

โรคไข้รูมาติกซ้ำและการติดเชื้อ ปีศาจโคมโรคสเตรปโตคอคคัส กรุปเอ ในผู้ป่วยโรคไข้รูมาติกที่ได้รับเบนซาทีนเพนนิซิลิน ป้องกันการเกิดโรคซ้ำอย่างสม่ำเสมอ

Rheumatic Fever Recurrences and Streptococcal Infections in rheumatic fever patients receiving regular Intramuscular Benzathine Penicillin Prophylaxis

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บทคัดย่อ

เนื่องจากในประเทศไทยยังไม่มีการศึกษาอุบัติการณ์การเกิดโรคซ้ำในผู้ป่วยโรคไข้รูมาติกที่ได้รับการป้องกันการเกิดโรคซ้ำอย่างสม่ำเสมอ ผู้วิจัยได้ศึกษาภาวะการติดเชื้อสเตรปโตคอคคัส และการเกิดโรคซ้ำในผู้ป่วยโรคไข้รูมาติกที่ได้รับการป้องกันการเกิดโรคซ้ำด้วยยา benzathine penicillin ทุก 4 สัปดาห์ ในผู้ป่วยเด็กที่เป็นโรคไข้รูมาติก และเคยเป็นโรคไข้รูมาติก จำนวน 105 ราย อายุ 3-20 ปี ที่รับการรักษาในภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ตั้งแต่ 1 ตุลาคม 2546-30 กันยายน 2547 จากการเพาะเชื้อ 210 ครั้ง พบว่าเป็น เชื้อ Group A beta hemolytic streptococcus 1 ครั้ง มีการติดเชื้อสเตรปโตคอคคัส 7 ครั้ง ใน 1,260 patient-months จากการตรวจของระดับ Antistreptolysin O titer และ Antideoxyribonuclease B titer ดังนั้นการให้การป้องกันการเกิดโรคซ้ำในผู้ป่วยที่เป็นโรคไข้รูมาติกในบริเวณภาคตะวันออกเฉียงเหนือของประเทศไทยนี้อาจจะต้องพิจารณาให้ฉีด benzathine penicillin ทุก 3 สัปดาห์ เพื่อลดอุบัติการณ์การเกิดโรคซ้ำ

Abstract

To study the incidence of streptococcal infections and the recurrences of rheumatic fever in rheumatic fever patients receiving regular intramuscular benzathine penicillin prophylaxis, we examined all patients with rheumatic fever who were followed at the Department of Pediatrics, Faculty of Medicine, Khon Kaen University during October 2003 to September 2004. There were 105 rheumatic fever patients and two hundred and four throat cultures were collected. Streptococcal infection occurred in 7 patients and throat swab cultures showed group A beta hemolytic streptococcus in one patient. The patients in Northeast Thailand who received benzathine penicillin prophylaxis every 4 weeks were still at risk of inter-current streptococcal infections. The 3-week regimen should be considered in these patients.

คำสำคัญ: โรคไข้รูมาติก โรคไข้รูมาติกซ้ำ การติดเชื้อสเตรปโตคอคคัส

Keywords: Acute rheumatic fever, Recurrent rheumatic fever, Streptococcal infection

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Introduction

Since 1952 the administration of 1.2 million units of benzathine penicillin G every 4 weeks has been recognized as the most effective method for the prevention of the recurrence of rheumatic fever (Feinstein et al., 1964 and Stollerman et al., 1956). Prophylaxis failure during regular administration of benzathine penicillin G every 4 weeks has occurred especially in developing countries (Lue et al., 1994) where rheumatic fever is still prevalent (Panamonta et al., 1993; Panamonta et al., 2004 and Stollerman, 1997).

The effects of benzathine penicillin G administrations every 4 weeks on the incidence of streptococcal infections and the recurrences of rheumatic fever from different areas of the world (Feinstein et al., 1964; Lue et al., 1994; Stollerman, 1997 and Stollerman et al., 1956) have been reported. Since there is no data on the incidence of streptococcal infections and the recurrences of rheumatic fever in patients receiving regular intramuscular benzathine penicillin prophylaxis in Thailand, this paper reports the situation in Northeast Thailand.

Patients and Methods

From October 2003 to September 2004, 105 consecutive patients with rheumatic fever and rheumatic heart disease who were followed at the Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Northeast Thailand were enrolled in this study. Patient's age ranged from 3 to 20 years. All patients and their families were informed by one of us (MP) and the parents of the patients provided written informed consent. All patients included in this study received a regular 4-week

regimen and received a card for recording benzathine penicillin injections. Each patient was examined in the Rheumatic Fever Clinic by two pediatric cardiologists every 1 to 3 months (Panamonta et al., 2004). At each visit, thorough histories included checks for sore throat, fever, arthralgia, arthritis, nocturnal cough, orthopnea, easy of fatigue, abnormal movement, subcutaneous nodules, and erythematous skin rash. Serum samples and throat swab cultures were obtained every 1 to 3 months for streptococcal tests. Two qualified pediatric cardiologists independently categorized the patients according to murmur types, location, intensity and transmission; the auscultatory diagnosis was based on the agreement of both independent observations. The documentation of auscultatory change was based on the agreement of these two pediatric cardiologists. The patients who had symptoms suggestive of recurrent rheumatic fever also had color Doppler echocardiograms and laboratory tests (i.e. ASO titers, anti-DNase B titers, erythrocyte sedimentation rate, C-reactive protein tests and throat swab cultures).

All specimens for throat culture were obtained with a cotton swab and directly inoculated on 5% blood agar and incubated overnight at 37°C. β -hemolytic streptococcal colonies were sub-cultured in blood agar plates and tested for susceptibility to bacitracin. GABHS were further sub-classified by emm gene sequence analysis at the WHO Reference Center for Streptococcus of the University of Minnesota. Determinations of anti-streptococcal antibodies were performed with commercial reagents, including ASO (Biotec Laboratory) and Anti DNase B (Dade Behring). Titer increases of >0.2 log (in two dilutions) increments were considered indicative of a recent

streptococcal infection. All sera were stored at -70°C for further re-evaluation. Diagnosis of acute rheumatic fever and recurrent rheumatic fever were according to the revised Jones' criteria (American Heart Association, 1992).

Results

During the 1-year study period, 105 patients with rheumatic fever and rheumatic heart disease were followed prospectively for streptococcal surveillance. A total of 210 throat cultures were performed and group A beta hemolytic streptococcus (GABHS) was identified in 1 isolate. GABHS were further sub-classified by emm gene sequence analysis at the WHO Reference Center for Streptococcus of the University of Minnesota. The results will be reported later. Seven instances of increases in antibody titer occurred in this 1,260 patient-month follow-up. There was no recurrence of acute rheumatic fever among these 105 patients.

Discussions

The incidence of rheumatic fever recurrence in our patients receiving regular intramuscular benzathine penicillin prophylaxis in Northeast Thailand during October 2003 to September 2004 was 0.0 per 100 patient-years. The reported rheumatic fever recurrence rates among patients receiving 4-week benzathine penicillin G prophylaxis varies from 0.0 to 2.8 per 100 patient-years (Feinstein et al., 1964; Lue et al., 1994; Tompkins et al., 1972; Stollerman, 1997 and Stollerman et al., 1956). The risk factors for recurrence are poor socioeconomic conditions, virulence of streptococcal infections, lower patients' age, and poor compliance to the prophylaxis regimen (Feinstein et al., 1964; Lue et al.,

1994; Stollerman, 1997 and Stollerman et al., 1956).

The incidence of streptococcal infections in rheumatic fever patients receiving regular intramuscular benzathine penicillin prophylaxis in Northeast Thailand during October 2003 to September 2004 was 6.7 per 100 patient-years. The incidence of streptococcal infections in rheumatic fever patients receiving regular intramuscular benzathine penicillin prophylaxis varied widely from 0.6 to 14 per 100 patient-years, depending on the epidemiology of streptococcal infections and the methodology used in monitoring the infections (Lue, 1994).

Our study revealed that the rheumatic fever patients in Northeast Thailand during October 2003 to September 2004 had recurrence per infection ratio of 0.0. This finding might be explained by the small sample size in this study.

This study indicates that rheumatic fever patients receiving 4-week benzathine penicillin G prophylaxis in Northeast Thailand are still at significant risk of developing streptococcal infections. The 3-week regimen might be more effective in the prophylaxis of streptococcal infections and moreover to prevent rheumatic fever recurrence among patients with rheumatic fever in this area of Thailand.

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