

Polymorphisms of CYP1A1 and its relationship to benzo(a)pyrene hemoglobin adducts in smokers and nonsmokersSteven Myers¹¹University Of Louisville

The cytochrome P450 isoform CYP1A1 has been widely studied because of its interactions with the PAH substrates such as BP. In addition to being a substrate for CYP1A1, BP is also a potent inducer of the enzyme. Because CYP1A1 plays such a pivotal role in the metabolism of BP, as well as several other PAH found in tobacco smoke, we deemed it justifiable to measure the levels of BP Hb adducts in cord blood samples with regards to CYP1A1 genetic polymorphisms of Msp I (T6235C) and Hinc II (A4889G). Matched maternal and fetal blood samples were obtained from smokers at delivery and stratified based on cotinine determinations. Subjects were divided into three groups based on CYP1A1 Msp I genotype: wild type (TT), heterozygous (TC), homozygous variant (CC). Subjects were divided into two groups based on CYP1A1 Hinc II genotype (AA) and heterozygous (AG). There were no homozygous variants for Hinc II. BP diol epoxide Hb adduct levels were highest in the cord blood samples with the CYP1A1 Msp I wild type (TT) genotype and lowest in the cord blood samples with the CYP1A1 Msp I homozygous variant (CC) genotype ($= 0.05$, $P < 0.39$). This was also the trend with BP-7,8-oxide Hb adduct levels ($= 0.05$, $P < 0.61$) and BP-4,5-oxide Hb adduct levels ($= 0.05$, $P < 0.13$). BP diol epoxide Hb adduct levels were slightly higher in cord blood samples with the CYP1A1 Hinc II heterozygous genotype than in the wild type ($= 0.05$, $P < 0.75$). Cord blood subjects with the CYP1A1 Hinc II wildtype genotype had higher BP-7,8-oxide Hb adduct levels than those with the heterozygous genotype ($= 0.05$, $P < 0.21$). BP-4,5-oxide Hb adduct levels were slightly higher in the cord subjects with the CYP1A1 Hinc II heterozygous genotype than in subjects with the wild type genotype ($= 0.05$, $P < 0.62$). These results suggest that polymorphisms of the CYP1A1 genotype may play a role in formation of hemoglobin adducts