PROJETO

"Aspectos Epidemiológicos da Infecção pelo Helicobacter pylori: transmissão intra-familiar, aquisição e eliminação espontânea da bactéria em crianças e frequência de anticorpos anti-CagA em uma população da área rural de MG"

Relatório Final

Relatório Técnico apresentado à FAPEMIG – Fundação de Amparo à Pesquisa do Estado de Minas Gerais, em cumprimento ao Processo CDS 687/01, vigente no período de 03 de dezembro de 2001 a 02 de dezembro de 2003.
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Relatório Final

Belo Horizonte, MG.

FUNDEP

Dezembro/2003
RELATÓRIO TÉCNICO

Nome do Pesquisador: Andreia Maria Camargos Rocha

Nº do Processo: CDS 687/01

Instituição: Universidade Federal de Minas Gerais

Área/subárea do projeto (por extenso): Ciências da Saúde

Título do projeto apoiado

"Aspectos epidemiológicos da infecção pelo Helicobacter pylori: transmissão intra-familiar, aquisição e eliminação espontânea da bactéria em crianças e frequência de anticorpos anti CagA em uma população de área rural de Minas Gerais"

O projeto está dentro da linha de pesquisa desenvolvida pelos pesquisadores do Laboratório de Pesquisa em Bacteriologia/FM/UFMG "Infecção por Helicobacter e doenças do aparelho digestivo".

Principais objetivos do projeto original:

1 - Determinar a prevalência da infecção bem como a prevalência de amostras de Helicobacter pylori com marcadores de virulência (Cag A) em adultos e crianças de Melquiades, MG;

2 - Avaliar os fatores de risco ambientais (nível sócio-econômico, uso de água não tratada, aglomeração, presença de rede de esgoto na moradia) associados à infecção pelo H. pylori;

3 - Avaliar a participação dos membros da família - pai, mãe e filhos - na transmissão do microrganismo por meio da comparação do perfil de anticorpos anti-H. pylori presentes no soro dos indivíduos infectados;

4 - Determinar as taxas de aquisição do microrganismo e de eliminação da infecção em crianças desta população.
Etapas executadas no período visando ao alcance dos objetivos:

1 - Realizada a colheita de material de crianças para a realização de teste respiratório. Para isso foram feitas duas "visitas" à região de Melquiades.

2 - Dados essenciais para a condução do projeto foram obtidos dos indivíduos através da aplicação de um questionário;

3 - As amostras obtidas para o teste respiratório foram enviadas ao Laboratório de Pesquisa em Bacteriologia onde foram realizadas as leituras dos testes;

Na realização das etapas 1, 2 e 3 participaram um estudante de mestrado (Luciana Silva) e três bolsistas de Iniciação Científica além de pesquisadores do Centro de Pesquisa René Rachou;

4 - O teste de ELISA para a pesquisa de anticorpos anti-H. pylori foi realizado em amostras de soro obtidas de adultos e crianças (idade superior a 12 anos) da região;

5 - A reação de Western blot foi realizada em amostras de soro dos indivíduos H. pylori-positivos, membros das famílias;

6 - ELISA para a pesquisa de anticorpos anti CagA foi realizada no soro dos indivíduos;

Na realização das etapas 4, 5 e 6 participaram estudantes de mestrado (Luciana Silva) e Iniciação Científica.

7 - Os dados obtidos foram analisados empregando o programa estatístico SPSS;

8 - Resultados parciais foram apresentados em Congressos Nacionais e Internacionais (anexo) e selecionados para apresentação oral no "XV International Workshop on gastroduodenal pathology and Helicobacter pylori. Atenas, 2002).

9 - O manuscrito foi publicado no "Tropical Medicine and International Health" 2003;8:987-991.
Apresentação e discussão dos principais resultados obtidos

Foram avaliados 673 indivíduos residentes em Melquiades, MG: 349 adultos e 324 crianças. A prevalência da infecção foi de 86,2% nos adultos e 51,9% nas crianças e aumentou progressivamente com o aumento da idade. Estes dados confirmam resultados obtidos por nós em populações de outras regiões do país como Araquai (região do Vale do Jequitinhonha, MG), Bela Fama (MG) e Nossa Senhora do Livramento (Mato Grosso do Sul). Nessas populações, a prevalência da infecção é bastante elevada tanto nos adultos como nas crianças. Considerando que o Brasil é um país de dimensões continentais e que a prevalência da infecção pelo H. pylori está relacionada a condições de vida dos indivíduos como, por exemplo, o número de cômodos da moradia, a presença de saneamento básico e os hábitos higiénicos, é essencial conhecer o comportamento da infecção em populações de diversas regiões do país, para que se tenha um conhecimento amplo das doenças a ela associadas, bem como das medidas de prevenção a serem tomadas.

Dos 673 indivíduos avaliados, 580 responderam a um questionário com dados sócio-demográficos. A análise pelo modelo de regressão logística mostrou associação entre a infecção e as variáveis idade e compartilhar a cama com outras pessoas na infância. Variáveis como sexo, presença de animais de estimação, uso de álcool e fumo e comer com as mãos não foram associadas à presença da infecção. Resultados semelhantes foram descritos por outros autores. Porém, na nossa população, é a primeira vez que a associação entre infecção e aglomeração, no caso, compartilhar a cama com outras pessoas na infância, é demonstrada. Este resultado reforça a hipótese de transmissão pessoa-pessoa do microrganismo (via oral-oral, fecal-oral ou ambas) também na população do Brasil.

A taxa estimada da aquisição da infecção variou de 5,8% nas crianças com menos de 5 anos de idade, 5,5% nas de 6 a 10 anos de idade e, aproximadamente 1% dos 11 aos 50 anos de idade. No grupo de indivíduos com mais de 60 anos de idade, esta taxa tornou-se negativa. Estes dados reforçam a ideia de que a infecção é adquirida
predominantemente na infância e que em países em desenvolvimento como o Brasil as crianças infectam-se principalmente em idade pré-escolar.

A pesquisa de anticorpos anti-CagA foi feita em 105 amostras de soro por meio do teste de ELISA. A frequência de anticorpos foi de 81,9% (65% em crianças e 92,3% em adultos), havendo aumento significativo com o aumento da idade. Estes resultados nos surpreenderam pois a frequência foi bem mais elevada que a observada em outras regiões do país e muito semelhante à observada por nós em doadores de sangue da Nigéria, África. O que determina esta alta frequência de anticorpos anti-CagA na população de Melquiades ainda precisa ser esclarecido. Também torna-se interessante verificar a prevalência das doenças associadas à infecção pelo H. pylori como úlcera péptica e carcinoma gástrico nesta população.

Quanto à transmissão intra-familiar, uma avaliação conduzida em 66 crianças de menos de 8 anos de idade e em seus pais (60), mães (63) e irmãos (134) mostrou que a prevalência da infecção foi maior nas mães de crianças infectadas que naquelas de crianças não infectadas (OR: 22,7; IC95% 2,3-223,21). Foi observado também que, ao contrário das crianças H. pylori-negativas, a maior parte das crianças infectadas tinha, pelo menos, 1 irmão infectado, bem como um número maior de irmãos (OR: 1,8; IC 95% 1,01-3,30). Estes resultados demonstram a importância da mãe e de irmãos na transmissão do H. pylori entre crianças na idade pré-escolar.

A transmissão intra-familiar foi também avaliada em 19 famílias, por meio da comparação do perfil de anticorpos anti-H. pylori empregando a técnica de blot. A concordância entre os perfis de anticorpos das amostras do mesmo domicílio foi analisada por meio do teste de Cohen's k e foi estabelecido um índice de número de comparações com concordância/número total de comparações. Desse modo 6 famílias apresentaram índice igual ou superior a 50%, 9 famílias apresentaram índice igual ou superior a 30% e inferior a 50% e, 4 famílias, índice inferior a 30%. Estes dados estão sendo analisados frente a aspectos genéticos relacionados à infecção com vistas a publicação de um segundo trabalho ("Role of additive genetic factors in the immune response to H. pylori infection").
Os objetivos propostos no projeto foram atingidos. Os resultados obtidos permitiram a aquisição de conhecimentos sobre importantes aspectos epidemiológicos da infecção pelo *H. pylori* como os fatores ambientais relacionados a uma maior prevalência da infecção e a importância da família, especialmente mãe e irmãos, na transmissão da infecção na população do Brasil. Além disso, o conhecimento da elevada frequência de amostras com marcadores de virulência nesta população abre caminho para novos estudos relacionados a doenças associadas a infecção pelo *H. pylori* nesta população.

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**Trabalho publicado em periódico internacional**


**Resumos publicados em periódicos internacionais**


Trabalho resumido em evento nacional


Dissertação de mestrado

Curso de Pós-Graduação em Medicina da Universidade Federal de Minas Gerais, área de concentração em Gastroenterologia

Aluna: Luciana Diniz Silva.

Co-orientadora: Profa. Andreia Maria Camargos Rocha


[Signature]
Transmission of Helicobacter pylori infection in families of preschool-aged children from Minas Gerais, Brazil

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Summary

We evaluated the role of the family in the transmission of Helicobacter pylori infection in preschool-aged children from a rural district in the State of Minas Gerais, Brazil. Sixty-six families (66 index children, 63 mothers, 60 fathers and 134 siblings), defined as at least one parent living in the same household with at least one offspring up to 8 years old, were studied. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by logistic regression controlling for age, gender, number of children in household and H. pylori status of the father, mother and siblings. The prevalence of the infection was 69.7% (469 of 673) and it increased with age (P < 0.001). Positive mothers were a strong and independent risk factor for infection (OR 22.70, 95% CI 2.31–223.21). Positive siblings were also positively associated with infection (OR 1.81, 95% CI 1.01–3.30).

Keywords Helicobacter pylori, transmission, epidemiology

Introduction

Helicobacter pylori is recognized as the main aetiologic agent of gastritis in humans and as an essential factor in the pathogenesis of peptic ulcer (NIH 1994). There is evidence that H. pylori infection is a risk factor in the genesis of the gastric carcinoma (IARC 1994) and mucosa associated lymphoid tissue (MALT) type gastric lymphoma (Wooterspoon et al. 1991).

The microorganism is responsible for one of the most frequent chronic bacterial infections and its acquisition seems to occur predominantly in childhood, especially at preschool age. In developing countries the prevalence of infection with H. pylori is low among children. This is in contrast to prevalence rates observed in developing countries, where most children are infected by 10 years of age (Graham et al. 1991; Sathar et al. 1997; Brown 2000; Nabwera et al. 2000). Although factors such as age, socioeconomic level and living conditions have been considered to be important risk factors for acquisition of H. pylori (Souto et al. 1998; Brown 2000; Malaty et al. 2001), the impact of other epidemiological aspects of the infection, such as the infection transmission pathways, are not clear.

Several studies have suggested that the family has an important role in the transmission of the infection (Malaty et al. 1991; Blecker et al. 1994; Ma et al. 1998; Dominici et al. 1999; Rothenbacher et al. 1999; Malaty et al. 2000). For example, Dominici et al. (1999) studied 416 Italian families and showed that children belonging to families where both parents were infected had significantly higher prevalence of H. pylori infection than children belonging to families where only one parent was infected. Rothenbacher et al. (1999), evaluating German children and their fathers or mothers, showed an association between maternal infection status and that of their children. Malaty et al. (2000) showed that H. pylori prevalence in Japan was significantly higher in children whose mothers were infected than in children whose mothers were uninfected. The authors also demonstrated a 1.5% seroconversion rate among children living with positive mothers. However, these previous studies had serious limitations which prevented them from fully describing the pathways of transmission between parents and offspring. For instance, Dominici et al. (1999) evaluated only children over 12 years of age, while Rothenbacher et al. (1999) failed to simultaneously measure the H. pylori status of mothers and fathers. Although Malaty et al. (2000) determined the H. pylori infection status of all family members, they did not evaluate the father's infection as a risk factor for infection of the child. Furthermore, all
of these studies except one (Ma et al. 1998) were carried out in developing countries, and in some of them the children were selected from clinical settings (Drumm et al. 1990; Blecker et al. 1994). In the only study conducted in a developing country, Ma et al. (1998) demonstrated that infection in the parents was significantly associated with infection in children. Despite the higher odds ratio (OR) observed among children with maternal vs. paternal infection, this difference was not statistically significant, possibly because of the small sample size of the study (Ma et al. 1998).

The aim was to determine the importance of the family in the transmission of H. pylori in preschool-aged children from a rural district in the State of Minas Gerais, Brazil.

Subjects and methods

This study was approved by the Ethics Committee of the Universidade Federal de Minas Gerais, Brazil and informed consent to take part was obtained from the children (whenever possible) and their parents, and from the adults.

The population studied was originally recruited in 1999 and 2000 to evaluate the prevalence of schistosomiasis in Melquiades, a rural area in the State of Minas Gerais, Southeast Brazil, with 867 inhabitants. The district is predominantly rural with subsistence agriculture and animal husbandry. All 197 households were visited. The overall response rate was 85.4% \((n = 168)\) of the homes surveyed, comprising 673 subjects. The annual increments in seropositivity for each period of 5 years for children and 10 years for adults were calculated by subtracting the non-susceptible population from the total seropositivity at the end of the period and dividing by the number of years in the period (Torres et al. 1998).

To evaluate the importance of the family in the transmission of the infection, the families were defined as follows: at least one parent living in the same household with, at least, one offspring up to 8 years of age. The first child with age ≤8 years was chosen as the index person for each family.

Helicobacter pylori infection was determined by ELISA for detection of IgG antibodies to specific H. pylori antigens in adults and children older than 12 years. As the sensitivity and specificity of serological methods for the diagnosis of H. pylori infection in children are low (Oliveira et al. 1999), the \(^{13}\)C-urea breath test was used in children under 12 years.

Serology

Sera were assayed for H. pylori antibodies using the Cobas Core anti-H. pylori IgG enzyme immunoassay (ELA) (Roche Diagnostic Systems, Basel, Switzerland), which had been previously validated for Brazilian population showing 95.4% and 100%, and 93.1% and 100% sensitivity and specificity, for adults and children over 12 years old, respectively (Rocha et al. 1998; Oliveira et al. 1999). The assays were performed according to manufacturer’s instructions.

\(^{13}\)C-urea breath test

The urea breath test was performed as follows: after a 6-h fast, one breath sample was obtained and an oral dose of urea comprising 50 or 75 mg \(^{13}\)C-urea if body weight was over 30 kg was administered with 100 and 200 ml of orange juice, respectively. The second sample was collected 30 min after the ingestion of the substrate. The breath samples were analysed by an isotope selective non-dispersive infrared spectrometer (NDIRIS; Wagner Analytical Systems, Bremen, Germany). A change of >4.05 in \(^{13}\)C-value over baseline was considered positive. The \(^{13}\)C-urea breath test is highly sensitive (99.5%) and specific (99.0%) for the diagnosis of H. pylori infection in our population even for children under 6 years of age (Cardinani et al. 2003).

Statistical analysis

Data were analysed with SPSS (SPSS Inc., Chicago, IL, USA) statistical software package version 10.0. The association of each variable with H. pylori infection was tested in univariate analyses. All variables with a P-value of 0.25 or less were included in the full logistic regression model. Odds ratios and 95% confidence intervals (CIs) were estimated, controlling for age, gender, number of children in household and H. pylori status of fathers, mothers and siblings.

Results

Of the 673 subjects evaluated, 349 were adults (162 men and 187 women, mean age 44.9 years, range 19–97) and 324 were children (161 boys and 163 girls, mean age 10.1 years, range 2 months to 18 years). The annual family income was less than US$2400 for 95% of the families. The population used water with no treatment and lived in dwellings with no sewer network.

The overall prevalence of the infection (469 of 673) was 69.7% (95% CI 66.0–73.1); 86.2% in adults (95% CI 66.0–73.1) and 51.9% in children (95% CI 46.3–57.4). The prevalence increased with age \((P < 0.001)\) and it ranged from 28.9% in children from 2 months to 5 years old to 90% in adults over 40 years old (Figure 1). The annual change in seroprevalence for children with ages:
Figure 1 Prevalence of Helicobacter pylori infection in children and adults from Melquiades, Brazil. The number above each bar indicates the number of positive individuals/number of tested individuals.

Figure 2 Estimated annual change in seroprevalence of Helicobacter pylori infection in Melquiades, Brazil, by 5- or 10-year periods.

(i) ≤5 years was 5.8%; 6–10 years was 5.5%; and 11–50 years was 1.0%. This rate decreased to 0.3% in persons aged 51–60 years. In individuals over 60 years old, the annual change in seropositivity became negative (Figure 2).

To evaluate the potential for intra-familial spread of H. pylori, 66 families (66 index children, 63 mothers, 60 fathers and 134 siblings) were studied. The index case, the mother and father were evaluated in 57 families; the child and the mother in six families; and the child and the father in three families. In these last families the sera could not be obtained from one of the parents, because they did not live in the household or they did not agree to participate. The prevalence of the infection in these groups was 47.0% (31 of 66) in children, 72.7% (48 of 63) in mothers and 68.2% (45 of 60) in fathers. In the group of parents of infected children, the prevalence of H. pylori infection was 90.0% whereas it was 61.9% (P = 0.0002) in the parents of non-infected children. Twenty-seven percent (18 of 66) of the children had more than two siblings: 32.2% (10 of 31) of the H. pylori positive and 22.8% (eight of 35) of the H. pylori negative (P = 0.392). The H. pylori-positive siblings (mean age 13.2 ± 4.6 years) of the negative-index children were significantly older than the infected siblings (mean age 11.5 ± 6.6 years) of the positive-index children (P = 0.04). In the univariate analysis H. pylori infection in the index child was associated with age, presence of infection in the mother, father and in the siblings (Table 1). Infection of both parents was also associated with infection in children (P = 0.001), but the risk associated with the presence of an infected mother (OR = 21.4) was greater than the risk associated with the infection in both parents (OR = 5.5), only the infected mother was included in the final model. In the multivariate analysis, only positive mothers and the number of infected siblings remained positively associated with the child’s infection. Helicobacter pylori status of the father was not associated with risk of infection in the offspring (Table 2).

Discussion

Although H. pylori infection is now recognized as a cause of digestive diseases, which has a major impact on public health, several epidemiological aspects of the infection are not fully understood. In this study, we used a healthy population, from a rural area with homogeneous

Table 1 Familial risk factors for Helicobacter pylori infection in 66 children up to 8 years old from Melquiades, Brazil

<table>
<thead>
<tr>
<th>Factors</th>
<th>Positive</th>
<th>Negative</th>
<th>P</th>
<th>OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (boys/girls)</td>
<td>16/15</td>
<td>16/19</td>
<td>0.633</td>
<td>1.3</td>
</tr>
<tr>
<td>Mean age (years ± SD)</td>
<td>5.3 ± 2.1</td>
<td>4.7 ± 1.9</td>
<td>0.241</td>
<td>1.1</td>
</tr>
<tr>
<td>Mother</td>
<td>29/01</td>
<td>19/14</td>
<td>≤0.001</td>
<td>21.4</td>
</tr>
<tr>
<td>Father</td>
<td>25/05</td>
<td>20/10</td>
<td>0.14</td>
<td>2.5</td>
</tr>
<tr>
<td>Positive siblings (≥2/2)</td>
<td>24/07</td>
<td>34/01</td>
<td>0.014</td>
<td>9.9</td>
</tr>
<tr>
<td>Number of siblings</td>
<td>2.2 ± 2.3</td>
<td>1.9 ± 1.3</td>
<td>0.524</td>
<td>1.1</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OD, odds ratio; CI, confidence interval; SD, standard deviation. * Univariate analyses.

Table 2 Adjusted OD for selected covariates on Helicobacter pylori positivity in children with age ≤8 years

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Adjusted OD</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.83</td>
<td>0.58–1.20</td>
<td>0.330</td>
</tr>
<tr>
<td>Positive mother</td>
<td>22.7</td>
<td>2.31–223.21</td>
<td>0.007</td>
</tr>
<tr>
<td>Positive father</td>
<td>0.72</td>
<td>0.14–3.75</td>
<td>0.701</td>
</tr>
<tr>
<td>Number of positive siblings</td>
<td>1.81</td>
<td>1.01–3.30</td>
<td>0.049</td>
</tr>
</tbody>
</table>

OD, odds ratio; CI, confidence interval. * Multivariate analysis.
socioeconomic status and sanitation conditions in order to minimize the number of variables possibly associated with H. pylori infection in the model of multivariate analysis.

As expected in poor, rural communities, the prevalence of the infection was high and it was significantly associated with increasing age. We also demonstrated, by evaluating the increments in H. pylori seropositivity, that by 10 years of age, 60% of the children were infected, suggesting that in Brazil most H. pylori infection occurs early in childhood. The observed pattern is similar to that reported in other developing countries (Ma et al. 1998; Torres et al. 1998).

From 11 to 50 years of age, there was a modest increase in seropositivity of approximately 1% per year. A decrease in the prevalence of infection was observed among individuals aged 60 years or older. This is a universal finding (Torres et al. 1998) which has been explained by the fall in general immunity among older individuals or by a decrease in bacterial load observed in older infected patients with gastric atrophy, which is an adverse condition for bacterial colonization.

Considering that H. pylori acquisition occurs mainly in childhood, we evaluated a large number of families and simultaneously the role of mother, father and siblings in the H. pylori status of preschool-aged children, adjusting for confounding factors such as age. Helicobacter pylori infection was much more prevalent in the parents of infected children (90.0%) than in those of H. pylori-negative children (61.9%). Furthermore, in families with both parents uninfected (n = 9), all children were H. pylori negative. However, in a multivariate analysis, only infected mothers remained associated with the infection of the children, even when the infection of both parents was included as a covariate in the model (data not shown). The association we observed between infection in mothers and their children, but not between fathers and offspring, may be explained by the fact that in Brazilian families, like in other countries (Ma et al. 1998; Malaty et al. 2000), the mother is the primary caretaker of children.

We also observed a positive association between positive siblings and infection in the child index. Similarly, Goodman and Correa (2000), studying rural Andean children younger than 10 years of age, observed that the risk of infection increased with the number of siblings in the household and that the number of H. pylori-positive siblings had a particularly strong gradient effect. However, Malaty et al. (2000) observed that Japanese children who seroconverted had older seronegative siblings or were the only child in the family. They hypothesized that the transmission between siblings may occur more commonly in families from developing countries, where there are several children in each family. Thus, our results suggest that children are more exposed to infection by close personal contact with infected mother and siblings.

In conclusion, the acquisition of H. pylori infection in a rural population of Brazil occurs mainly in childhood. Infected mothers or siblings may have a primary role in the transmission of the infection, which suggests person-to-person as the most important mode of passing the infection. Knowledge of the mechanism of mother to child transmission is important for the spread of H. pylori infection, as it could allow the identification of target groups for eventual interventions.

Acknowledgement

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Abstracts of Scientific Presentations
prevalence of H. pylori antigen was found between S. aureus positive specimens and all other groups: H. pylori vs. H. pylori x E. coli p=0.0013; S. aureus vs. rotavirus p=0.0017: S. aureus vs. controls p=0.0043.

Conclusions: H. pylori infection in small children is associated with S. aureus gastrointestinalis, but not with salmonella or rotavirus gastrointestinalis. The association warrants further investigation.

6.13 Role of host additive genetic factors in the immune response to H. pylori infection

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Our previous study pointed to the importance of intracellular transmission of Helicobacter pylori infection. However, an aspect overlooked was the overlap between shared residence and kinship. Therefore, we evaluated the influence of demographic, environmental and host additive genetic factors in the acquisition of HP infection and in the immune response to the infection. 583 subjects were studied. Genealogical, demographic and environmental informations were collected by interview. Multihousehold, extended pedigrees were constructed using the pedigree data management system PEDSYS. Individuals were defined as belonging to the same pedigree if they were related biologically to any one of the H. pylori in the pedigrees. Unrelated spouses and 10 unrelated single individuals were retained and included to improve the estimation of non-genetic effects. The individuals could be assembled into 6 extended pedigrees with more than 15,000 relative pairs, and nearly one quarter of these are third degree relatives. H. pylori infection was determined by ELISA and PCR in area birth test (younger than 12 yrs.). The data were analyzed by logistic regression to evaluate risk factors associated with the infection and by multivariate analysis (covariates data) to study the familial immune response (HP-positive patients). Infection was associated with age (p<0.01) and much more proximally (shared residence or bed; p=0.006) that accounted for 41% and 24% of infectivity, respectively, but not with gender, socio-economic level, sanitation, water supply, alcohol use, smoking, having pets and a helmet infection. Infection did not have also a genetic compound. In order to the immune response, host additive genetic factors accounted for 70% of IgG response to HP antigens (p<0.001). Age remained as an important factor. This study adds to the literature on the genetic component of HP infection by demonstrating the role of additive effects of genes in immune response, but not on infectivity, that depends on age and shared residence. Supported by FAPEMIG, CNPq(Brazil).

6.14 Prevalence of H. pylori infection and its association with environmental conditions in Warsao Lineage communities of Delta Amacuro State, Venezuela

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Helicobacter pylori colonization about 50% of the world population and it has been reported that prevalence of H. pylori infection in children varies between 10% and 80%. The purpose of this study was to evaluate H. pylori infection prevalence in children and adults of indigenous communities of Delta Amacuro State of Venezuela. The evaluation was performed in 98 children (mean age 7 ± 3.37 years) and their mothers (53.96 ± 13.77 years) from two communities of Warsao lineage. Anti-H. pylori serum IgG and secretory anti-H. pylori IgA antibodies were determined, as well as total secretory IgA and H. pylori antibodies in feces; a bacteriological analysis for water quality in the corresponding communities was also carried out. Serological prevalence of H. pylori infection was 38% in children and 84% in women. Children from the community that had the most deficient sanitary and environmental conditions had significantly lower titers of specific IgG antibodies and total secretory IgA (P<0.0001) and a high percentage of them had H. pylori antigens in their feces (P<0.0001), whereas water quality studies reported a larger number of total coliform colonies. The levels of specific IgA were positive and similar in both groups. The results indicate that in these populations there is a high prevalence of H. pylori infection and that environmental conditions can modulate the immune response directing the course of the infection. Grant FONACIT 96001408

6.15 Helicobacter pylori infection in Polish shepherds and their families from Tatra Mountains

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Background: Helicobacter pylori (Hp) infection is widespread but the rates of transmission are unclear and non-human reservoirs (domestic animals) of Hp have been proposed by several authors. Since then, Hp infection might be considered in some instances as zoonosis. The aim of this study was to assess the Hp prevalence in Polish Tatra Mountains shepherds and in their families as compared to controls not contacting sheep at all.

Methods: 42 shepherds from Tatra Mountains (mean age 46 ± 17.6 yr) with full contact with sheep, 28 members of their families with incidental contacts (mean age 45.4 ± 19.1 yr) and 61 age- and gender-matched controls without such contacts were involved in this study. Hp detection was performed using our low dose (about 40 mg of urea) capsulated 13C-Urea breath test (UBT). Serology was used to measure anti-Hp and anti-CagA IgG. Plasma gastrin concentrations, interleukin-8 (IL-8) and tumor necrosis factor-alpha (TNF-alpha) were also measured using either RIA or ELISA methods.

Results: The prevalence reached 97.6% in shepherds, 86% in their family members, but significantly less 65.1%, in controls without contacts with sheep. Anti-Hp IgG, anti-CagA in control groups were significantly higher than in controls. Also plasma gastrin concentrations, IL-8 and TNF-alpha values were had significantly higher that in controls.

Conclusions: Shepherds showed almost 100% Hp prevalence and higher incidence of CagA serositivity, plasma gastrin and pro-inflammatory cytokine concentrations. Considering 100% positive UBT in sheep, it may be reasonable to suggest that Hp infection in shepherds and their family members originate from sheep and Hp infection might be, therefore, considered as zoonosis.

6.16 Vector potential of cockroaches for Helicobacter pylori

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Background and Aims: The route by which humans become infected with Helicobacter pylori (Hp) is still unknown. As one of the possible routes of infection, vectorial spread by houseflies has been suggested, while no other possible vectors have been reported. We have chosen to study cockroaches as another possible vector to determine if they could transmit Hp.

Materials and methods: We used a common species of cockroaches (Periplaneta fuliginosa) and the Sydney strain of Hp. After 3-day fasting, freshly grown Hp on an agar plate was used to challenge the cockroaches. The roaches were kept in a disinfected container. As controls, a sterile agar plate without H. pylori was given to cockroaches in another container. After 24-hour challenge period, the plates were removed and autoclaved food and water was provided to the roaches. Excreta of the cockroaches were sampled for testing by culture, rapid urease test, and PCR analysis. To avoid contamination, all cockroaches were removed to a new disinfected container after each sampling.

Result: Hp colonies, whose identity was confirmed by PCR were cultured on Day 1. Positive rapid urea test results were confirmed up to Day 3. PCR analysis showed most of the samples to be positive up to Day 7. After Day 7, all samples were negative. In control group, all samples were negative.

Conclusions: Culturability, viability and existence in excreta of cockroaches led us to believe that Hp was shown in this study. Cockroaches usually live in insanitary environments with a variety of bacterial pathogens, including Hp. They, like houseflies also habitually ingest foodstuffs and/or food contamination areas (e.g., pantries) such that they have direct access to foods we consume daily. In developing countries or rural areas with poor sanitation facilities, dissemination of Hp infection could achieve via inadvertent ingestion of foods contaminated with reach excreta containing viable Hp.
Gastroenterology 

Digestive Disease Week 
and the 
102nd Annual Meeting of the American 
Gastroenterological Association 
May 20-23, 2001, Atlanta, GA 

Program of the Annual Meeting of the American 
Gastroenterological Association, the American 
Association for the Study of Liver Diseases, the 
Gastroenterology Research Group, the Society for 
Surgery of the Alimentary Tract, and the American 
Society for Gastrointestinal Endoscopy 

Abstracts of Papers Accepted by the American 
Gastroenterological Association 

Abstracts of Papers Accepted by the American 
Association for the Study of Liver Diseases 

Abstracts of Papers Accepted by the Society for 
Surgery of the Alimentary Tract
662 Natural History of Helicobacter pylori infection from infancy to adulthood: A 21-year follow-up Cohort Study

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Aim: To examine H. pylori infection from infancy to young adulthood. Methods: A longitudinal cohort was selected retrospectively from a population followed over a 21-year period. 220 children (144 boys; 51% females) first studied in 1978-79 at ages 1, 2, and 3 years were re-examined at 18 months through 1998-99 as young adults. H. pylori status was assessed by presence of serum IgG H. pylori antibodies. Results: 9% of the cohort had H. pylori infection at ages 1-3. There were no associations with age or gender. There was a significant association with race (14% at blacks vs. 4% in whites, p = 0.008). By 10-20 years, the infection rate was higher and remained significantly higher among blacks (20% in blacks vs. 10% in whites). The seroconversion rate was higher at ages 2-5 and 7-9% at ages 13-15. 15% at ages 18-20 and 20-23% at ages 21-23. 45% (10% in non-infected children at age 1) became infected at age 21. 7% became infected after age 21. 7% of children were infected at H. pylori at ages 2-4 and 12-15% of children were infected after age 21. The infection persisted into young adulthood. The incidence of infections was higher after the age of 10. The highest rate of loss was before age 5. These findings suggest that treatment and preventive strategies must be aimed at the children below the age of 5.

664 The Natural History of H. pylori (HP) Infection in Asymptomatic Individuals: Should We Test and Treat Everyone?

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Background: The natural history of asymptomatic HP infection in Caucasian subjects is unclear. Consequently, there is uncertainty about whether eradication is worthwhile in asymptomatic subjects. Aim: To determine the outcome of persistent HP infection in asymptomatic subjects compared with subjects with successful eradication over a 10-year time frame. Methods: In 1990-92, 359 healthy blood donors agreed to be re-examined after 10 years to test for HP. 230 donors were found to be eradicated, the table shows the incidence of intestinal metaplasia (IM) over the follow-up interval evaluating ulcer disease in 9.12%, 3.6 duodenal, 1.9 gastric, and 3.5% of the eradicated groups respectively. The odds ratio for IM development was 3.85 (95% CI 1.6-7.7) for HP positive donors compared to HP negative donors. A positive IM was present in 17 of 38 (55%) HP positive subjects with IM. The odds ratio for the development of IM was 3.0 (95% CI 1.5-6.1) for H. pylori - Cag A samples. Conclusion: Over a 6.5-year follow-up period HP - asymptomatic donors have a 3.5 fold increased risk of developing IM compared to HP- donors. 2 Cag A positive strains were associated with a 3 fold increased risk of IM compared to Cag A negative strains. The risk for developing ulcer disease is 1.5 fold higher in asymptomatic subjects. These results support the need for eradication even in asymptomatic subjects.

665 Transmission of H. pylori Infection: Study of Families of Primary-aged Children in Brazil

Dionne M M, Guerreiro, Gilce A. Roga, Andresa Santos, Ana C. Bocchiatti, Andreia M C Rocha, Ushik Feijes de Barros, Braco Horizonte Brazil; Andrea Boccia, Crs de Pesquisa Renata Rocha, Prot Nesse Renata Rocha, Braco Horizonte Brazil. Background: Several studies have demonstrated that family has an important role in the transmission of H. pylori. However, these studies have been done in developing countries and most of them have been limited by the small sample size. Therefore, we evaluated the role of the family in the transmission of the infection among preschool-aged children living in a rural area of the State of Mato Grosso, Brazil. The study was supported by municipal water and lives in dwellings with no sewer network. The annual income was less than US$ 2,500.00 for 95% of the families studied. Subjects and Methods: Firstly, we determined the prevalence of infection in 29 children and 300 adults. Children aged 2 months to 35 years old. H. pylori infection in children > 12 years old and adults was evaluated by ELISA (Coates-Corey, Roches. in children < 12 yrs the test was diagnosed by 42 sera breath test (100% sensitive and specific for our population, even in children < 8 yrs old). In children > 8 yrs old and families (63 mothers, 69 fathers and 132 siblings) were studied in order to determine the role of the family in the transmission of the infection. The oldest child in each family was considered the index case. Then, we evaluated < 15 yrs old and their families (63 mothers, 67 fathers and 132 siblings). Use of food and clothing items was measured by logistic regression, controlling for age, gender, number of children in household and risk status of siblings. Results: The prevalence of the infection was 24% (CI 0.88-0.97) in children 2 months to 12 yrs old and became significant at those over 60 yrs old. In the group of preschool children 41% were HP positive and positive mothers were a strong and independent risk factor for infection (OR = 2.13, CI 2.61-1.75). Positive siblings were also significantly and positively associated with infection (OR = 1.5, CI 1.2-1.85). When all children were analyzed, a positive and independent association was also observed between H. pylori infection (OR = 1.2, CI 1.1-1.3). In both groups the association was observed between positive fathers and risk for infection. Conclusion: Concordance of infection status among siblings and offspring as well as among age-mate but not others is consistent with person to person transmission of H. pylori infection.

666 A 21-Year Cohort Study of the Seroprevalence of Helicobacter pylori Infection and Helicobacter A virus in Rural Japan

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Background: Recent studies have compared the seroprevalence patterns of Hp pylori and Helicobacter A virus (HAV) in attempts to establish the definitive mode of transmission of H. pylori infection. The aim of this study is to evaluate the seroprevalence of Helicobacter A virus and Helicobacter pylori in Japan. Methods: We conducted a cohort study of Japanese children and adults residing in rural Japan who were monitored from 1978 to 1994. Each individual completed questionnaires and a blood sample was collected. The seroprevalence of H. pylori and HAV infection was determined by ELISA. Results: The overall seroprevalence of H. pylori infection was 63.4% in children and 67.8% in adults. In adults, there was no significant difference between age groups. During the 7-year follow-up study, the seroconversion rates (i.e., the incidence of HAV infection) were 0.0% and 0.7% per year for children and adults, respectively. During the follow-up period, there was no significant difference between age groups. The seroprevalence of HAV was 9% among adults and 16% among children. The prevalence of both infections increased parallel with age. The prevalence of HAV infection in the children group was 63.4% and in the adults group was 67.8%. There was a significant difference between the two age groups. The seroprevalence of HAV was 16% among children and 9% among adults. In both groups, the seroprevalence of both infections among the population is a marker for the level of sanitation and hygienic practices.
Universidade Federal de Minas Gerais

Pró-Reitoria de Pesquisa

II SEMANA DO CONHECIMENTO DA UFMG
X SEMANA DE INICIAÇÃO CIENTÍFICA

21 a 23 de Fevereiro de 2002

BELO HORIZONTE – MG
2.214. FATORES DE RISCO PARA A PRESENÇA DE CICATRIZES REFINADAS NA ADIÇÃO DE PACIENTES COM REFLUXO VÉSECO-UРЕTERAL PRIMÁRIO.


DEPARTAMENTO DE PEDIATRIA

ÁREA PEDIATRIA

PALAVRAS-CHAVE: CICATRIZ RENAL / REFLUXO VÉSECO-UРЕTERAL PRIMÁRIO

Objetivo: Identificar fatores associados à presença de cicatrices renales na admissão dos pacientes portadores de RVUP na UFP entre 1969-1990.

Metodologia: Prontuários de 402 pacientes foram revisados. Desses, 394 (98%) foram avaliados na admissão quanto ao dano renal. Os métodos de avaliação foram UE, DMSA e US. O método variou com a época de admissão: 94% dos pacientes admitidos até 1985 foram submetidos a UE; após, 71% foram submetidos a DMSA ou US. Variáveis analisadas foram: sexo, idade do diagnóstico, pressão arterial, função renal e dano renal. O reflexo foi encontrado em 2 vezes maior do que a UE (p < 0,001). Variáveis não associadas a dano renal: sexo (p = 0,13), cor (0,45), idade do diagnóstico (< 6 meses), diagnóstico fetal (0,61), reflexo bilateral (0,12) e fatores variáveis (0,66). No reflexo bilateral, variáveis preditivas de dano renal: reflexo bilateral > 18 mm (RR = 1,43, IC95% = 1,14-1,80, p < 0,003), refractário acima de 2 anos de idade (RR = 1,8, IC95% = 1,11-2,89, p = 0,006) e reflexo maior que 22 mm (RR = 2,35, IC95% = 0,56-0,98, p < 0,001). A associação entre reflexo e cicatriz renales foi: 3 (55%), 1 (29%), 1 (2%) e 1 (2%) (V = 77%). Conclusões: Houve associação entre reflexo e dano renal a admissão com reflexo no diagnóstico e com reflexo maior ou igual a III.

APOIO: CNPQ / PROGRAD


DEPARTAMENTO DE PROFEDÊNCIA COMPLEMENTAR

ÁREA: GASTROENTEROLOGIA

PALAVRAS-CHAVE: EPINEFRINA; EPINEFRINA / CLÁSSICA

Objetivo: Avaliar o efeito da administração de epinefrina na maternidade do Hospital das Clínicas (UFMG) nos partos ecológicos, no período de 1995-2000.

Metodologia: Foi realizado um estudo prospectivo, observacional, no qual foram incluídos 150 partos consecutivos. Os partos foram divididos em dois grupos: grupo A (n=75) e grupo B (n=75). Os partos do grupo A receberam epinefrina nas doses de 5mg/min, enquanto os do grupo B receberam placebo. Os resultados foram analisados através de testes estatísticos adequados.

Conclusões: Não houve diferença estatisticamente significativa entre os dois grupos em relação à taxa de parto prematuro, taxa de cesariana e taxa de morbidade neonatal.

APOIO: CNPQ / FAPERJ

II Semana do Conhecimento da UFMG

X Semana da Iniciação Científica

21 a 23 de Fevereiro de 2002
Infecção pelo *Helicobacter pylori*: prevalência e transmissão intra-familiar em uma população da área rural de Minas Gerais

Dissertação apresentada ao Curso de Pós-Graduação em Medicina da Faculdade de Medicina da Universidade Federal de Minas Gerais, como requisito parcial para a obtenção de título de Mestre em Medicina.
Área de concentração: Gastroenterologia

Orientadora: Profª Dulciene Maria de Magalhães Queiroz
Co-orientadora: Profª Andreia Maria Camargos Rocha

Universidade Federal de Minas Gerais
Belo Horizonte
2002