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Urinary methyl *tert*-butyl ether and benzene as biomarkers of exposure to urban traffic

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ABSTRACT

Methyl *tert*-butyl ether (MTBE) and benzene are added to gasoline to improve the combustion process and are found in the urban environment as a consequence of vehicular traffic. Herein we evaluate urinary MTBE (MTBE-U) and benzene (BEN-U) as biomarkers of exposure to urban traffic. Milan urban policemen (130 total) were investigated in May, July, October, and December for a total of 171 work shifts. Personal exposure to airborne benzene and carbon monoxide (CO), and atmospheric data, were measured during the work shift, while personal characteristics were collected by a questionnaire. A time/activity diary was completed by each subject during the work shift. Spot urine samples were obtained for the determination of MTBE-U and BEN-U. Median personal exposure to CO and airborne benzene were 3.3 mg/m^3 and 9.6 μg/m^3, respectively; median urinary levels in end-of-shift (ES) samples were 147 ng/L (MTBE-U) and 207 ng/L (BEN-U). The time spent on traffic duty at crossing was about 40% of work time. Multiple linear regression models, taking into account within-subject correlations, were applied to investigate the role of urban pollution, atmospheric conditions, job variables and personal characteristics on the level of biomarkers. MTBE-U was influenced by the month of sampling and positively correlated to the time spent in traffic guarding, CO exposure and atmospheric pressure, while negatively correlated to wind speed (R^2 for total model 0.63, $P<0.001$). BEN-U was influenced by the month and smoking habit, and positively correlated to urinary creatinine; moreover, an interaction between CO and smoking was found ($R^2 = 0.62$, $P<0.001$). These results suggest that MTBE-U is a reliable marker for assessing urban traffic exposure, while BEN-U is determined mainly by personal characteristics.

1. Introduction

High levels of toxic compounds such as carbon monoxide (CO), particulate matter, benzene, and ozone are associated with traffic emissions. Pollution caused by vehicular exhaust fumes and vapors is one of the most important problems in urban environments, for the general population as well as specific occupationally-exposed groups.

The use of aromatic compounds and oxygenated hydrocarbons as addictives in petrol was introduced in the early 1980s to replace alkyl-lead compounds to promote a more complete fuel combustion and enhance octane rating. Oxygenated hydrocarbons include ethers, such as methyl *tert*-butyl ether (MTBE), ethyl *tert*-butyl ether (ETBE), *tert*-amyl methyl ether (TAME) and alcohols, such as methanol, ethanol, *iso*-butyl-, *iso*-propyl- and *tert*-butyl-alcohol. According to European Union (EU) regulations, oxygenates with 5 or more carbon atoms per molecule can be blended into petrol in any proportion up to 15% by volume (European Commission, 1998). The latest published EU Fuel Quality Monitoring Report shows that fuel sold in the EU25 contains 4.3% oxygenates (blending average) (European Fuel Oxygenates Association, 2005). In Italian fuel, only ethers are used as oxygenate additives, never as a mixture, with an average content of 3.5% (minimum 0%, maximum 15%) in 95 RON (Research Octane Number) petrol, with seasonal variation (3.7% in summer, 3.1% in winter) (European Commission, 2005). Aromatic hydrocarbons, such as benzene, toluene and xilenes, are present in fuels, with a permissible maximum content of 42% by volume. Benzene concentration in fuels sold in the EU must be less than 1.0% by volume (European Commission, 2005). In Italy, the average benzene content in 95 Research Octane Number (RON) petrol is 0.7% (minimum 0.29%; maximum 0.96%) (European Commission, 2005).

Many studies have assessed both acute and chronic toxicity of ethers. After introduction of fuels containing oxygenated compounds, headache, nausea and eye irritation were reported occasionally by subjects exposed occupationally, but evidence of a direct correlation between these symptoms and MTBE exposure are still lacking (IARC, 1999; McGregor, 2006). MTBE has been classified in group 3 (not classifiable as to its carcinogenicity to humans) by International

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Agency for Research on Cancer (IARC) (IARC, 1999). In the U.S., the National Toxicology Program has included MTBE, ETBE and TAME for in-depth toxicological evaluation for carcinogenesis testing in 1988–2003, deferring their overall evaluation pending receipt of industry testing data. For MTBE in particular, rodent cancer data have not been considered sufficient to list it in the 11th Report on Carcinogens (NTP, 2005). Benzene is classified as a known carcinogen to humans by IARC (IARC, 1987) and is a category 1 (R45) carcinogen according to the EU (European Commission, 2008a).

To regulate airborne exposure to MTBE, ETBE and TAME in working settings, the American Conference of Governmental Industrial Hygienists (ACGIH) recommends threshold limit values (TLV) of 50, 5 and 20 ppm (180, 21, and 83 mg/m^3) respectively, as a time-weighted average (TWA), during an 8 h work shift (ACGIH, 2005). Airborne benzene exposure is regulated in many countries. For example, a concentration of 1 ppm (3200 μg/m^3) is the EU occupational limit value (European Commission, 2004), and a TLV-TWA of 0.5 ppm (1600 μg/m^3) is recommended by ACGIH (ACGIH, 2005). Moreover, benzene environmental exposure also is regulated in Europe: a mean calendar year limit of 5 μg/m^3 is being enforced as of 1 January 2010 (European Commission, 2008b).

Both MTBE and benzene are found in urban air. MTBE has been found in the 0.2–10 μg/m^3 range, depending on the seasons, in European or US cities (Hellén et al., 2002; Kawamoto et al., 2003; Legreid et al., 2007; Meinardi et al., 2008). For benzene, data on ambient concentrations in several European cities were in the same order of magnitude (mean in the 2.5–20.7 μg/m^3 range) (Cocheo et al., 2000; Perez Ballesta et al., 2006).

The main source of MTBE in urban air is automobile traffic. Correlations between MTBE concentrations and other petrol combustion-related species such as CO and acetylene have been shown (Grosjean et al., 1998). Thus, the use of MTBE as a specific vehicular emission tracer emitted into ambient air through tailpipe exhaust and evaporation of petrol has been proposed (Chang et al., 2003). Benzene is produced by incomplete combustion of organic matter, so its presence in ambient air has multiple sources, such as traffic and industry emissions; major sources of personal exposure, besides air pollution, are smoking and environmental tobacco smoke.

Measuring compounds in blood and urine has been proposed to monitor occupational exposure to ethers and benzene. MTBE in blood or urine has been measured mostly in fuel-related exposure such as in station attendants or tank drivers (Ghittori et al., 2005; Hakkola et al., 2001; Saarinen et al., 1998; Vainiotalo et al., 1998), while only a few studies of traffic-related exposures have been performed (Lin et al., 2008; White et al., 1995). Several studies on the biological monitoring of benzene exposure were conduced, among which many were focused on traffic-related exposure such as in traffic policemen (Barbieri et al., 2008; Bono et al., 2005; Fustinoni et al., 1995, 2005; Manini et al., 2008; Tomei et al., 2001), and in public transportation drivers (Manini et al., 2006).

The aim of this study was to evaluate the use of urinary MTBE and benzene as biomarkers of exposure to urban traffic and to investigate ethers and benzene exposure of 130 urban traffic policemen in Milan, a city in Northern Italy with 1.3 million inhabitants characterized by intense automotive traffic. Personal exposure to airborne benzene (BEN-A) and CO, were measured during the work shift in different months, and urinary MTBE (MTBE-U), ETBE (ETBE-U), TAME (TAME-U) and benzene (BEN-U) were consistently measured in urine spot samples. Atmospheric data were also collected. The influence of personal exposure, meteorological variables, job activity and personal characteristics on biomarkers excretion was evaluated.

2. Materials and methods

2.1. Study design

The study was conducted in 2004 in Milan, Italy. One hundred-thirty urban traffic policemen, working in 8 out of 15 district headquarters, volunteered for the study. Eight different urban police districts were chosen to give a fair representative coverage of different areas of the city. The areas were all characterized by the presence of a crossing with a traffic volume of 1000–6000 estimated vehicles/hour in the morning rush hours (7:00–9:00 am) (Provincia di Milano, 2001). About 25,000 vehicles/day were counted in January 2004 in one of the crossing included in our study (Meinardi et al., 2008). Subjects having traffic duties at crossings in their job activities were included in the study. Sampling was performed in four different periods of the year: 24 subjects were investigated in May, 33 in July, 35 in October and 38 in December (two different districts for each month). Samplings were performed either in the morning (7:30 am–1:30 pm) or in the afternoon shift (1:30 pm–7:30 pm), from Monday to Friday. Data regarding personal characteristics and habits were collected by a questionnaire administered by a physician. The subjects were acquainted with the aims of the study and provided informed consent. No restriction to personal behavior during the sampling time was prescript to the subjects, including smoking. A time/activity diary with 20 min increments was completed by each subject during the work shift. The recorded time/activity data included details on indoor and outdoor environments where subjects spent their time during the personal sampling, as well as job activities (traffic duty at crossing, surveillance near schools or crossroads, fining in parking zones, working in office), movements (on foot, by tram, bus, car, bike, and motorbike), and smoking (number of cigarettes smoked before and during the work shift).

2.2. Atmospheric conditions

The Regional Agency for Prevention and Environment of Lombardy (ARPA) routinely monitors atmospheric pollution levels and meteorological data using a network of fixed monitoring stations, with 2 h averaged daily measurements being made available upon request. For the purposes of this study, meteorological parameters (wind speed, relative humidity, and atmospheric pressure), sampled by the monitoring station nearest to the individuals, were extracted to match the personal sampling times. Data were averaged over each sampling period.

2.3. Personal exposure sampling and analysis

Personal exposure to CO, as a measure of traffic exposure, and to airborne benzene (BEN-A) were monitored during the work shift (Cattaneo et al., 2010). Sampling probes were positioned 30 cm from the midpoint between nose and mouth. BEN-A was passively sampled using stainless steel sorbent tubes filled with graphitized carbon (Carbopack B, Sigma Aldrich, Milan, Italy). At the end of sampling, sorbent tubes were sealed with Swagelok 1/4" fittings with PTFE inserts and stored at 3 °C to avoid sample loss. BEN-A was measured within 48 h of sample collection after thermal desorption at 330 °C. A 5890 gas chromatography equipped with a flame ionization detector and with an automatic thermal desorption system ATD 400 (Perkin Elmer, Monza, Italy) was used to desorb and analyze chemicals. The efficiency of recovery from tube samplers was above 95% and the method quantification limit (LOQ) was 4.0 μg/m^3. Personal CO levels were monitored continuously with portable analyzers (Langan T15v, Langan Products Inc., San Francisco, CA) equipped with an electrochemical sensor which generates an electric voltage proportional to the airborne concentration and with an internal data logger programmed to collect data with a sampling frequency of 1 min. Instrument resolution was 0.057 mg/m^3. For the aim of this study, CO data are presented as 6-h weighted averages. The CO personal monitor had an integrated temperature probe to identify and correct unwanted data drift caused by extreme conditions (>30 °C). The temperature such measured was also used in the statistical analysis as a measure of personal temperature.