RECOMMENDATION

1- The critical period of *H. pylori* acquisition is in childhood so, genotyping at childhood is important in future policies for the identification of those at risk of sever disease and will help in planning of eradication programme.

2- The relation between the genotypes of causative strain and clinical outcome should be considered in different geographic regions in order to make a true estimation of prognosis.

3- Further studies are needed to clarify the exact pathognicity role of babA2 gene also with the use of animal models and with in vitro studies.

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RELATIONSHIP BETWEEN HELICOBACTER PYLORI GENOTYPES, CLINICAL MANIFESTATION AND SEVERITY OF GASTRITIS IN CHILDREN

العلاقة بين موروثات الميكروب الحلزونى وشدة المظاهر السريرية والتهابات المعدة عند الأطفال

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الباحث المساعد

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INTRODUCTION

Helicobacter pylori is a spiral, microaerophilic, gram negative bacterium that permanently colonizes gastric epithelial cells in approximately 25% of the population in developed countries and 70% - 90% in developing countries.[1]

Humans appear to be the only reservoir of H.pylori infection and therefore human contacts remain the major mode for its transmission. Iatrogenic spread through contaminated gastrointestinal equipment has been documented.[2] Water has been shown to be a source for H.pylori infection.[3]

Histological gastritis is essential universal among H.pylori infected individuals .Whereas most infected individuals are asymptomatic, chronic H.pylori infection in susceptible individuals is associated with a variable degree of mucosal damage ranging from mild gastritis and ulcer disease to gastric carcinoma and mucosa–associated lymphoid tissue (MALT) lymphoma.[4] One reason for this phenomenon may be the different pathogenicity of infective H .pylori strains.[5]

The most important virulence determinants of H. pylori are CagA protein and the vaculating cytotoxin A (VacA)[6,7] .Approximately 50% to 60% of H. pylori contain the cagA gene, encoding the CagA protein.The cagA gene is part of cag pathogenicity island (cagPAI),which contains many genes that are related to the virulence and pathogenicity of H. pylori strain. The presence of cagA is a confirmed marker for cag PAI and is associated with more virulent H. pylori strains.[8-10]

5.

The vaculating cytotoxin A gene, which is another important virulence factor of H. pylori, encodes an 87 kD protein that induces vaculation of epithelial cells[11]. The vacA gene is present in all strains of H. pylori and comprises two variable parts. The H. pylori strains have one of two types of vacA signal sequence (s1 and s2)and two types of mid region (m1 and m2).[12,13]

Among the bacterial factors, the ability to adhere to epithelial cells is crucial in the initiation of a gastric inflammatory response.[14-16]. The blood group antigen-binding adhesion BabA has been shown to mediate adherence of H. pylori to human Lewis b (a-1,3/4-difucosylated) blood group antigens on gastric epithelial cells [5]. This attachment resulted in the development of chronic gastritis and gastric atrophy.[16-18]

AIM OF THE WORK

The aim of the work is to correlate the virulence factor, (cagA, VacA and BabA2) with:

1- The histologic parameters of H.pylori related gastritis.

2- The clinical presentations.

7.

PATIENTS

Fifty patients infected with H.pylori (stool Ag positive) referred for endoscopy with upper gastrointestinal symptoms (mostly recurrent abdominal pain, haematemsis...etc.), suggestive of organic disease and severe enough to require endoscopic evaluation, will be included in the study.

Informed consent from the parents will be obtained.

Exclusion criteria were treatment with antisecretory, antimicrobial, or anti-inflammatory medication, for the 3 months preceding the endoscopy.

Twenty five clinically health children (no gastrointestinal symptoms) with H.pylori stool antigen positive will be included as a control group.

8.

METHODS

All patients of this study will be subjected to the following:

1- Through history taking and clinical examination with special stress on age and clinical manifestation, exclusion of patients who received proton pump inhibitor or antibiotic for the last three months.

2- Upper GIT endoscopy (after written consent):

Biopsy specimens will be systemically taken from duodenum, gastric antrum, and body. One of gastric biopsies will be processed for rapid ureasc test, other biopsy specimen will be processed, paraffin blocked, sectioned into 5μm thick section and submitted for the following:

1- Histopathological assessment according to Sydney classification for gastritis.

2- The Polymerase clain reaction will be used to detect cagA, vacA and $babA_2$ genes of H.pylori using specific primers.

3- In the stool specimens of the control group, polymerase clain reaction will be used to detect cagA, vacA and $babA_2$ genes of H.pylori using specific primers.

9.

RESULTS

The results will be tabulated and analyzed using appropriate statistical methods.

10.

DISCUSSION

Results will be discussed in view of achievement of the aim and compared with other studies published in the literature.

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الملخص العربى

تعتبر الاصابه بالعدوى بالميكروب الحلزوني من العدوى البكتيريه الشائعه عالميا. وقد اصاب اكثر من ثلاثه ارباع السكان في الدول الناميه وتم حيازته في الغالب في مرحله الطفوله. اما في البلدان المتقدمه فالعدوى في الاطفال اقل توترا. انها السبب الاكثر شيوعا لالتهاب المعده المزمن وايضا قرحه المعده وهى مرتبطة مباشرة بسرطان المعدة.

وهدفنا في هذه الرساله هو ربط العوامل الرئيسيه لضراوه البكتيريا وهي الجينات (cagA, vacA, babA) مع كلا من الاعراض المرضيه والمحددات النسيجيه والمرضيه لالتهاب المعده المرتبط بالميكروب الحلزوني وأيضا بالصوره المنظاريه وهذا سوف يكون مهما لوضع سياسات مستقبليه للقضاء على الميكروب الحلزوني من اجل منع الامراض الاكثر شده في كلا من الاطفال والبالغين ولدراستنا اضافات جديده في هذا الصدد.

ولتحقيق هذا الهدف اجريت هذه الدراسه على ٩٥ من الاطفال الذين احيلو لعمل منظار علوي بسبب معاناتهم من آلام البطن والترجيع والقئ الدموي. ٥٠ من هؤلاء الاطفال تم اثبات اصابتهم بالميكروب الحلزوني بواسطه اختبار اليورياز السريع والفحص الدقيق للانسجه (هستوباثولوجي) والفحص الجيني PCR وايضا ٤٥ طفلا تم اثبات خلوهم من العدوى وقد تم تشخيص ٢٥ طفلا لا يشتكون باعراض مرضيه انهم حالات ايجابيه بواسطه اختبار المولد المضاد للميكروب الحلزوني في البراز.

واظهر التحليل الاحصائي للبيانات التي تم الحصول عليها من هذه الدراسه النتائج التاليه:

١- القئ الدموي هو عرض من الاعراض المرضيه الاكثر شيوعا في الاطفال الذين احيلو الى عياده الجهاز الهضمي للاطفال لعمل التنظير العلوي (٥٤.٧%) وتوجد علاقه ذات دلاله بين القئ الدموي والاصابه بالميكروب الحلزوني.
٢- وجود العقيدات المعديه هو مؤشر كبير على الاصابه بالبكتيريا الحلزونيه.
٣- قد تميزت الصوره النسيجيه للاطفال ذوي الاعراض المرضيه والمصابين للميكروب الحلزوني بوجود التهاب شديد واكثر عمقا مع زياده في عدد البصيلات الليمفاويه مقارنه بالحالات السالبه.
٤- الصوره النسيجيه للحالات المصابه بالميكروب الحلزوني والتي تعاني من الام البطن المتكرره وأيضا التي تعاني من القئ الدموي تتميز بالتهاب حاد بشكل ملحوظ مقارنه بالذين لا يشتكون من نفس الشكاوى.
٥- الجينات الاكثر شيوعا في حالات الميكروب الحلزوني الايجابيه هي vacA (٧٢%) ثم cagA (٥٢%) ثم babA2 (٤٤%).
٦- توجد علاقات هامه بين وجود كلا من الجينات babA2، cagA، vacA s1، s1 / m1وs2 / m2 ووجود الأعراض المرضية فى الحالات المصابة بالميكروب الحلزونى.
٧- تعتبر العقيدات المعديه اكثر شيوعا في العينات الايجابيه لكلا من cagA و vacA S1.
٨- ترتبط الجينات cagA و vacA s1 ببعض الاعراض المرضيه واالتغيرات النسيجيه
٩- لا توجد علاقه ذات دلاله بين الجين babA2 والتغيرات في الصوره المنظاريه والصوره النسيجيه بالمجهر.
١٠- تم العثور على الثلاثي (cagA, vacA, babA2) في خمسه حالات تشتكي من أعراض الميكروب الحلزوني من عدم وجود هذا الثلاثي في الاطفال بدون أعراض.

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العلاقة بين موروثات الميكروب الحلزونى وشدة المظاهر السريرية والتهابات المعدة عند الأطفال

رسالة مقدمة

لقسم طب الأطفال ـ كلية الطب ـ جامعة الإسكندرية
ضمن متطلبات درجة

الماجستير

فى

طب الأطفال

مـــن

أميرة حامد حسب النبى
بكالوريوس الطب والجراحة ،
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[٢٠١٥]

جامعة الإسكندرية
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رسالة مقدمة من

أميرة حامد حسب النبى

للحصول على درجة

الماجستير

فى

طب الأطفال

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