

# Estimating systemic exposure to ethinyl estradiol from an oral contraceptive



Carolyn L. Westhoff, Malcolm C. Pike, Rosalind Tang, Marianne N. DiNapoli, Monica Sull, Serge Cremers

## Objective

This study was conducted to compare single-dose pharmacokinetics of ethinyl estradiol in an oral contraceptive with steady-state values and to assess whether any simpler measures could provide an adequate proxy of the “gold standard” 24-hour steady-state area under the curve (AUC) value. Identification of a simple, less expensive measure of systemic ethinyl estradiol exposure would be useful for larger studies that are designed to assess the relationship between an individual’s ethinyl estradiol exposure and side-effects.

## Study Design

We collected 13 samples over 24 hours for pharmacokinetic analysis on days 1 and 21 of the first cycle of a monophasic oral contraceptive that contained 30 µg ethinyl estradiol and 150 µg levonorgestrel in 17 nonobese healthy white women. We also conducted an abbreviated single-dose 9-sample pharmacokinetic analysis after a month washout. Ethinyl estradiol was measured by liquid chromatography-tandem mass spectrometry. We compared results of a full 13-sample steady-state pharmacokinetic analysis with results that had been calculated with the use of fewer samples (9 or 5) and after the single doses. We calculated Pearson correlation coefficients to evaluate the relationships between these estimates of systemic ethinyl estradiol exposure.

## Results

The AUC, maximum, and 24-hour values were similar after the 2 single oral contraceptive doses (AUC;  $r = 0.92$ ). The steady-state 13-sample 24-hour AUC value was correlated highly with the average 9-sample AUC value after the 2 single doses ( $r = 0.81$ ;  $P = .0002$ ). This correlation remained the same if the number of single-dose samples was reduced to 4, taken at time 1, 2.5, 4, and 24 hours. The 24-hour value at steady-state was correlated highly with the 24-hour steady-state AUC value ( $r = 0.92$ ;  $P < .0001$ ). The average of the 24-hour values after the 2 single doses was also correlated quite highly with the steady-state AUC value ( $r = 0.72$ ;  $P = .0026$ ).

## Conclusion

Limited blood sampling, including results from 2 single doses, gave highly correlated estimates of an oral contraceptive user’s steady-state ethinyl estradiol exposure.

