

## **Rosuvastatin is transferred into human breast milk: A case report.**

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**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.<sup>1</sup> 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 is available on the transfer of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors via breast milk in humans.

**CASE SUMMARY:**

We present a case of a 31-year old Caucasian 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)(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 nine days postpartum. Thirty-three days postpartum a daily dose of 40 mg rosuvastatin treatment was resumed.

Figure A demonstrates the hourly increases in rosuvastatin concentrations in breast milk after oral ingestion, whereas Figure B shows the breast milk concentrations on various days after initiation of treatment. Rosuvastatin concentrations in breast milk increased steeply from hour 1 to 7 (i.e. 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 Figure B, but the foremilk-to-hindmilk ratio may be different for the hourly samples in Figure 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 three test days (Figure B) with sampling done after 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 transferral of rosuvastatin into breast milk, confirming a study in rats.<sup>1</sup> Breast milk rosuvastatin concentrations were higher than in serum (22.4 versus 18ng/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 this data adds 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 al* suggests the earlier the better,<sup>2</sup> in line with the American Heart Association recommendation of  $\geq 10$  years in males and at the onset of menses in females.<sup>3</sup> Elahi *et al* found reduced cardiovascular risk in offspring of mice exposed to a high-fat diet and pravastatin during pregnancy and lactation.<sup>4</sup>

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 HMG-CoA 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.

## References

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## Figure Legend

### FIGURE 1.

#### **A. Hourly concentrations of rosuvastatin in breastmilk after intake of a 40 mg**

**dose.**(Concentration at -3hrs: 21 hrs after dose intake)

#### **B. Breast milk and serum rosuvastatin concentrations on different days after initiation of treatment**

(Day 4: 3 hrs after dose intake; Day 24: 3.8 hrs after dose intake; Day 25: 23 hrs after dose intake; Day 80; 21 hrs after dose intake).

**TABLE. Serum cholesterol profile**

	<b>Treatment</b>	<b>TC</b> (mmol/L)	<b>LDL-C</b> (mmol/L)	<b>HDL-C</b> (mmol/L)
A month before pregnancy	40 mg rosuvastatin	5.8	3.6	1.6
Nine days postpartum	None	14.6	12.6	1.4

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

Figure(s)

