WHO/FCH/CAH/05.08

A Review of the Technical Basis for the Control of Conditions Associated with Group A Streptococcal Infections

Department of Child and Adolescent Health and Development
World Health Organization

Acknowledgements

WHO/CAH wishes to thank Prof. Jonathan R Carapetis, Centre for International Child Health, University of Melbourne Department of Paediatrics, Royal Children's Hospital, Melbourne, Australia for undertaking this review, and Dr. Andrew C Steer and Prof. E. Kim Mulholland, Royal Children's Hospital, Melbourne, Australia, for contributing to it. WHO/CAH is grateful to Drs. Alan Bisno, Singh Chhatwal, Hala Hamsa, Ed Kaplan, Fran Rubin, and Anne Schuchat for reviewing the draft manuscript and providing valuable comments.

Table of Contents

Executive summary

Group A streptococcus (GAS) causes a diverse spectrum of disease. In the past, most GAS control activities have fallen under the categories of register-based rheumatic heart disease (RHD) secondary prophylaxis programs, and management of acute rheumatic fever (ARF), RHD and sore throat / GAS pharyngitis. The prevention and control of ARF/ RHD and streptococcal pharyngitis have also been the most researched topics in the literature. However, these activities do not encompass the entire range of potential strategies for controlling GAS diseases.

Of the available control strategies, secondary prophylaxis (defined as the delivery of regular doses of penicillin to ARF/RHD patients to prevent recurrent ARF and worsening RHD) is the only one that has been shown to be both effective and cost-effective at the community/population level. In populations with high prevalence of RHD, delivery of secondary prophylaxis should be the major priority for control of GAS diseases. Coordinated register-based RHD control programs appear to be the most effective method for delivering secondary prophylaxis and have the added benefit of improving clinical follow-up of patients and providing a mechanism for delivery of targeted health promotional messages. Past efforts to expand RHD control programs have had mixed success. Future strategies should concentrate on ensuring that programs are properly resourced, not overly ambitious in their early stages, and are systematically evaluated. The issue of the availability and quality of BPG supplies requires urgent attention. The diagnosis of ARF remains difficult in many countries, and the American Heart Association's Jones Criteria Working Group has called for more clinical research in this area. It is clear that this research should particularly be focused in developing countries and other populations with high ARF incidence.

Tertiary prevention of RHD (the provision of medical and surgical treatment to patients with RHD and heart failure) is expensive and largely palliative. Moreover, it deals with the provision of care to patients with preventable disease. Therefore, tertiary prevention of RHD should theoretically be the least important and therefore least resourced aspect of GAS control. Unfortunately, in many countries this strategy has become the focus of RHD control and consumes the majority of the RHD control budget (and a substantial proportion of the entire health budget). While the importance of treating patients in cardiac failure from RHD cannot be ignored, the cost-effectiveness of improving adherence to secondary prophylaxis - and thus reducing the number of RHD patients requiring surgical and medical treatment - clearly argues in favour of secondary rather than tertiary prevention.

There is currently no strategy for primary prevention of GAS diseases that has a proven cost-effective benefit at the population level. Of the existing primary prevention interventions, primary prophylaxis of ARF (antibiotic treatment of symptomatic GAS pharyngitis) has been the most intensively studied, advocated and practised. In particular, the use of simpler antibiotic treatment regimens (e.g. once-daily oral amoxicillin) and clinical algorithms for the diagnosis of GAS pharyngitis have received considerable attention in recent years. However, the available evidence suggests that, even when implemented at an optimal level using school-based surveillance and treatment (programs that are neither practical nor affordable for most less developed countries), primary prophylaxis can prevent only a minority of cases of ARF. The efficacy of large-scale primary prophylaxis programs in reducing transmission of GAS and incidence of GAS pharyngitis has been demonstrated, although this strategy is unlikely to be cost-effective. The impact of this approach on invasive GAS disease and acute post-streptococcal glomerulonephritis (APSGN) is not known. Although some middle-income countries may choose to implement surveillance-based primary prophylaxis programs on a large scale for the prevention of ARF, this strategy cannot be recommended for poorer countries, where the major burden of ARF exists.

Community-based approaches for controlling scabies have had demonstrated success in reducing the prevalence and severity of GAS skin infections. It is possible that mass administration of ivermectin for filariasis in many countries may have had an important secondary benefit by reducing scabies and skin infections; this is not known, but could be relatively easily determined. There is the potential for other strategies addressing personal and community hygiene (including swimming pools), insect bites, and targeted antibiotic treatment to be added to scabies programs to further reduce rates of skin infections; this has not been properly studied. The control of GAS skin infections and the likely effect of preventing APSGN and invasive disease is sufficient argument to support the widespread implementation of healthy skin programs in communities with high rates of scabies and pyoderma. The possibility that these programs may have the added benefits of preventing ARF and improving other aspects of child health is further impetus for their implementation and for a detailed evaluation of their health impact. This strategy has the potential to be the most effective and practical approach for primary prevention of GAS diseases in less developed countries.

Mass antibiotic treatment remains a valid strategy for prevention and control of outbreaks of GAS diseases in particular situations. These include the prevention of ARF in military institutions and control of focal APSGN outbreaks. Targeted antibiotic treatment - e.g. to family contacts of cases of invasive GAS disease - is of unproven efficacy and could potentially only prevent a very small minority of cases.

The most successful GAS control activities have combined multiple strategies including primary prophylaxis, treatment of skin infections, health promotion, secondary prophylaxis and RHD registers. Although effective, these comprehensive programs require a substantial commitment from individuals and organisations (including Ministries of Health).

In light of the current lack of a clear strategy for primary prevention of GAS infections, there is definitely a place for a safe, effective, affordable and practical GAS vaccine. It appears likely that the vaccine most advanced in development - a multivalent, type-specific vaccine - will not provide sufficient and long-lasting protection in less developed countries, although this should be assessed.

Introduction

Large-scale activities to control GAS diseases historically have fallen mainly under the categories of register-based rheumatic heart disease (RHD) secondary prophylaxis programs, and management of acute rheumatic fever (ARF), RHD and sore throat / GAS pharyngitis. The prevention and control of ARF/ RHD and streptococcal pharyngitis have also been the most researched topics in the literature. However, because these activities do not encompass the entire range of potential strategies for controlling GAS diseases, this review will cover the technical basis for past and current approaches, as well as other potential approaches.

Because some diseases caused by GAS are not due to active infections (e.g. ARF, RHD, and acute post-streptococcal glomerulonephritis - APSGN), this report will refer to GAS diseases rather than GAS infections, except where specific active infections are inferred (e.g. invasive GAS infections).

Potential approaches to controlling GAS diseases

Figure 1 outlines a simplified approach to understanding the spectrum of GAS diseases, and Table 1 details the types of prevention strategies that could potentially be used. There is some debate as to whether the following interventions technically fall into the categories of primary, secondary and tertiary prevention as defined by Last. (1) For example, it can be argued that secondary prophylaxis is tertiary, rather than secondary prevention. However, such arguments are largely semantic. These categories are retained for simplicity.

Figure 1. A simplified approach to the spectrum of GAS diseases and potential prevention strategies