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Alcohol and Aldehyde Dehydrogenase Polymorphisms in Chinese and Indian Populations

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The association between two functional polymorphisms in alcohol dehydrogenase (ADH2/ADH1B) and aldehyde dehydrogenase (ALDH2) genes and alcohol dependence was examined in 182 Chinese and Indian patients undergoing treatment for alcohol dependence and 184 screened control subjects from Singapore. All subjects were screened by the Alcohol Use Disorders Identification Test (AUDIT). Patients were also administered the Severity of Alcohol Dependence Questionnaire (SADQ). Polymorphisms were genotyped by allele-specific polymerase chain reaction and selected genotypes confirmed by DNA sequencing or restriction fragment length polymorphism. Our results showed that frequencies of ADH1B*2 and ALDH2*2 were higher in controls compared to alcohol-dependent subjects for both Chinese and Indians. Frequencies of these two alleles were also higher in the 104 Chinese controls compared to the 80 Indian controls. None of the eight Chinese who were homozygous for both protective alleles was alcohol dependent. The higher frequencies of the protective alleles could explain the lower rate of alcohol dependence in Chinese.

Keywords alcoholism; alcohol dehydrogenase; aldehyde dehydrogenase; alleles; genetic polymorphisms

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Introduction

Several lines of evidence suggest that genes are involved in the etiology of alcohol dependence and abuse. For both alcohol dependence and abuse, twin studies show that the concordance rate for monozygotic twins is higher than same-sex dizygotic twins, and prevalence rate for adoptees is closer to biological than foster fathers (Prescott and Kendler, 1999; Schuckit and Smith, 2001; Warner and Rosett, 1975). In terms of drinking patterns and amount of alcohol consumed, there is also more similarity between genetically related individuals, being more alike for monozygotic twins than for same-sex dizygotic twins (Whitfield et al., 2004). The involvement of genes is further substantiated by the successful identification of positive regions from genomewide linkage studies (Corbett et al., 2005; Hill et al., 2004; Lappalainen et al., 2004; Long et al., 1998; Nurnberger et al., 2001; Prescott et al., 2006).

Alcohol abuse and dependence often occur together, although a significant proportion of alcohol-dependent individuals did not meet the criteria for alcohol abuse (Hasin and Grant, 2004). While abuse is likely to involve behavioral and psychosocial risk factors, alcohol dependence is closely related to an individual’s biological response to alcohol consumption. This response is known to have wide variability between individuals which is highly heritable, with the low response which is a risk factor for alcohol dependence several times more common in children of alcoholics (Schuckit, Smith, Kalmijn, and Danko, 2005; Schuckit, Tsuang, Anthenelli, Tipp, and Nurnberger, 1996). This difference in response is attributed to the actions of different allelic variants of genes encoding enzymes essential for alcohol metabolism. Among the genetic polymorphisms with the strongest effect on alcohol metabolism are the genes encoding alcohol dehydrogenase on chromosome 4 (ADH1B) and aldehyde dehydrogenase on chromosome 12 (ALDH2) and specifically the ADH2*1/2 Arg47His and ALDH2*1/2 Glu487Lys polymorphisms. Other genes which have been associated with alcohol use and dependence include other members of the alcohol dehydrogenase and aldehyde dehydrogenase families such as neurotransmitters such as gamma-aminobutyric acid A receptors, mu-opioid receptors, muscarinic acetylcholine receptors, neuropeptide Y and its receptors, and genes in the serotonin system such as the serotonin transporter and receptors (Higuchi, Matsushita, and Kashima, 2006).

Epidemiological studies show that the prevalence rates of alcohol dependence is different for different population groups (Hasin and Grant, 2004; Smith et al., 2006). Among the main ethnic groups in Singapore, the Indians most of whom originated from the Southern part of India have a high rate of alcohol abuse and dependence while the rate for those of Chinese ancestry is low (Kua, 1998). According to Singapore’s 1998 National Health Survey, among Singaporeans aged 18–69 years old, Chinese (2.9%) and Indians (2.9%) consumed alcohol more regularly than Malays (0.5%). There was no significant change in regular (defined as drinking at least 4 days a week) alcohol intake between 1992 and 1998 in all three ethnic groups. Indians (6.9%) had the highest prevalence of binge drinking (defined as consumption of five or more alcoholic drinks on a single occasion at least once during the past month) compared to Chinese (5.5%) and Malays (1.8%) (Ministry of Health, 1998). During the study period, treatment seekers were approximately 60% Indians and 40% Chinese when they comprised 8% and 70% of the population, respectively (Immigration and Checkpoints Authority, 2002).

In the present study, we sought to confirm the protective effect of ADH1B*2 and ALDH2*2 on alcohol dependence in these two ethnic groups in our population. The different rates of alcohol dependence in the two groups suggested that the population frequencies of the protective alleles might be different. There was also no previous report on the frequencies
of both functional polymorphisms for alcohol-dependent subjects of Asian Indian descent. Our study is the first comparing normal controls with alcohol-dependent subjects of Asian Indian descent. The results for the corresponding finding for subjects of Chinese ancestry in Southeast Asia were also presented.

Methods

Study Groups

The study was approved by the Hospital Ethics Committee. Chinese and Indian subjects between the ages of 19 and 71 (mean age 45 years old, SD ± 9.9; 70 Chinese males, 8 Chinese females; 98 Indian males, 6 Indian females) were recruited from patients who attended the addiction clinics at the Institute of Mental Health (IMH) and IMH’s Addiction Medicine Service located at Alexandra Hospital from 2001 to 2005. Patients were invited to join the study and written informed consent was obtained from those who met DSM-IV criteria for alcohol dependence after the study procedures were explained to them by a member of the study staff. Alcohol dependence was assessed by the Alcohol Use Disorders Identification Test (AUDIT) (Saunders, Aasland, Babor, de la Fuente, and Grant, 1993). The severity of dependence was assessed by the Severity of Alcohol Dependence Questionnaire (SADQ) (Stockwell, Murphy, and Hodgson, 1983). An English version of both tests was given to the subjects by a medical staff who was also a member of the study team and who would also answer queries and record the answers.

Controls between the ages of 19 and 65 (mean age 34 years old, SD ± 13.1; 30 Chinese males, 74 Chinese females; 26 Indian males, 54 Indian females) with no personal or family history of alcohol abuse were recruited from Chinese and Indian staff of Woodbridge Hospital. Control subjects were screened for alcohol abuse and dependence by structured interview and AUDIT. All subjects gave written informed consent after the study was explained to them by a member of the research team. All the samples were coded when sent to the laboratory for DNA extraction and genotyping to protect the identity of the subjects.

Laboratory Procedures

Genomic DNA was extracted from peripheral blood with the QIAamp Blood Kit (Qiagen Inc., Hilden, Germany). Duplex polymerase chain reaction with confronting two-pair primers (PCR-CTPP) was used to genotype the two polymorphisms (Tamakoshi et al., 2003). Some genotypes were also confirmed by PCR-RFLP according to Chen, Loh, Hsu, and Cheng (1997) and by DNA sequencing on MegaBASE 1000.

Statistical Analyses

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 11.5. Chi-square test was used to determine whether the distribution of genotypes was in accordance to Hardy–Weinberg equilibrium, and to assess difference in genotype distribution and allele frequency between groups. For multiloci analysis, difference in the distribution of genotypes and alleles between groups within each genotype was assessed by Fisher’s exact test due to the small numbers in each group. Bonferroni correction was applied for multiple testing in multiloci comparisons.
Results

Comparison Between Chinese and Indians

The distribution of the genotypic groups was in Hardy–Weinberg equilibrium for the two markers for both case and control groups in the two populations. For $ADH1B$, there was statistically significant difference in genotype distribution and allele frequencies between Chinese controls and Indian controls (genotype: $\chi^2 = 38.825$, d.f. = 2, $p = .000$; allele: $\chi^2 = 37.584$, d.f. = 1, $p = .000$). In the Chinese population, the allele with higher activity ($ADH1B^*2$ or His) that was reported to be protective was the major allele while for Indians the major allele was the lower activity wild type ($ADH1B^*1$ or His) as in Western populations. For $ALDH2$, the major allele in both ethnic groups was the wild-type allele ($ALDH2^*1$ or Glu) but there was still highly significant difference in genotype distribution between Chinese controls and Indian controls ($\chi^2 = 43.634$, d.f. = 2, $p = .000$). Difference in allele frequencies between the two groups was also statistically significant ($\chi^2 = 48.083$, d.f. = 1, $p = .000$). No Indian had the $ALDH2^*2/2$ genotype.

Because of the statistically significant differences in genotype and allele frequency for both markers between Chinese and Indians, subjects were stratified according to ethnic groups for comparison between cases and controls in subsequent analyses.

Chinese Samples

For both $ADH1B$ and $ALDH2$, frequencies for Chinese were similar to previous studies (Goedde et al., 1992; Muramatsu et al., 1995; Thomasson et al., 1991). There was statistically significant difference in genotype and allele frequencies between Chinese alcoholics and Chinese controls for both markers (Table 1). The direction of association was also the same as in previous studies; with the alleles identified to have protective effect for each marker present at higher frequency in controls compared to cases ($ADH1B$: OR = 0.253, 95% CI: 0.086–0.742 with allele $^*1$ as the comparison group; $ALDH2$: OR = 0.157, 95% CI: 0.071–0.347 with allele $^*1$ as the comparison group).

As there was significant difference in gender distribution between the case and control groups and there were significantly more males, a separate analysis was performed including only male subjects. With the smaller sample size the association with $ADH1B$ was no longer statistically significant (genotype distribution: $\chi^2 = 2.047$, d.f. = 2, $p = .359$; allele frequency: $\chi^2 = 1.187$, d.f. = 1, $p = .276$, OR = 1.511, 95% CI: 0.314–1.395). Analysis showed that the sample size has only 69% power to detect OR of 0.25 (OR obtained for Chinese samples in this study) or 18% for OR of 0.50 (OR obtained for Indian samples in this study). However, the association with $ALDH2$ remained (genotype distribution: $\chi^2 = 18.401$, $p = .000$; allele frequency: $\chi^2 = 16.893$, $p = .000$, OR = 0.107, 95% CI: 0.033–0.346).

Indian Samples

For the Asian Indian group that had not been studied previously, the trend for both markers was the same as for Chinese with both protective alleles at higher frequency for the control group (Table 1). However, the difference did not reach statistical significance ($ADH1B$: OR = 0.701, 95% CI: 0.459–1.072; $ALDH2$: OR = 0.572, 95% CI: 0.126–2.594). The frequency of the protective allele for both markers in this population which is geographically Asian was more similar to that reported for European populations than to populations of Asian origin such as Chinese, Japanese, or Koreans.
Table 1
Distribution of genotype and allele frequency of ADH1B and ALDH2 in the two ethnic groups

<table>
<thead>
<tr>
<th>Group</th>
<th>ADH1B(^*)</th>
<th>ADH1B(^*)</th>
<th>ADH1B(^*)</th>
<th>ADH1B(^*)</th>
<th>ADH1B(^*)</th>
<th>ADH1B(^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/1</td>
<td>1/2</td>
<td>2/2</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Chinese cases (78)</td>
<td>0.167</td>
<td>0.385</td>
<td>0.449</td>
<td>0.359</td>
<td>0.641</td>
<td></td>
</tr>
<tr>
<td>Chinese controls (104)</td>
<td>0.048</td>
<td>0.423</td>
<td>0.529</td>
<td>0.260</td>
<td>0.740</td>
<td></td>
</tr>
<tr>
<td>(\chi^2 = 7.079, p = .029)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian cases (104)</td>
<td>0.442</td>
<td>0.433</td>
<td>0.125</td>
<td>0.659</td>
<td>0.341</td>
<td></td>
</tr>
<tr>
<td>Indian controls (80)</td>
<td>0.300</td>
<td>0.550</td>
<td>0.150</td>
<td>0.575</td>
<td>0.425</td>
<td></td>
</tr>
<tr>
<td>(\chi^2 = 3.901, p = .142)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ALDH2(^*)</td>
<td>ALDH2(^*)</td>
<td>ALDH2(^*)</td>
<td>ALDH2(^*)</td>
<td>ALDH2(^*)</td>
<td>ALDH2(^*)</td>
</tr>
<tr>
<td></td>
<td>1/1</td>
<td>1/2</td>
<td>2/2</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Chinese cases (76)(^b)</td>
<td>0.882</td>
<td>0.105</td>
<td>0.013</td>
<td>0.934</td>
<td>0.066</td>
<td></td>
</tr>
<tr>
<td>Chinese controls (104)</td>
<td>0.538</td>
<td>0.356</td>
<td>0.106</td>
<td>0.716</td>
<td>0.284</td>
<td></td>
</tr>
<tr>
<td>(\chi^2 = 24.237, p = .000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian cases (104)</td>
<td>0.990</td>
<td>0.010</td>
<td>0</td>
<td>0.995</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Indian controls (80)</td>
<td>0.975</td>
<td>0.025</td>
<td>0</td>
<td>0.986</td>
<td>0.013</td>
<td></td>
</tr>
<tr>
<td>(\chi^2 = 0.701, p = .704)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Frequencies are rounded up to three significant decimal places and may not add up to 1.000.

\(^b\)Genotyping failed for two of the subjects.

Multiloci Analysis

Because of the small number of subjects in each group when distributed into the nine possible genotype combinations, there was not enough power to assess the effect of combined genotypes for both Chinese and Indian populations. To meaningfully apply statistical measures to assess the effect of each marker independently, comparisons were made for the three genotypes and two alleles of each marker while controlling for the genotype/allele of the other marker (Table 2). Among Chinese, the largest group comprised those homozygous for the wild-type allele (ALDH2\(^*1\)) with 67 cases and 56 controls. For this group with ALDH2\(^*1\)/\(^*1\) genotype, ADH1B genotype distribution was very similar for case and control groups with no statistically significant association between genotype or allele frequencies and alcohol dependence. For those who were heterozygous at this locus (ALDH2\(^*1\)/\(^*2\)), ADH1B genotype/allele appeared to have statistically significant association on the risk of alcohol dependence but the direction was opposite that expected. It could be a false positive association as the case group had only eight individuals. There was no significant association for the very small group of 12 individuals (1 case, 11 controls) homozygous for the protective allele (Table 2). However, the sample sizes of these two groups were small and the analysis might not be reliable.

When stratified according to the ADH1B genotype, there was statistically significant difference for ALDH2 genotype and allele frequency for the group with one copy of the ADH1B\(^*2\) (OR = 0.22, 95%CI: 0.066–0.747) or the group homozygous for this allele (OR = 0.029, 95%CI: 0.004–0.229). The number of Indians with ALDH2\(^*2\) was too small for a similar two-loci analysis.
### Table 2
Distribution of genotype and allele frequency for each marker among Chinese individuals (proportion within diagnostic class in parentheses) grouped according to genotype for the other locus

<table>
<thead>
<tr>
<th>Genotype and group</th>
<th>Genotype distribution(^a)</th>
<th>Allele frequency (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(ADH1B^*1/1)</td>
<td>(ADH1B^*1/2)</td>
</tr>
<tr>
<td><strong>ALDH2*1/1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese cases</td>
<td>33 (0.493)</td>
<td>26 (0.388)</td>
</tr>
<tr>
<td>Chinese controls</td>
<td>27 (0.482)</td>
<td>26 (0.464)</td>
</tr>
<tr>
<td>(Fisher's exact)</td>
<td>(\text{significant (corrected) = 1})</td>
<td>(\text{significant (corrected) = 1})</td>
</tr>
<tr>
<td><strong>ALDH2*1/2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese cases</td>
<td>1 (0.125)</td>
<td>3 (0.375)</td>
</tr>
<tr>
<td>Chinese controls</td>
<td>20 (0.541)</td>
<td>15 (0.405)</td>
</tr>
<tr>
<td>(Fisher's exact)</td>
<td>(\text{significant (corrected) = 0.015})</td>
<td>(\text{significant (corrected) = 0.003})</td>
</tr>
<tr>
<td><strong>ALDH2*2/2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese cases</td>
<td>0</td>
<td>1 (1.000)</td>
</tr>
<tr>
<td>Chinese controls</td>
<td>8 (0.727)</td>
<td>3 (0.273)</td>
</tr>
<tr>
<td>(Fisher's exact)</td>
<td>(\text{significant (corrected) = 1})</td>
<td>(\text{significant (corrected) = 0.936})</td>
</tr>
<tr>
<td><strong>ADH1B*1/1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese cases</td>
<td>4 (0.333)</td>
<td>8 (0.667)</td>
</tr>
<tr>
<td>Chinese controls</td>
<td>2 (0.400)</td>
<td>3 (0.600)</td>
</tr>
<tr>
<td>(Fisher's exact)</td>
<td>(\text{significant (corrected) = 1})</td>
<td>(\text{significant (corrected) = 1})</td>
</tr>
<tr>
<td><strong>ADH1B*1/2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese cases</td>
<td>26 (0.867)</td>
<td>3 (0.100)</td>
</tr>
<tr>
<td>Chinese controls</td>
<td>26 (0.591)</td>
<td>15 (0.341)</td>
</tr>
<tr>
<td>(Fisher's exact)</td>
<td>(\text{significant (corrected) = 0.087})</td>
<td>(\text{significant (corrected) = 0.021})</td>
</tr>
<tr>
<td><strong>ADH1B*2/2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese cases</td>
<td>33 (0.971)</td>
<td>1 (0.029)</td>
</tr>
<tr>
<td>Chinese controls</td>
<td>27 (0.491)</td>
<td>20 (0.364)</td>
</tr>
<tr>
<td>(Fisher's exact)</td>
<td>(\text{significant (corrected) = 0.000})</td>
<td>(\text{significant (corrected) = 0.000})</td>
</tr>
</tbody>
</table>

\(^a\)Frequencies are rounded up to three significant decimal places and may not add up to 1.000.
Discussion

Several studies have investigated the frequencies of polymorphisms in these two genes in various ethnic groups. It is found that the high-activity allele of alcohol dehydrogenase (ADH1B*2 or 47His) which is protective against alcohol abuse and dependence is only present in significant frequency in Middle Eastern and East Asian populations (Goedde et al., 1992; Hasin et al., 2002; Mulligan et al., 2003; Santos, Monteiro, and Thomasson, 1997). For aldehyde dehydrogenase, the protective effect of the allele deficient in catalytic activity (ALDH2*2 or 487Lys) is even stronger. To date, this null enzyme has only been documented in East Asians (Goedde et al., 1992; Mulligan et al., 2003; Oota et al., 2004; Santos et al., 1997).

Our results showed positive association between the two polymorphisms and alcohol dependence in our Chinese population, further extending the association to the Chinese in Southeast Asia. The Asian Indian population was investigated for the first time, with the trend being the same except that the difference did not reach statistical significance and the frequencies of the protective alleles were much lower overall. It should be pointed out that although these two groups in the study were classified based on their ancestry as defined by the country of birth of their ancestors, there would still be some genetic heterogeneity for both ethnic groups as both China and India are large countries with some differences between Southern and Northern areas. The Chinese in Singapore are mostly descendants of those who came from the two Southern provinces of China, Fujian, and Kwangtung in the 1800s and early 1900s. The Indians are mostly second, third, or fourth generation immigrants from various provinces of India. Approximately two-thirds are Tamil-speaking and originate from the South of India and Sri Lanka (Ceylonese Tamils).

For the two ethnic groups in this study with very different rates of alcohol dependence (Kua, 1998), statistically significant difference in genotype and allele frequencies was found. In the case of alcohol dehydrogenase β subunit encoded by ADH1B, the frequency of the protective allele ADH1B*2 in Indian controls (population with higher incidence of alcohol dependence) was 42.5% compared to 74% for the Chinese controls. The frequency of this allele in our study was higher compared to a previous study but the country origin of the Indian samples in that study was not stated (Goedde et al., 1992). For the Indians in Singapore, the majority were third and fourth generation migrants from the Tamil-speaking regions of Southern India (Chua, 1996).

For alcohol dehydrogenase, the protective allele with no enzyme activity was very rare in Indians at about 1% for controls, while its frequency in Chinese was close to 30%. Out of the 12 Chinese ALDH2*2 homozygotes identified in this study, only 1 was alcohol dependent, adding to the very small number of only 3 other alcohol-dependent ALDH2*2 homozygotes reported to date worldwide (Chen et al., 1999; Luczak, Wall, Cook, Shea, and Carr, 2004). This individual was heterozygous for the other marker (ADH1B). He did not have any family history of alcohol dependence but started drinking as a teenager. At the time of treatment he also had financial problem with debts from gambling.

Combined analysis of genotypes for both markers did not reach statistical significance for both ethnic groups but sample size was also small for such analysis. Controlling for the presence of the protective allele at either locus, there was statistically significant association for some groups for the Chinese population. However, the results should be interpreted with caution as the number in each group was small.

None of the eight Chinese who were homozygous for both protective alleles was alcohol dependent, showing that homozygosity for both polymorphisms offered almost
complete protection from alcohol dependence. This protection is not absolute as one alcohol-dependent individual with such combined genotypes has been reported in Taiwan (Chen et al., 1999).

**Study Limitations**

The major limitations of our study were the small sample size in each group, and that the controls and cases for both ethnic groups were not matched for both age and gender. The control group had more females and a lower mean age than the case group. Although we screened for family and personal history of alcohol abuse and dependence, some control subjects might still develop alcohol dependence in later life. However, given that family history is an important risk factor and all the control subjects had no family history, there would probably not be many such conversions.

**Conclusions**

Our results appeared to support the hypothesis that individuals might be protected from alcohol dependence due to the presence of genetic variants that influence alcohol metabolism and consequent drinking behavior. An inverse relationship between the frequencies of the protective alleles and the prevalence of alcohol dependence was noted for both high-risk (Indian) and low-risk (Chinese) groups. The population with higher prevalence of alcohol dependence seemed to have lower frequency of protective alleles for both enzymes. Within each ethnic group, frequencies of protective alleles for both enzymes were also higher in controls compared to alcohol-dependent individuals.

**Declaration of Interest**

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the article.

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**RÉSUMÉ**

Polymorphismes dans des gènes d’alcool déshydrégénase et d’aldéhyde déshydrégénase dans chinois et indiens

L’association entre deux polymorphismes fonctionnels dans des gènes d’alcool déshydrégénase (ADH2/ADH1B) et d’aldéhyde déshydrégénase (ALDH2) et la dépendance à l’alcool ont été examinées dans 182 patients chinois et indiens subissant un traitement.
pour la dépendance d’alcool et 184 patients criblés du groupe contrôle résidant à Singapour. Nos résultats ont montré que les fréquences des gènes ADH1B*2 et ALDH2*2 étaient plus élevées dans le groupe contrôle par rapport aux sujets dépendant de l’alcool à la fois pour les Chinois et les Indiens. Les fréquences de ces deux allèles sont également plus élevées dans les 104 contrôles chinois par rapport aux 80 contrôles Indiens. Aucun des huit Chinois qui étaient homozygotes pour les deux allèles protecteurs n’était fortement dépendants d’alcool. Les basses fréquences des allèles protecteurs Indiens de l’Asie devrait être confirmée dans un autre groupe d’échantillons d’indiens asiatiques.

RÉSUMÉN

Polimorfismos de la alcohol y de la aldehido deshidrogenasas en sujetos chinos e indios

La asociación entre dos polimorfismos funcionales en los genes de la alcohol deshidrogenasa (ADH2/ADH1B) y de la aldehido deshidrogenasa (ALDH2), y la dependencia alcohólica fueron examinadas en 182 pacientes chinos y indios tratados para la dependencia alcohólica y en 184 personas como control experimental de Singapour. Todos los sujetos fueron sometidos al test de identificación de enfermedades producidas por el consumo del alcohol. Los pacientes también recibieron el cuestionario sobre la gravedad de la dependencia alcohólica. El genotipaje de los polimorfismos se realizó mediante PCR de alelos específicos. Los genotipajes seleccionados fueron confirmados mediante secuenciación de ADN o mediante determinación del tamaño de los fragmentos digeridos por enzimas de restricción. Nuestros resultados demostraron que las frecuencias de ADH1B*2 y de ALDH2*2 eran más altas en los controles que en chinos e indios alcohólicos. Las frecuencias de estos dos alelos fueron también más altas en los 104 controles de sujetos chinos comparados a los 80 controles de sujetos indios. Ninguno de los ocho sujetos chinos que eran homocigotos para ambos alelos protectores era alcohólico. Las frecuencias altas de los alelos protectores podrían explicar el índice bajo de la dependencia del alcohol en sujetos chinos.

THE AUTHORS

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Glossary

Case–control methods: Comparisons of cases (defined as those that have a condition such as alcohol dependence) and controls (defined as those without the condition).

Concordance rate: The rate at which twins or siblings have the same affected status.

Genetic markers: A segment of DNA of specific sequence which is coinherited with a phenotype.

Polymorphism: A variation of common occurrence (>1% in the population) in the sequence of DNA.

Protective allele: A genetic factor which protects an individual against developing a specific condition or disease despite the presence of other risk factors.

Risk factor: A factor which increases the occurrence of a condition or disease and is overrepresented in affected individuals.

References


Alcohol and Aldehyde Dehydrogenase Polymorphisms


