influence of GSTT1 null genotype on the offspring sex ratio of gasoline filling station workers

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The aim of this study was to investigate whether the occupational exposure to gasoline of men employed at filling stations affects the sex of their children. Altogether 115 offspring (47 males, 68 females) were identified within families of 49 men working in filling stations in Shiraz (Fars province, south of Iran) and 345 offspring (178 males, 167 females) from 147 families of unexposed persons from the general population of Shiraz, which were matched by age of fathers (±2 years) and number of children as a control group. The offspring sex ratio at birth (male proportion) in the filling station workers was significantly lower than the ratio in control group (OR = 0.65; 95% confidence intervals (CI) 0.42 to 0.99). Genotypes of glutathione S-transferase M1 (GSTM1) and T1 (GSTT1) were investigated on extracted genomic DNA of 37 exposed workers using the polymerase chain reaction based method. In exposed group with active GSTM1 and GSTT1 genes, offspring sex ratio was the same as the ratio in the control group (OR = 0.66; 95% CI 0.34 to 1.28). However, in the exposed group with active GSTM1 and null genotype of GSTT1, the offspring sex ratio statistically decreased (OR = 0.45; 95% CI = 0.21 to 0.96). It seems that GSTT1 null genotype has an effect on offspring sex ratio in the filling station workers.

Many demographic and environmental factors have been shown to be associated with variation in human sex ratio at birth. It has been shown that exposure to environmental toxins changes the sex ratio of live births in humans.1 There are several studies that have shown the association between fathers’ occupation and sex ratio of offspring.2–4 Male reproductive hazards may usefully be monitored by low offspring male to female ratio.5

The glutathione S-transferases (GSTs) are involved in cellular detoxification.6 The GSTs have been divided into a number of subclasses, α, μ, π, and θ. There are well-defined genetic polymorphisms in the expression of GSTM1 (a member of class μ) and GSTT1 (a member of class θ) enzymes with non-functional null-alleles named GSTM1-0 and GSTT1-0, respectively. The homozygosity for these null-alleles is associated with the absence of the corresponding enzyme activity.7,8 The GSTs involved in detoxification of several toxins including some of compounds present in gasoline.2 On the other hand, the reported data provide some evidence of an association between GSTs polymorphisms and risk of recurrent early pregnancy loss.9,10 Therefore, we speculate that paternal GSTM1 and GSTT1 genotypes might be associated with offspring sex ratio in gasoline filling station workers, who have long term exposure to gasoline.

METHODS

Using a simple questionnaire, number of sons and daughters of 49 men working in filling stations in Shiraz (Fars province, south of Iran) were determined. We identified 115 offspring (47 males, 68 females) within these families. The mean duration of employment in the filling station was 7.7 years (range 1.8–29 years). Because it is reported that paternal age and birth order have some effect on offspring sex ratio,11 for each exposed subjects, three unexposed persons from the general population of Shiraz (without occupational exposure to gasoline) were matched by age of fathers (±2 years) and number of children as a control group. In the control group, 345 offspring (178 males, 167 females) were identified.

Blood samples were obtained from 37 of 49 filling station workers participating in the study. Genomic DNA was isolated from whole blood. The polymerase chain reaction (PCR) conditions for determining GSTM1 and GSTT1 genotypes were the same as that reported previously.5,11 The absence of amplified product was consistent with the null genotype. Successful amplification by β-globin specific primers confirmed the proper function of the PCR reaction.11 The sex ratio expressed as the proportion of total live births that were male (male proportion). The odds ratio (OR) (the odds of being male) and 95% confidence intervals (CI) were calculated. An OR >1.0 indicates an increase in the sex ratio and an OR <1.0 indicates a decrease in the sex ratio. Comparison of paternal age and number of children was done using two tailed unpaired Student’s t test. A probability of p<0.05 was considered a significant difference.

RESULTS

The sex ratio at birth of exposed and unexposed groups were 0.409 (total birth = 115) and 0.516 (total birth = 345), respectively. The offspring sex ratio at birth in the filling station workers was significantly lower than the ratio in the control group (OR = 0.65; 95% CI = 0.42 to 0.99). Statistical analysis for the two other combinations was not performed, because the sample size was too small.

It should be noted that there was no statistical difference for paternal age (t = 0.86, df = 28, p = 0.40) and number of children (t = 0.72, df = 28, p = 0.48) between the group with two active genes and the group with active GSTM1 and GSTT1 null genotype.

Abbreviations: PCR, polymerase chain reaction; GST, glutathione S-transferase
populations. A few strong men could sire many grandchildren, and this supports the Trivers and Willard hypothesis in human males. There is some evidence that under favourable environmental conditions males would be more likely to sire offspring than females. This is disruption of detoxification processes of some gasoline metabolites. In this status conditions became unfavourable. The finding reported here is in agreement with the hypothesis of Trivers and Willard. They hypothesised that under favourable environmental conditions males would be more likely to sire offspring than females. This is disruption of detoxification processes of some gasoline metabolites. In this status conditions became unfavourable. The finding reported here is in agreement with the hypothesis of Trivers and Willard. They hypothesised that under favourable environmental conditions males would be more likely to sire offspring than females. 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