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COMMENTARY

Muconic Acid in Urine: A Reliable Indicator of Occupational Exposure to Benzene

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In male subjects not occupationally exposed to benzene, the concentration of muconic acid (MA) in urine is usually below 0.5 mg/g creatinine. At ambient levels of benzene exposure (below 0.01 pprn), the mean MA level was greater in 21 smokers than in 14 nonsmokers. In 38 male subjects employed in garages and coke ovens, a statistically significant correlation was found between the airborne concentration of benzene measured with passive monitors and MA in postshift urine. The mean postshift MA concentrations corresponding to a benzene 8-hour time-weighted average exposure (TWA) of 0.5 and 1 ppm were 0.8 and 1.4 mg/g creatinine, respectively.

Key words: benzene exposure, biological monitoring, smoking exposures, biological markers

INTRODUCTION

Johnson and Lucier [1992] have recently drawn the attention to the interest of urinary muconic acid (MA) as a biomarker of exposure to benzene. Our own data, briefly summarized below, support this conclusion but suggest that the background level of MA in not occupationally exposed male subjects and the relation between the airborne concentration of benzene at workplaces and MA (end of shift) permit the detection of occupational exposure as low as 0.5 ppm (8 hour TWA).

MUCONIC ACID CONCENTRATION IN ADULT MALE SUBJECTS NOT OCCUPATIONALLY EXPOSED TO BENZENE

We have measured MA in morning and afternoon urine samples collected from adult male subjects (21 nonsmokers and 14 smokers). We used the method described by Ducos et al. [1990]. Ambient exposure to benzene during the day of urine collection was below 0.01 ppm. For both groups combined, the 95 percentile value of MA (afternoon sample) amoanted to 0.41 mg/g creatinine. This result is in agreement with that reported by Bechtold et al. [1991]. However, the geometric mean value of

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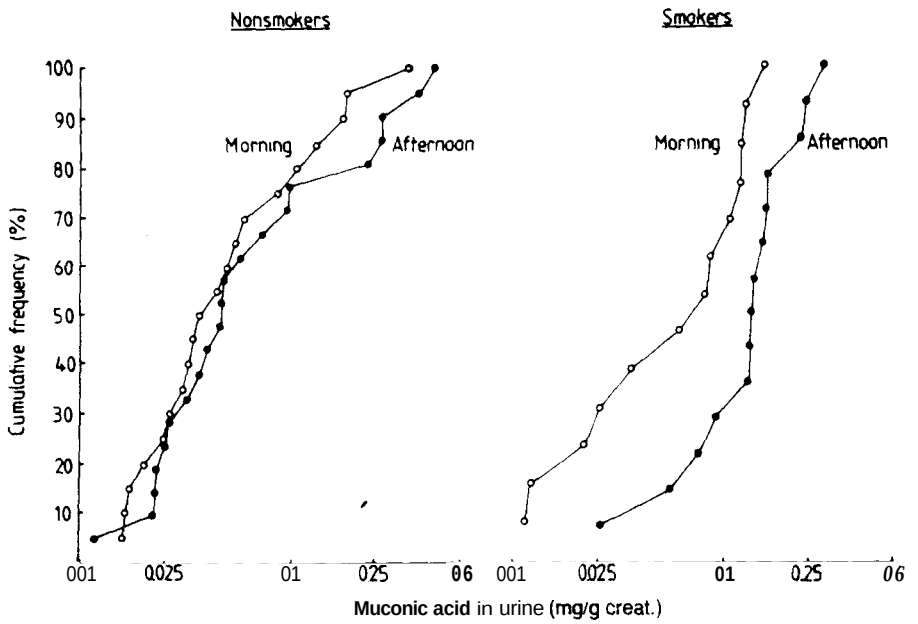

Fig. 1. Cumulative frequency distributions of **MA** in male nonsmokers and smokers not **occupationally** exposed to benzene.

MA is twice as high in smokers (0.130mg/g creatinine) as in nonsmokers (0.06).The impact of cigarette consumption on **MA** is clearly illustrated in Figure 1. In nonsmokers, the morning and afternoon **MA** are not significantly different; in smokers, the cumulative frequency distribution of **MA** is shifted to significantly higher values in the afternoon, apparently reflecting exposure to benzene present in tobacco smoke (paired t test $p < 0.05$). The highest individual values, however, were found in nonsmokers, an observation possibly due *to* small numbers or high environmental exposure of some nonsmokers to benzene. Johnson and Lucier {1992} state **that** the only significant source of **MA** formation in the body is through the metabolism of benzene, suggesting that even the background **MA** level found in nonsmokers results from environmental exposure to benzene. However, **it** has been demonstrated by Ducos et al. {1990} that sorbitol, which is present in certain foods, may also be biotransformed to **MA.** Therefore, the different background levels of **MA** reported in nonsmokers not occupationally exposed to benzene may also partly reflect differences in dietary habits.

Whatever the main factors responsible for the background level **of MA,** our preliminary data suggest that in Belgium the average **MA** level in not occupationally exposed subjects (smokers and nonsmokers combined) is usually below 0.5 mg/g creatinine.

RELATION BETWEEN MUCONIC ACID CONCENTRATION IN POSTSHIFT URINE AND OCCUPATIONAL EXPOSURE TO BENZENE

We have also assessed whether in workers moderately exposed to benzene (up to *2* ppm) in garages and coke ovens there was a relationship between benzene in air

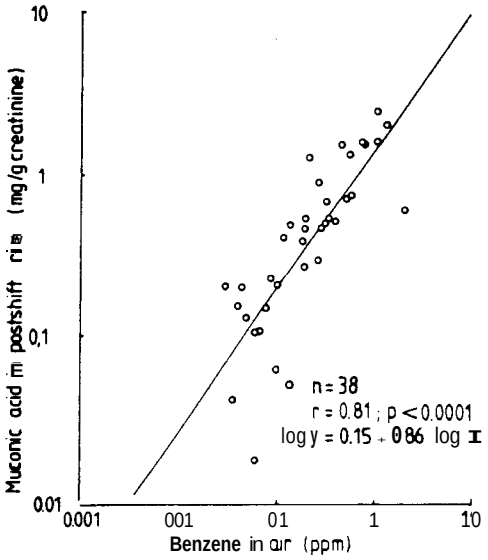

Fig. 2. Relation between benzene in air and MA in postshift urine.

(measured with 3 M 3500 organic vapor monitor) and MA in postshift urine. As illustrated in Figure 2, a statistically significant relation was found. No difference between smokers and nonsmokers could be ascertained. This suggests that either the impact of occupational exposure to benzene on MA has masked the influence of smoking habits or the amount of benzene collected on passive samplers reflects both the amount present in cigarette smoke and that contaminating the work environment. Another possibility is that the number of observations was too limited to detect an additive effect of smoking and occupational exposure to benzene. Our results (Fig. 2) indicate that the mean postshift **MA** levels in subjects exposed to 0.5 or 1 ppm benzene **(8** hour TWA) ranged from 0.8 or 1.4 mg/g creatinine, respectively; these values are significantly higher than the background MA level found in subjects not occupationally exposed.

It should be noted that in the two groups reported here, benzene in air was monitored with passive personal samplers. It would be useful to assess whether the same relationship holds when benzene in air is collected with a dynamic (pump) personal sampling system to clarify the possibility of underestimated exposures. Such a study has recently been reported by Ducos et al. [1992], but it involved workers from **3** perfume-producing factories whose average exposure to benzene (9 ppm) was higher than in our study. Nevertheless, their estimate of the mean MA (1.17 mg/l) corresponding to a benzene TWA of 1 ppm is in rather good agreement with our results. In conclusion, our preliminary findings suggest that MA is a reliable indicator of exposure to benzene, even at a TWA level as low as 0.5 ppm.

ACKNOWLEDGMENTS

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