K47 Buprenorphine and Norbuprenorphine Concentrations in the Hair of OpiateDependent Pregnant Women and Their Newborn Infants

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After attending this presentation, attendees will have a better understanding of the application of hair analysis for the determination of buprenorphine and norbuprenorphine in women maintained on buprenorphine and their infants exposed in utero.

This presentation will impact the forensic community and/or humanity by addressing the usefulness of hair analysis as a tool for the determination of illicit and therapeutic drugs.

Accurate identification of in utero illicit and therapeutic drug exposure has important implications to mothers and infants. Buprenorphine, a partial μ agonist, is under investigation as a pharmacotherapy for treating opioid dependence in pregnant women. Hair testing may be a useful tool for the determination of drug exposure during pregnancy; however, data are limited on the disposition of buprenorphine and norbuprenorphine in maternal and infant hair.

This study examined buprenorphine and norbuprenorphine concentrations in hair obtained from nine (8 African-American, 1 Caucasian) buprenorphine-maintained pregnant women and four of their infants. Women received 4 – 24 mg daily sublingual buprenorphine throughout gestation, an average of 16.3 ± 2.8 weeks; 13 – 21 (mean ± SD; range). Mean total maternal buprenorphine dose was 1742.4 ± 385.3; (range, 1204 – 2270 mg). Mean cumulative third trimester maternal buprenorphine dose was 1347.6 ± 241.6 mg; (range, 920 – 1672mg).

Maternal hair specimens (N=52) were collected, root to tip, approximately every 4 weeks throughout enrollment and stored at -20°C until time of analysis. Specimens were analyzed at the Center for Human Toxicology, Salt Lake City, UT utilizing liquid chromatography-tandem mass spectrometry with limits of quantification of 3.0 pg/mg for buprenorphine and norbuprenorphine in hair. Prior to analysis, hair specimens were cut into 3 cm segments, representing approximately 3 months of hair growth. Hair specimens were washed twice with 5 mL of methylene chloride at ambient temperature. Of 52 washed maternal hair specimens, 40 were positive for buprenorphine (46.4 ± 33.74; 8.6 – 161.8 pg/mg) and 41 positive for norbuprenorphine (607.5 ± 496.9; 8.2 – 1733.7 pg/mg) in the first segment of hair (closest to the scalp). Ratios of buprenorphine to norbuprenorphine ranged from 0.04 to 0.70 (0.14 ± 0.17). When sufficient amounts of hair were available (N=20), specimens also were analyzed without washing. Of the 20 unwashed specimens, 18 were positive for buprenorphine (47.7 ± 35.6; 4.6 – 151.3 pg/mg) and 17 for norbuprenorphine (714.0 ± 554.3; 46.5 2018.6 pg/mg) in the unwashed first hair segment. There was no statistically significant difference between the concentrations of buprenorphine (p=0.64) or norbuprenorphine (p= .86) in the washed and unwashed hair specimens. Ratios of buprenorphine to norbuprenorphine in the unwashed specimens ranged from 0.04 – 0.49 (0.15 ± 0.14) and were not significantly different in washed hair specimens (p=0.89).

Infant hair specimens (N=4) were collected within 48 hours of delivery and were not washed prior to analysis. Neonatal hair was not washed because drug concentrations could have been lower than in the mother, and it was not known if washing would remove excess amounts of drug due to the fine texture of the hair, and there was an insufficient amount of hair to test both washed and unwashed specimens. All infant specimens were positive for buprenorphine (54.7 ± 21.7; 36.8 – 82.1 pg/mg) and norbuprenorphine (785.6 ± 190.2; 579.9 – 1037.1 pg/mg). The ratio of buprenorphine to norbuprenorphine in infant hair ranged from 0.05 to 0.08 (0.07 ± 0.02). There was no correlation between maternal total buprenorphine dose and buprenorphine (r^2=0.05, p=0.95) or norbuprenorphine (r^2=0.18, p=0.82) concentrations in infant hair. There also was no correlation between 3rd trimester maternal buprenorphine dose and buprenorphine (r^2=0.29, p=0.71) or norbuprenorphine (r^2=0.09, p=0.91) in infant hair.

Higher concentrations of norbuprenorphine as compared to buprenorphine were found in maternal and neonatal hair following daily maintenance doses of buprenorphine to opiate-dependent pregnant women. Washing maternal hair with methylene chloride did not significantly decrease parent or metabolite concentrations in the specimens. Although buprenorphine pharmacotherapy offered the opportunity to evaluate doseconcentration relationships in this vulnerable population, no significant correlations were observed between maternal buprenorphine dose and buprenorphine or norbuprenorphine concentrations in maternal or neonatal hair. Research supported by NIDA R01-12220 and NIH DA 09096.

Buprenorphine, Hair, In Utero

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