18th Expert Committee on the Selection and Use of Essential Medicines

(21 to 25 March 2011)

Section 2 Analgesics, antipyretics, NSAIMs, DMARDs

2.4 Disease-modifying agents used in rheumatoid disorders

Review of Disease-Modifying Anti Rheumatic Drugs in Paediatric Rheumatic disease

September 2010

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Contents

3. Sulphasalazine
    1. Mechanism of action and Pharmacology
    2. Efficacy in Juvenile Idiopathic Arthritis
    3. Dose and administration
    4. Safety
    5. Drug interaction
    6. Monitoring and supervision
    7. Formulary
    8. Summary recommendations

4. Cyclosporin
    1. Mechanism of action and Pharmacology
    2. Efficacy in Juvenile Idiopathic Arthritis and Macrophage Activation Syndrome
    3. Efficacy in Juvenile Dermatomyositis
    4. Dose and administration
    5. Safety
    6. Drug interaction
    7. Monitoring and supervision
    8. Formulary
    9. Summary recommendations

5. Azathioprine
    1. Mechanism of action and Pharmacology
    2. Efficacy in SLE
    3. Efficacy in JIA
    4. Dose and administration
    5. Safety
    6. Drug interaction
    7. Monitoring and supervision
    8. Formulary
    9. Summary recommendations

6. Hydroxychloroquine
    1. Mechanism of action and Pharmacology
    2. Efficacy in SLE
    3. Dose and administration
    4. Safety
    5. Drug interaction
    6. Monitoring and supervision
    7. Formulary
    8. Summary recommendations

1. Intent of review

- To identify priority rheumatological conditions in children
- To outline the treatment options for these conditions
- To outline the role of DMARDs in the treatment of priority rheumatological conditions
- To review the literature and collate the evidence for the efficacy of DMARDs in priority conditions
- To review the safety of DMARDs and outline monitoring and supervision required
- To give recommendations for the inclusion of DMARDs on the WHO Essential Medicines List

2. Identification of priority conditions

Paediatric Rheumatology encompasses a broad range of inflammatory disorders involving the joints and connective tissues in children. Juvenile idiopathic arthritis is perhaps the most well recognised of the rheumatic diseases of childhood however the specialty's scope includes conditions such as acute rheumatic fever, post-streptococcal reactive arthritis, Kawasaki disease and Lyme disease as well as chronic systemic conditions including Systemic Lupus Erythematosus (SLE), Juvenile Dermatomyositis (JDM), and the vasculitides.

The most common rheumatic disease affecting children is chronic arthritis. The functional impact of this disease can be significant and the timely administration of appropriate therapy, including DMARDs, can be effective in improving outcome. While less common, SLE and JDM are also are potentially devastating conditions and DMARD therapy plays an equally important role in their management.

3. Review of priority conditions

3.1 Juvenile Idiopathic Arthritis

Chronic arthritis is a complex group of disorders comprising a number of clinical entities with the common feature of arthritis. Each type is characterised by a different mode of presentation and different disease course and outcome.
The three main groups of chronic arthritis are: those affecting few joints (oligoarticular); those affecting many joints (polyarticular); and those systemic in onset. The classification of chronic arthritis has been problematic over the past few decades especially in terms of universally agreed upon definitions. This, in part, largely reflects the complex and heterogeneous nature of this group of conditions and the as yet not clearly defined immunogenetic factors contributing to their onset. It is also important to remember the population (mostly Caucasian) in which each of the major classification criteria have been described. For the purposes of this paper, the International League of Association for Rheumatology (ILAR) criteria for classification of juvenile idiopathic arthritis (JIA) has been used.[1]

3.1.1 Epidemiology

JIA remains an uncommon but by no means rare condition affecting children worldwide. [2] Estimates of incidence and prevalence however have been difficult to ascertain for many reasons including: variation in diagnostic criteria; differences in ascertainment (community vs clinical based studies); differences in study design; low frequency of disease and small study numbers. [3]

In 2002 Manners and Bower summarised the most recent epidemiological studies to that point and found a reported prevalence of 0.07 to 4.01 per 1000 children and an annual incidence of 0.008 to 0.226 per 1000 children. [3] The large difference in reported prevalence is considered to be largely due to varying study characteristics. The highest prevalence was reported in community based studies where children were examined in classrooms or homes. In 1993, Meilants performed an epidemiological study using a questionnaire followed by clinical examination and found a prevalence of definite JIA of 1.67 per 1000.[4] In 1996 Manners et al found a significantly higher prevalence (4.01 per 1000) in an urban Australian community.[5] Similarly, Tayel et al found a prevalence of JIA amongst 10-15 year old school children in Alexandria, Egypt, of 3.3 per 1000.[6] Clinic based studies on the other hand appear to report lower prevalence rates - perhaps reflecting that many clinicians fail to recognise JIA and therefore these children do not make their way to medical care in large study centres, therefore underestimating the true prevalence.[7]

There is very little comparable data outlining the prevalence of JIA in populations other than those of European descent. In fact, in the most heavily populated areas of the world epidemiological data is very scarce. Outside of the US, UK and Canada some studies reveal very different data. Lower frequencies of JIA have been reported in children in Japan (annual incidence 0.0083 per 1000) and Costa Rica (annual incidence 0.068 per 10000 Arguedes 1998 and 0.054 per 1000 Arguedes 1995). In 1983 Hochberg reported an annual incidence of 0.066 per 1000 children and a prevalence of 0.26 per 1000 in urban black children in the USA however other studies suggest that this is an underestimate. [8] Many of these studies are ultimately limited by the small sample size and selection bias. One retrospective study undertaken by Kurahara et al in 2002 demonstrated lower frequency of JIA in Hawaiians of Filipino, Japanese and Samoan descent compared with Caucasians.[9] In a similar population Kurahara also found increased prevalence of JIA in rural areas compared with urban areas.[10]

The extent of juvenile arthritis in the developing world and the epidemiological impact of ethnicity and geography needs further consideration especially in considering the impact and burden of disease of this group of conditions.

3.1.2 Burden of Disease and outcome

The disease outcome and prognosis in JIA is variable and to some degree predictable based on the different disease subtypes. For example, sero-positive polyarticular JIA has a relatively poor outcome compared with oligoarticular JIA whose outcome is generally very good. [11, 12] However, the latter group are also the most at risk of debilitating uveitis as a complication of their disease. Many children with JIA have an excellent prognosis and for the

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