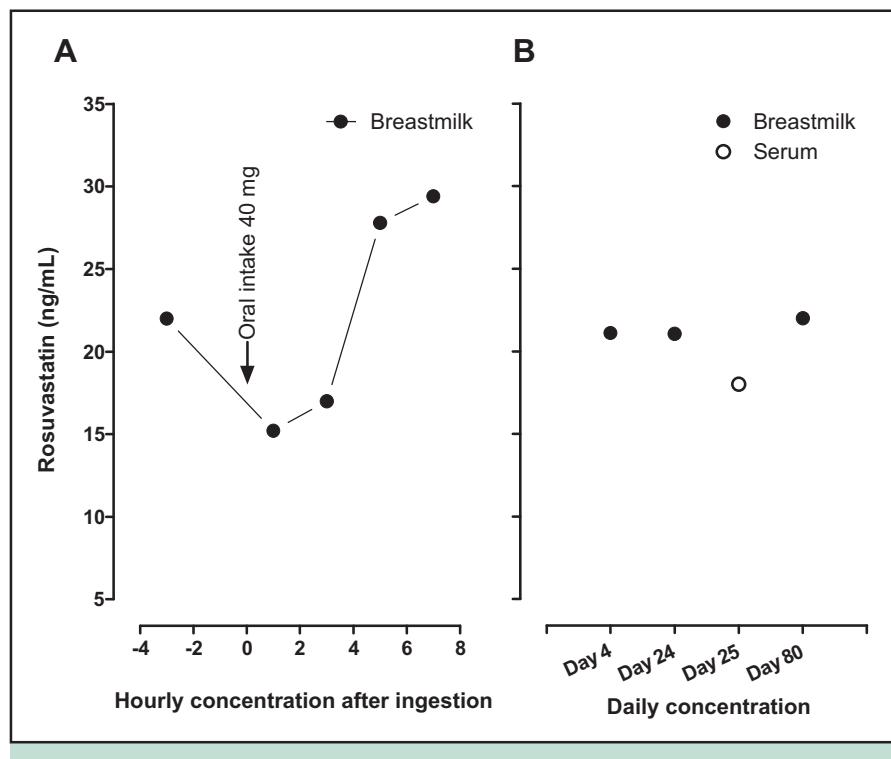


Figure (A) Hourly concentrations of rosuvastatin in breast milk after intake of a 40-mg dose. (Concentration at -3 hours: 21 hours after dose intake). (B) Breast milk and serum rosuvastatin concentrations on different days after initiation of treatment. (Day 4: 3 hours after dose intake; Day 24: 3.8 hours after dose intake; Day 25: 23 hours after dose intake; Day 80; 21 hours after dose intake).

hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors transferred via breast milk may have a potential to cause serious adverse reactions in nursing infants.

CONCLUSIONS

Rosuvastatin transfers into human breast milk at high concentrations. After 21-23 hours, breast milk concentrations were approximately 4 ng/mL higher than in serum.

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