VITAMIN D RECEPTOR TAQI GENE VARIANT IN EXON 9 AND APAI IN INTRON 8 IN UNCONTROLLED PAEDIATRIC ASTHMA.

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BACKGROUND

Asthma is a chronic heterogeneous respiratory disease with a strong genetic and immunological component and it affects about one of every five children in Ireland. The results of recent studies imply that vitamin D receptor (VDR) genetic variants may be associated with asthma. Fig. 1. We aimed a) to determine the VDR gene variants TaqI in exon 9 (T/C) and ApaI (C/T) between uncontrolled paediatric asthmatic and b) to investigate the impact of these polymorphisms in asthma susceptibility in relation to vitamin D status and other biochemical and immunological indices.

MATERIALS AND METHODS

In this study, carried out in Ireland (at a high latitude and during the winter season), 45 Caucasian children with uncontrolled asthma and 57 healthy volunteers participated. Outcome measured lung function, full blood count (FBC), biomarkers of allergy, immunity, airway and systemic inflammation. Serum 25-hydroxyvitamin D (25OHD), parathyroid hormone, total calcium, alkaline phosphatase, phosphate, total Ige, IgA, and C - reactive protein were analysed on the Abbott Architect c8000. Eosinophil cationic protein was performed on Phadia 250. The Interleukin-10 (IL-10) and Cathelicidin antimicrobial peptide were determined by human ELISA. FBC was measured on the Sysmex XE-2100D.

Genotypes of VDR TaqI and ApaI were determined using TaqMan® SNP Genotyping Assay on Applied Biosystems Real-Time PCR-7500. The software used for the statistical analysis was GraphPad Prism 5, Version 5.01.

RESULTS

We found that the distribution of T and C alleles and genotype frequencies differed significantly between asthmatics and controls for both polymorphisms (p value < 0.05). Tab.1. In uncontrolled asthma no association was found between VDR polymorphism and suppressed effects on action of 1,25(OH)2D. Table 1:

<table>
<thead>
<tr>
<th>Enzyme analysis</th>
<th>Patients n (%)</th>
<th>Controls n (%)</th>
<th>χ2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TaqI Genotypes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT (40 %)</td>
<td>18 (40 %)</td>
<td>34 (60 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT (46.7%)</td>
<td>21 (46.7%)</td>
<td>23 (46.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC (13.3%)</td>
<td>6 (13.3%)</td>
<td>0 (0 %)</td>
<td>9.737</td>
<td>0.008*</td>
</tr>
<tr>
<td>ApaI Genotypes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT (28%)</td>
<td>11 (28 %)</td>
<td>5 (9 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT (50%)</td>
<td>23 (50 %)</td>
<td>20 (35 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC (24%)</td>
<td>12 (24 %)</td>
<td>32 (56 %)</td>
<td>10.5</td>
<td>0.005*</td>
</tr>
</tbody>
</table>

* Denotes statistically significant.

Conclusions

This report, the first of its kind on Irish paediatric patients, suggests that the CC genotype and presence of C allele of VDR TaqI polymorphism and TT genotype and presence of T allele of VDR Apal are associated with uncontrolled asthma in children. Further studies are warranted to investigate the importance of decreased IL-10 levels and increased WBC in uncontrolled paediatric asthmatics with specific genotypes. These could help us to understand the mechanisms involved in the development of paediatric asthma.

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FIG.1

VDR polymorphism and suppressed effects on action of 1,25(OH)2D. (Adapted from D. Bikle 2010)

FIG.2

Average IL-10 levels According to TaqI genotypes. (Tukey’s Multiple Comparison Test: TT vs TC, p < 0.05*)

FIG.3

Average WBC levels According to TaqI genotypes. (Tukey’s Multiple Comparison Test: TT vs TC, p < 0.05*)

FIG.4

Average IL-10 levels According to Apal genotypes. (Tukey’s Multiple Comparison Test: CC vs TT and for TT vs CT, p < 0.05*)

FIG.5

Average WBC levels According to Apal genotypes. (Tukey’s Multiple Comparison Test: TT vs CC, p < 0.05*)

TABLE 1:

Genotypic analysis of VDR single-nucleotide polymorphisms TaqI (T=C) and ApaI (C>T) between uncontrolled paediatric asthmatic patients and control individuals.