Am. Ind. Hyg. Assoc. J. 48(11):900-908 (1987)

Formate in Urine as a Biological Indicator of Formaldehyde Exposure: A Review

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The presence of a small amount of endogenously derived formate in human urine is normal; however, formate derived from the metabolism of formaldehyde, several other industrial compounds and some pharmaceuticals may elevate the urine formate concentration above the normally expected values. This elevation in the urine formate concentration presents the possibility of using this as a tool for monitoring exposure to chemicals. Unfortunately, the use of urine formate as a technique for monitoring personal chemical exposure has yet to be evaluated. This review identifies several potentially important variables that could alter the extent to which formate is eliminated through the urine and that could affect the accuracy of using urine formate concentration as an indicator of chemical exposure. Some potentially important confounders that have been identified, but not evaluated adequately, include dietary intake, nutritional status and exposure to cigarette smoke. Furthermore, the metabolism and elimination kinetics have yet to be adequately demonstrated in humans. Without having controlled for potential confounders in previous pharmacokinetic studies, it is unknown whether or not the large range and variation observed in human studies is due to the confounders or to innate individual variability. Given the poor understanding of the normal variation of formate concentration in the urine, the use of it as a biological indicator of chemical exposure becomes questionnable. Without appreciable skin penetration, as in this case, the reliance upon air monitoring alone may be more practical. The evidence at this time suggests that the use of urine formate to monitor chemical exposure offers a broad opportunity for investigative research. At the present time, however, the interpretation of urine formate concentration in samples obtained from workers would be difficult.

Introduction

Formate, an endogenous product of single carbon (C_1) metabolism, is normally found in the urine of healthy individuals. Exposure to several common industrial compounds — such as formaldehyde, methanol and acetone — may contribute to increasing the amounts of formate in the body. It might be expected that any external exposure resulting in an elevation of the internal C_1 body load should lead to an increase in the rate of formate elimination. In practice, a simple predictable relationship between dose and elimination has not been demonstrated yet.

The analysis of biological media to determine the effect or extent of personal exposure to a substance is receiving increasing attention. To date, over 1000 substances reportedly have been determined in human biological media.[1] In theory, the application of biological monitoring offers benefits beyond the capabilities offered by environmental sampling.[2,3] First, the routes of exposure that contribute to the total body burden may be multiple and the amounts of exposure ambiguous. Therefore, a single short-term sample of a person's breathing zone air, for example, may poorly represent the actual total exposure. Furthermore, biological sampling may be related more closely to the extent of contaminant absorption. It may better reflect workload and individual uptake and it therefore may more closely parallel the personal hazard potential. Biological monitoring also can be used to assess the effectiveness of worker protective equipment. Finally, where cumulative body burden is of toxicologic consequence, the time integrated measurement of exposure — as determined in a biological sample — should be more meaningful than short-term environmental measurements. This is particularly advantageous when wide fluctuations in exposure concentration occur over a period of time.

To be useful for the practical application of assessing personal exposure, a biological monitoring procedure must meet certain requirements. Obviously, the analytical methods used should be accurate, precise, specific and as sensitive as possible. The procedure preferably should be non-invasive and should present minimal risk of injury. Overall, it should be inexpensive and easy to perform. Of equal importance is that the investigator know when to collect a sample or samples and whether to take any special precautions to prevent contamination or loss. To interpret the results, the investigator will require a knowledge of the normally expected median concentration and range for non-exposed individuals. If possible, potential confounding effects — such as diet, personal habits (*e.g.*, smoking and alcoholic beverage consumption), hobbies, age, sex, body weight, state of health, use of medications, and workload — should be taken into account. The above factors may influence directly the intrapersonal, and especially the interpersonal, variability of the results within the normal range. One can best understand these interdependent factors through the study and understanding of the metabolism, excretory pathways and pharmacokinetics of the compound of interest.

This communication attempts to review the literature and provide a perspective on the many biological and exogenous