Nicotine Metabolite Ratio and Biomarkers of Exposure among American Indian Tobacco Users

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Background: Smokers with a normal or fast nicotine metabolism have higher nicotine intake and more exposure to and bioactivation of carcinogens than smokers with a slow metabolism. CYP2A6 is the main enzyme that metabolizes nicotine and the nicotine metabolite ratio (NMR) of 3'hydroxycotinine to cotinine is a genetically-informed biomarker of CYP2A6. We examined the NMR and its relationship with biomarkers of exposure in American Indian (AI) cigarette smokers (n=27), electronic nicotine delivery system (ENDS) users (n=21), and dual users (n=26).

Methods: Participants of AI descent were recruited in 2016 throughout the state of Oklahoma. Urine samples were analyzed for NMR, total nicotine equivalents (TNE), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and its glucuronides (NNAL). A measurement of expired-air carbon monoxide (CO) was collected. Geometric means (GM) and 95% confidence intervals (CI) were computed. Associations between log-transformed values of NMR, TNE, NNAL, and CO were examined using Pearson's product-moment correlation coefficient (r)

Results: NMR in smokers (GM: 3.10; CI: 2.27, 4.22), END users (GM: 4.85; CI: 3.52, 6.69), and dual users (GM: 3.36; CI: 2.52, 4.47) did not differ (p-value=0.13). NMR and TNE were not associated in smokers (r=-0.32; p-value=0.11), ENDS users (r=0.06; p-value=0.78), or dual users (r=0.15; p-value=0.45). NMR was not correlated with NNAL in smokers (r=-0.30; p-value=0.12) or dual users (r= 0.04; p-value=0.85). In smokers, NMR was negatively correlated with CO (r=-0.41; p-value<0.05). There was no relationship between NMR and CO in dual users (r=0.01; p-value=0.96).

Conclusions: Nicotine and toxicant exposure within AI tobacco users may not be related to the rate of nicotine metabolism as demonstrated in other race groups. Given the study's small-scaled nature, further research is needed to elucidate the relationships between nicotine metabolism, nicotine intake, and toxicant exposure in AIs. Such research is of upmost importance given the high rates of tobacco use and subsequent health disparities in AIs.

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