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# The excretion of enalapril and enalaprilat in human breast milk

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Puerperal hypertension often necessitates urgent therapy to minimise post partum morbidity. A variety of antihypertensive agents have been used to date, however many of them have unwanted side effects such as depression, lethargy and tiredness. Diuretics cannot be used as they may interfere with lactation.

The angiotensin converting enzyme inhibitor enalapril maleate has been shown to be effective in the treatment of essential hypertension of all grades of severity and thus its use may be considered for the treatment of puerperal hypertension. Enalapril administered orally is converted by hydrolysis in the liver to the active diacid parent compound enalaprilat. Animal data have shown that minimal radioactivity from labelled enalapril is detectable in milk (MSD Research Laboratories, Data on file). The oral administration to lactating rats of phenylpropyl 2,3 $^{14}$C-enalapril in a dose of 10 mg/kg resulted in mean milk concentrations of $^{14}$C-enalapril equivalents of 0.09 ug/ml at 1 h and 0.36 ug/ml at 4 h post dose. Plasma concentrations at these times were 3.64 and 0.59 ug equivalents/ml, respectively. No data are available on whether either enalapril or its active metabolite enalaprilat are excreted in human breast milk and we therefore undertook a project to evaluate the extent to which this might occur. Patients requiring treatment of puerperal hypertension and who had opted not to breast feed were studied. Baseline blood and milk samples were taken and then enalapril 20 mg was administered orally. Milk samples were taken 4, 6 and 24 h later for assessment of enalapril and enalaprilat. Specimens of milk were centrifuged and aliquots of the supernatant deproteinated using acetonitrile. After evaporation and reconstitution in assay buffer, specimens were assayed as for serum by the method of Hichens et al. [1]. This radioimmunoassay measures enalaprilat. Concentrations of enalapril were measured as enalaprilat after enzymatic conversion by overnight incubation with a rat liver homogenate. Concentrations of enalaprilat were calculated by difference and multiplication by the appropriate molecular weight factor. Blood samples were taken at 2 and 4 h to measure serum concentrations of enalapril and enalaprilat.

Five patients were studied. In one patient however, only a single milk sample was available (4 h). The milk and serum concentrations of enalapril and enalaprilat, together with the maximum milk/serum ratios, are shown in Table 1. Small amounts of enalapril and enalaprilat were detected in the milk. On the assumption that the average neonate consumes between 500 ml and 850 ml milk per day, the total daily dose of enalaprilat received would not be in excess of approximately 2 ug (assuming the maximum milk levels noted in this study are maintained) following an oral dose of enalapril 20 mg to the mother.

In confirmation of animal studies, we have demonstrated that both enalapril and enalaprilat do appear in milk to a small degree following the administration of a single dose of enalapril. While the amounts are small this observation should be taken into account when selecting antihypertensive therapy for the mother who wishes to breast feed.

**Table 1.** Serum and milk concentrations of enalapril and enalaprilat after a single 20 mg dose of enalapril

| Enalapril patient No. | Milk (ng/ml) | | | | Maximum M/S ratio | Maximum serum concentration (ng/ml) |
|---|---|---|---|---|---|---|
| | 0 | 4 | 6 | 24 | | |
| 1 | 0 | 0 | 5.9 | 1.8 | 0.043 | 136 |
| 2 | 0 | 0 | 0 | 0 | 0 | 151 |
| 3 | 0 | 0.54 | 0 | 0 | 0.006 | 92 |
| 4 | 0 | 1.2 | 1.7 | 0 | 0.012 | 143 |
| 5 | 0 | 0.54 | – | – | 0.005 | 93 |

Mean maximum milk concentration = 1.74 ng/ml

| Enalaprilat patient No. | Milk (ng/ml) | | | | Maximum M/S ratio | Maximum serum concentration (ng/ml) |
|---|---|---|---|---|---|---|
| | 0 | 4 | 6 | 24 | | |
| 1 | 0 | 1.0 | 1.6 | 1.9 | 0.023 | 83 |
| 2 | 0 | 0 | 0 | 1.2 | 0.031 | 39 |
| 3 | 0 | 1.5 | 2.3 | 1.8 | 0.021 | 112 |
| 4 | 0 | 1.2 | 1.1 | 1.7 | 0.026 | 64 |
| 5 | 0 | 1.5 | – | – | (0.028) | 54 |

Mean maximum milk concentration = 1.72 ng/ml

## Reference

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