Update of rheumatic fever in children - A review

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Acute rheumatic fever (ARF) is an inflammatory, autoimmune disease resulting from inadequate treated group A β-hemolytic streptococci (GAS) tonsillopharyngitis. This disease commonly affect, heart, joints, skin, and brain. Carditis, arthritis, chorea, subcutaneous nodules, and erythema marginatum are the major manifestations. Fever, arthralgia, raised acute phase reactants (ESR and CRP), and prolonged PR interval on ECG are the minor manifestations of ARF. In 1944 Thomas Jones described Jones criteria for proper diagnosis of ARF. To control unnecessary treatment after over diagnosis and lacks of treatment due to under diagnosis, the Jones criteria was modified four times and the latest update were published in 1992. According to Jones criteria ,(if 2 major or 1 major and 2 minor manifestation plus supporting evidence of antecedent group A beta hemolytic streptococci pharyngitis) has probability of ARF. In 2006 and 2012 Australian heart association introduced a new guideline for the diagnosis of RF in high risk and aboriginal patients. Developing countries are more affected by ARF than industrialized countries. It is the most common cause of acquired heart disease worldwide. Most common affected structures are Mitral valve and aortic valves as regurgitations. Penicillin is the first line antibacterial therapy for eradication of GAS infection as well as secondary prophylaxis. Macrolide (erythromycin) are acceptable alternatives in penicillin-allergic patients. Paracetamol is sufficient anti-inflammatory for fever and atypical arthralgia where as Aspirin and naproxen is the traditional NSAID for diagnosed ARF cases. For carditis and heart failure, oral prednisolone with supportive therapy is mandatory. Secondary prophylaxis therapy can prevent recurrence of ARF and cardiac complication. Rheumatic heart disease (RHD) with permanent heart damage and heart failure are the late sequela of ARF.

Key word: ARF, Streptococcal pharyngitis, major manifestations, minor manifestations, Jones criteria, RHD, aspirin, penicillin.

INTRODUCTION

Rheumatic fever is inflammatory diseases which can be developed due to partially treated throat infection and scarlet fever caused by beta hemolytic streptococci of group A. But sometimes, group G or group C streptococci which contain certain GAS antigen or enzyme may be the cause of acute rheumatic fever (McDonald et al., 2004. Because some positive throat culture of group G and group C streptococci have been found from Australian patient of ARF (McDonald et al., 2004; Andrews et al., 2006) . Just after 14 - 28 days after throat infection and scarlet fever. Most common affected age by ARF is 5 - 15 years. It is rare among children younger than 5 years, representing less than 5% of first attack, very rare and occasionally seen among children less than 2 years and

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people older than 45 year (BenDov and Berry 1980; Carapetis et al., 2000; Tani et al., 2003; Uner et al., 2010)

It can also affect younger children and adult rarely. Most common organ involved in this disease is Heart (carditis), joints (arthritis, arthralgia), Skin (erythema marginatum and subcutaneous nodules) and Brain (chorea), till fully damaged of heart valves and heart failure.

ARF has the features of an autoimmune response of GAS pharyngitis and affects commonly the connective tissue that principally involves the heart, blood vessels, joints, subcutaneous tissues, and central nervous system (El-Said, 1994). Acute rheumatic fever is a major healthcare problem in developing and poor countries and remains to be the leading cause of acquired heart disease (RHD) in children all over the world (Mc Laren and Markowitz 1994; Balat et al., 2005).

About 1 - 2% general population are effected by ARF worldwide (Carapetis et al., 2000; Uner et al., 2010). Major public health effects of ARF are acute illness, considerable morbidity, some mortality, and long term damage of the heart and joints.

Acute rheumatic fever (ARF) is generally preceded by group A streptococcal (GAS) tonsillopharyngitis, but not by GAS skin infection infections (Guidelines for the diagnosis of rheumatic fever. Jones Criteria, 1992 update).

ARF is commonly target in children and characterized as an acute febrile illness. Polyarthritis presents as redness, swelling, heat, and tenderness or pain, and decreased function of multiple major joints. Carditis manifest with new cardiac murmur representing mitral or aortic regurgitation with or without cardiomegaly, and congestive heart failure (Williamson et al., 2004).

Rheumatic carditis is the leading cause of permanent disability in ARF patients, being present in 68 - 70% of the patients (Childhood acute rheumatic fever in Greece (2001); Veasy et al., 1994) the degree of cardiac involvement improves in about 2/3 of them with early and standard treatment (Veasy et al., 1994).

Carditis prevailed as the major criterium of ARF, while in most series from the United States and Europe arthritis is the main major criterium (Veasy et al., 1994; Hosier et al., 1987).

Even after introduction of several new molecules of antibiotics, penicillin still represents as the drug of choice for streptococcal pharyngitis; however, its utility can be substituted if there is allergic, or failure to adhere, to the multiple dosing schedule (Dajani et al., 1995). Cephalosporin and amoxicillin are the commonly traditional alternatives. Macrolides such as erythromycin and azithromycin have been established as second-line alternatives for the treatment of group A streptococcal pharyngitis.

**EPIDEMIOLOGY**

Rheumatic fever is most common in the age of 5 - 15 years but it can also occur in any age (Lawrence et al., 2013; Parnaby and Carapetis, 2010; Seckeler et al., 2010). It is about 20 million in developing countries and the most common cause of acquired RHD (Miyake et al., 2007) According to population based data, approximately 336,000 cases of acute rheumatic fever occur per year in children aged 5 - 14 years, and more than 471,000 cases of ARF occur in all ages (Carapetis et al., 2005). The incidence of rheumatic fever each year is 470,000 and death is 233,000 worldwide (Miyake et al., 2007). Most common incidence is in developing countries in which mean incidence is 19 per 100,000 (Tibazarwa et al., 2008). But the same incidence in developed countries like America is about 2 to 14 per 100,000 because of regular and successful vaccination programme, good hygiene, and more sincerity about health, regular and standard antibiotic use for upper respiratory bacterial infection (Miyake et al., 2007; Gordis, 1985). Some study clarified that only limited M serotypes (type 3, 5, 6, 14, 18, 19, 24 and 29) strains of group A streptococcus can be the cause of out breaks of rheumatic fever (Stollerman, 1997; Markowitz and Gerber 1987; Shulman et al., 2006; Johnson et al., 1992). It is clear that to suffer from rheumatic fever, is necessary to suffer from streptococcal pharyngitis, with their toxins or scarlet fever (Whitnack and Bisno 1980; Kaplan and Bisno, 2006).

Predisposing factor of rheumatic fever is group A streptococcal (GAS) tonsillopharyngitis, but not GAS skin infection infections. If we can treat streptococcal pharyngitis adequately, we can subsequent reduce the incidence of rheumatic fever (Bisno et al., 2002) and by regular use of prophylactic antimicrobial therapy who had already rheumatic fever, recurrence of the disease is reduced (Markowitz and Gerber 1987; Shulman et al., 1994). The patients who once suffered from rheumatic fever, he always finds increased anti streptococcal antibody atleast one among the three antibodies (streptolysin “O”, streptokinase and hyaluronidase) (Stollerman et al., 1956).

**CLINICAL MANIFESTATION AND DIAGNOSIS**

In 1944 T. Duckett Jones proposed a guideline known as the Jones criteria for diagnosis of acute rheumatic fever
which was again revised in 1965 (Jones, 1944; Forster, 1993), and 4 times till 1992. Jones criteria are revised by American Heart Association for the diagnosis of initial attack of rheumatic fever, not for recurrence. And finally Jones criteria working group of the American Heart Association (AHA) reviewed this guideline in 2002 (Guidelines for the diagnosis of rheumatic fever. Jones Criteria, 1992; Ferrieri, 2002). Jones criteria is the current ‘gold-standard’ guideline for diagnosis of ARF ( Special writing group of the committee on rheumatic fever, endocarditis, and Kawasaki disease, 1992).

Acute rheumatic fever is characterized by group A streptococcal (GAS) infection followed by clinical manifestations explained below as major and minor manifestation.

There are 5 major manifestations and 4 minor manifestations and an absolute requirement for evidence (microbiology or serology) of recent group A streptococcal infection (GAS) infection.

**5 Major criteria are (major clinical manifestations)**

1. Migratory arthritis (predominantly involving the large joints)
2. Carditis and valvulitis.
3. Central nervous system involvement (Sydenham chorea)
4. Erythema marginatum
5. Subcutaneous nodules

**4 Minor criteria are (minor clinical manifestations)**

1. Arthralgia
2. Fever
3. Elevated acute phase reactants [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)]
4. Prolonged PR interval on ECG

**Essential criteria**

1. Evidence of prior group A streptococcal infection
2. Positive throat culture or rapid antigen test for group A streptococcus
3. Raised or rising streptococcal antibody titre.

According to Jones criteria, acute rheumatic fever can be diagnosed only when

2 major criteria or 1 major and 2 minor criterias with the evidence of recent GAS pharyngitis in both scenarios (Ferrieri, 2002; Rheumatic fever and rheumatic heart disease: report of a WHO Expert Consulatation, 2001).

But for recurrence cases, requires only one major or several minor manifestations, with evidence of prior group A streptococcal infection.

Even with strict follow of Jones criteria, underdiagnosis or over diagnosis of acute rheumatic fever can occur. That’s why there are 3 circumstances in which acute rheumatic fever can be diagnosed without strict adherence to the above mentioned Jones criteria.

1. Chorea as the single manifestation of acute rheumatic fever
2. Indolent carditis as the single manifestation in patients who 1st come to medical attention months after acute GAS infection.
3. Finally, in patients with recurrence of rheumatic fever or who have rheumatic heart disease (RHD), one major or several minor manifestations will be sufficient to diagnose ARF with strong evidence of recent Group A Streptococcal pharyngitis.


**MAJOR CLINICAL MANIFESTATION OF ACUTE RHEUMATIC FEVER**

**Polyarthritis**

Polyarthritis is also called migratory polyarthritis as involvement of each joint overlapping to give the impression that the process ‘migrates’ (severely affected joint can improve within one week and 1 or more other joints become involved). Usually, arthritis is the earliest symptomatic manifestation of acute rheumatic fever. Involvement of arthritis in patients of rheumatic fever is about 75% and typically the large joints knee, ankle, wrist and elbows. The leg joints (knee, ankle) are typically involved first and each last for a few days to a week (Al-Eissa et al., 1993). In rare cases we can find the involvement of the spine, smalls joint of the hand and feet or hip. Teenagers and young adult are more affected from rheumatic arthritis than children (Wallace et al., 1989) with the sign and symptoms of inflammation redness, hot, swelling, and massive tenderness to palpation and limitation of joint range of motion. The joints involvements are migratory in nature and dramatically response even after small dose of salicylate.
therapy which supports to diagnose rheumatic arthritis. If not responding after 48 h of salicylate therapy, diagnosis should be considered. A single large joint was common in the patients with rheumatic fever who were treated for associated arthritis (Al-Eissa et al., 1993). In other study in aboriginal patients in Australia found 17% cases of monoarticular arthritis cases in 555 patients of rheumatic fever (Carapetis and Currie, 2001). No radiological changes are found in arthritis affected joint except some effusion which is generally transudative fluid.

**Carditis**

Carditis and chronic rheumatic heart disease are the most serious manifestation of acute rheumatic fever. It occurs in 50 - 60% of patients in rheumatic fever. Carditis can cause permanent cardiac damage, and more than 60% of patients with ARF develop RHD (Carapetis and Currie, 1999) Carditis is characterized as pericardium, epicardium, myocardium, and endocardium but in some cases cardiac involvement limited till endocarditis (valvulitis) which manifest by 1 or more cardiac murmur. The heart valves are the most commonly affected structure if occurs recurrence of the disease. The damaged valves may characterize as regurgitation (fail to close properly and leak) or as stenosis (fail to open properly). Commonest affecting structures are the mitral and aortic valves (Special Writing Group of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young of the American Heart Association. Guidelines for the diagnosis of rheumatic fever: jones criteria, 1992 update 1992; Marcus, 1994). Mitral valve as mitral regurgitation about (85%). The aortic valve is affected in about 54% of patients and both tricuspid and pulmonary valves in less than 5% of patients. Pericarditis characterized as typical pericardial pain and a friction rub. Mitral regurgitation is characterized as high pitched apical holosystolic murmur radiating towards the axial where as aortic regurgitation is characterized by high-pitched diastolic murmur at the upper left sternal border. Echocardiography is the gold standart test to confirm the diagnosis and stage of rheumatic carditis. Carditis may culminate in chronic valvular disease (rheumatic heart disease) and can lead to heart failure and, ultimately, death.

**Chorea**

Chorea is a neuropsychiatric sequela of ARF characterized by rapid involuntary, purposeless movements (Involuntary jerky movements of the limbs and face) associated with emotional liability and muscular weakness (Cardoso et al., 1997). Chorea is also called Sydenham chorea (also known as chorea minor or “St. Vitus dance”) and it occurs about 10 - 15% in patients with rheumatic fever. Thomas Sydenham first described Sydenham’s chorea (SC) in 1686 (Al-Eissa, 1993). The latent period of chorea is longer than Arthritis and carditis (Eshel et al., 1993). Chorea is generally unilaterally (hemichorea) and characterized by ataxia, poor school performance, incoordination, facial grimacing, slurring of speech, crying, and restlessness, and symptoms disappear during sleep. Muscles weakness can be noted when the patients is ashked to squeeze examiners fingers as irregular contraction of the muscles of the hand and the phenomena is called a relapsing grip or “milk maids sign. As chorea is late manifestation of ARF, we should evaluate carditis with echocardiogram if chorea is noted.

**Erythema marginatum**

Erythema marginatum is an evanescent, non-itchy, pink or slightly red, non-pruritic rash involving the trunk and rarely the extremities but not the face (Johnston, 1996). Erythema is reported to be found in only about (4 – 15%) patients with acute rheumatic fever. The rash may be fleeting, vary in size and disappear within hours. A hot bath or shower may make them more evident. Many studies have been reported that erythema is more common in patients with chronic carditis (Feinstein and Spanguolo, 1962). It is rare but typical characteristic rash of acute rheumatic fever.

**Subcutaneous nodules**

Subcutaneous nodules occur rarely, (≤1% in patients with acute rheumatic fever) and typically only in severe cases. The common sites of appearing nodules are near the bony prominences, over the joints, tendon, scalp and spinous processes of the thoracic or lumbar vertebrae. The nodules are painless lesions ranging from a few millimeters to 2 cm in size. The skin site is not inflamed and the nodule is freely moveable. Nodules are generally symmetric and the number varies from a single lesion up to average of three or four.

**Minor manifestation**

Minor manifestations of the Jones criteria contains both clinical and laboratory findings. Arthralgia and fever are non-specific clinical features of acute rheumatic fever,
whereas Elevated acute phase reactants (erythrocyte sedimentation rate ESR and C-reactive protein CRP) are the laboratory findings. Prolong PR interval (more than $\geq 0.16$ s on ECG), is another ECG finding of minor criteria.

**CLINICAL FINDINGS**

**Arthralgia**

Arthralgia is defined as pain in one or more joints in the absence of polyarthritis as major criteria. Significantly if arthritis is noted as a major manifestation of the Jones criteria, arthralgia is not counted as a minor manifestation. It is non-specific clinical features of ARF. It occurs frequently in rheumatic fever, as well as in many other disease states. Arthralgia is characterized as pain in joints, not in the muscles or periarticular tissues, without objective evidence of inflammation or trauma. It appears as pain and stiffness in knee, hip, ankle and less commonly in arm joint.

**Fever**

Fever is defined most often in ARF as typically body temperature of at least 39°C ($\geq$102°F) and occurring early in the course of disease. Fever is not categorized as a major manifestation because like arthralgia, it is also non-specific clinical feature of rheumatic fever.

**Laboratory findings**

Both acute-phase reactants, serum C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) are raised in ARF (Serum CRP level of $\geq 30$ mg/L or ESR of $\geq 30$ mm/h). Both are invariably elevated during the active rheumatic phase unless they are suppressed by antirheumatic drug (Saxena et al., 2008). Among both the CRP is more useful because it typically normalize as soon as acute inflammation subsides but the ESR may stay elevated longer than 6 - 8 weeks after a transient inflammatory stimulus.

Except these CRP and ESR changes, we can found increase in levels of Cu and Fe in the serum of ARF patients (Beisel, 2004). These trace elements play important role in the development and maintenance of the immune system. Tumor necrosis factor [TNF]), cytokines (interleukin [IL]-1, IL-6, and ceruloplasmin and are Cu- or Zn-binding proteins.

Streptococcal tonsillopharyngitis can be diagnosed in one of the following condition when,

1. If positive throat culture for group A beta-hemolytic streptococci
2. If rapid streptococcal antigen test is positive
3. Elevated or rising antistreptolysin (ASO) antibody titer

Some times ASO titre will be negative even in documented patients of ARF (Only about 80% of patients with documented ARF found raised ASO titre). So some times needs more specific test (antistreptococcal antibodies) to confirm GAS pharyngitis. Such as, anti-DNAse B, streptokinase, and antihyaluronidase which are positive even after long duration (3months) of active streptococcal infection. But not antistreptolysin titre, which antibody titers fall off rapidly after 6 - 8 weeks (Massell, 1997). The reference range for these antibody titres varies with age and geographical location.

These are the recommended investigations to be done in all ARF suspected patients.

1. White blood cell count (WBC)
2. Blood cultures
3. Erythrocyte sedimentation rate (ESR)
4. C-reactive protein (CRP)
5. Electrocardiogram (repeat in 2 weeks and 2 months if prolonged P-R interval or other rhythm abnormality)
6. Echocardiogram (consider repeating after 1 month if negative)
7. Chest x-ray if clinical or echocardiography evidence of carditis
8. Throat swab (preferably before giving antibiotics) — culture for group A streptococcus
9. Anti-streptococcal serology; both anti-streptolysin O and anti-DNase B titres, and again (repeat 10–14 days later if first test not confirmatory).

**Other symptoms**

Except these all above manifestation, some other manifestation are found in patients of acute rheumatic fever such as pain abdomen, malaise, epistaxis, normochromic normocytic anemia, Tachycardia out of propotion to the fever.

**Differential diagnosis**

Many of the clinical manifestation of ARF are nonspecific, so a broad range of differential diagnoses should be considered.

Post-streptococcal syndromes such as Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and post-
Table 1. Treatment of tonsillopharyngitis.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Doses</th>
<th>Mode</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin V (Phenoxymethyl penicillin)</td>
<td>Children 250mg 2-3 times daily or Adolescent 500mg 2-3 times daily</td>
<td>Oral</td>
<td>10 days</td>
</tr>
<tr>
<td>Benzathine Penicillin G</td>
<td>600,000 I.U. for patients&lt;20kg or 1,200,000 I.U for patients&gt;20kg</td>
<td>Intra muscular</td>
<td>10 days</td>
</tr>
</tbody>
</table>

Table 2. For individual allergy to penicillin.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Doses</th>
<th>Mode</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrow spectrum cephalosporin (cephalexin, cefadroxil)</td>
<td>Variable or 30-50mg/kg/day 2-4 times daily</td>
<td>Oral</td>
<td>10 days</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>12 mg/kg once daily or 15 mg/kg/day in 2 divided doses</td>
<td>Oral</td>
<td>5 days</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td></td>
<td>oral</td>
<td>10 days</td>
</tr>
</tbody>
</table>

streptococcal reactive arthritis (PSRA) may be confused with ARF.

1. The latent period of classical acute rheumatic fever is longer (2 to 3 weeks) than the antecedent streptococcal infection and the onset of migratory arthritis for 2 weeks.
2. We can see dramatically response of aspirin or any other non NSAID therapy in classical ARF patients which will be poorly response in PANDAS or PSRA patients.
3. Acute phase reactants (ESR) and (CRP) will be high in ARF patients than PANDAS and PSRA patients.
4. Cardiac involvement (carditis or valvulitis) is not seen in these patients, but in 50 - 60% of ARF, cardiac involvement is documented.

With these above mentioned evaluations we can differentiate PANDAS and PSRA with classical ARF patient (Barash et al., 2008; Van Bemmel et al., 2009).

There are some other diseases ((Kawasaki disease, sepsis bacterial, septic arthritis, systemic lupus erythematosus, juvenile rheumatoid arthritis) whose clinical features may similar with ARF, they must be rule out.

**Treatment**

Each suspected patients of ARF should be admitted for close monitoring, to confirm diagnosis, and rest till full recovery of the symptoms (Expert Consultation on Rheumatic Fever and Rheumatic Heart Disease, 2001).

Strictly monitoring of vital signs (temperature, heart rate, blood pressure, and respiration rate).

Close monitoring of input and output charting. Till fully confirmation of ARF, paracetamol should be prescribed as first line drug for arthralgia or fever.

**Antibiotic therapy**

After diagnosis of ARF, oral administration of penicillin V (250 mg twice a day) or a single dose of intramuscular benzathine penicillin G (BPG) {(600,000 I.U should be administered if ≤ 20 kg, and 12000,00 I.U if ≥20 kg of body weight (Table 1) or erythromycin (250 mg twice a day) if allergy to penicillin for 10 days as the firstline antibiotic therapy(Table 2). Then long term secondary prophylaxis for about 10 years since the last attack or till 21 years of age whichever is longer (Table 3) doses and (Table 4) durations. (Dajani et al., 1995; American Heart Association Rheumatic Fever 2009; Dajani et al., 1995; Berrios et al., 1993). Many studies have proved that penicillin is the first line of drugs not only to eradicate GAS tonsilopharingitis, but long term prophylaxis therapy, which also reduce recurrent attacks of ARF, frequency and duration of hospitalization in patients with ARF and rheumatic heart disease. Secondary long term antibiotic prophylaxis with BPG is recommended for all people suffering from ARF or RHD. Intramuscular Benzathine penicillin G for every 4 weekly is the drug of choice. In high risk patients with severe carditis or recurrent ARF, 3 weekly intramuscular injection of BPG is preferred
### Table 3. Secondary prophylaxis of rheumatic fever.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Doses</th>
<th>Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzathine Penicillin</td>
<td>600000 I.U. for patients&lt;20kg or 1 200 000 I.U. for patients&gt;20kg every 4 weeks.</td>
<td>I/M</td>
</tr>
<tr>
<td>Penicillin V</td>
<td>250 mg twice a day or 1 gm once daily for patients&gt;27 kg</td>
<td>Oral</td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>500 mg twice a day for patients&lt;27 kg or 1 gm once daily for patients&gt;27 kg</td>
<td>Oral</td>
</tr>
<tr>
<td>For Individual allergy to Penicillin and sulfadiazine</td>
<td>Variable</td>
<td>Oral</td>
</tr>
</tbody>
</table>

### Table 4. Duration of secondary prophylaxis for rheumatic fever.

<table>
<thead>
<tr>
<th>Type</th>
<th>Duration after last attack</th>
<th>Evidence rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic fever with carditis and residual heart disease (persistent valvular disease)</td>
<td>10 years or until 40 years of age (which is longer) life time prophylaxis may be needed</td>
<td>1C</td>
</tr>
<tr>
<td>Rheumatic fever with carditis but no residual heart disease (no valvular disease)</td>
<td>10 years or until age 21 years (which is longer)</td>
<td>1C</td>
</tr>
<tr>
<td>Rheumatic fever without carditis</td>
<td>5 years or until age 21 year (which is longer)</td>
<td>1C</td>
</tr>
</tbody>
</table>

instead of 4 weekly. The patients with the history of penicillin allergy, oral erythromycin can be used as an alternative drug.

**Anti inflammatory therapy:** For fever and arthralgia or a typical arthritis, before confirm diagnosis of ARF, paracetamol (15 mg/kg/dose, 3 to 4 times a day) is the choice of drug. Once the diagnosis is confirmed, aspirin or naproxen (10 - 20 mg/kg/d) is the first line anti-inflammatory drugs. Dramatically, response to aspirin is found, with relief of fever and arthritis after 1 to 3 days (Denny et al., 1986; Homer and Shulman, 1991). The dose of aspirin is 100 to 125 mg/kg/day in 4 to 5 divided doses till pain subside (3 – 5 days), then 75 mg/kg/day in 4 to 5 divided doses for 6 - 12 weeks as clinical response and laboratory measurement of inflammatory markers. But about 5% of patients of ARF may need 6 months or more of aspirin therapy (Stollerman, 1975).

Some studies have concluded that the efficacy and outcome of treatment for fever and arthritis related to RF with Naproxen and Aspirin are same. Naproxen (10 – 20 mg/kg/day) has been safer alternative to aspirin (Hashkes, 2003; Uziel, 2000). Naproxen is easy to give pediatric patients in syrup form and only two times a day but aspirin 4 - 5 times and available only in tablet form. Using aspirin have more chances of liver, gastrointestinal, dermatologic or renal side effects which are very rare to naproxen. Naproxen is well tolerated, less hepatotoxicity, and no risk of complication of Reye’s syndrome (Singh et al., 1992).

**Carditis or congestive heart failure**

Only for severe carditis and heart failure, need glucocorticoids for rapid resolution of cardiac compromise, and as life-saving in severe acute carditis (Cilliers, 2003; Albert, 1995). Drug of choice is oral prednisone or prednisolone (1 – 2 mg/kg/day, in 3 to 4 divided doses) to a maximum of 80 mg daily). First 2 to 3 weeks the doses are as above mentioned, and then is tapered as 5 mg/24 h in every 2 - 3 days. In a very severe case, carditis intravenous methyl prednisolone (10 – 20 mg/kg/day) can be used instead of oral prednisone or prednisolone. Total duration of glucocorticoids therapy is 6 - 12 weeks.

There are no more roles of aspirin to reduce the valves damage in patients with acute rheumatic fever. So if needed, Aspirin is started parallel with steroid in low doses as 60 – 70 mg/kg/day in 3 - 4 divided doses. Supportive treatment for severe carditis and heart failure needs diuretic, fluid restriction and, ACE inhibitor, therapy.

Valve surgery (valve repair, mechanical valve replacement, or bioprosthetic valve replacement according to types and stage of lesions) may be necessary when there is heart failure due to severe mitral regurgitation. Many studied have proved that the valve...
repair to be better operation of choice than replacement for dominant or pure rheumatic mitral or aortic regurgitation. (Thourani, 2003; Yau, 2000). 3 weeks intramuscular BPG injection is mandatory as secondary prophylaxis after valve surgery to prevent infective endocarditis and recurrent valve damage.

For chorea: Sydenham chorea is a self limiting but some rare cases may last for 2 - 3 years (Carapetis and Currie, 1999; Al-Eissa, 1993). This is the reason why there is no need of any specific treatment in mild condition. For severe chorea, haloperidol, which was previously considered the first-line medical treatment, replaced by carbamazepine and valproic acid are now preferred (Daoud, 1990; Genel, 2000). Some studies have proved valproic acid as the first-line agent in the treatment of SC (Cardoso, 2008). Dose of carbamazepine (15 mg/kg/day) and sodium valproate (20 - 25 mg/kg/day) in 2 or 3 divided doses. Haloperidol’s pediatric dose is (0.025 - 0.05 mg/kg/day) in divided doses, and slowly can be increased up to a maximum of (0.15 mg/kg/day). The total duration of this therapy is 12 weeks.

Conclusion

Acute rheumatic fever (ARF) is an auto-immune, nonsuppurative sequela of group A streptococcus tonsillopharyngitis which occurs 2 to 4 weeks after infection resulting in damage to heart valves. Clinical manifestation of ARF can be divided into major and minor criteria. Arthralgia, carditis, sydenham chorea, subcutaneous nodules and erythema marginatum are the major manifestation. Fever, arthralgia, elevated acute phase reactants (ESR and CRP) and prolonged PR interval are the minor manifestation. Jones criteria ([2major or 1major and 2 minor plus the evidence of recent GAS infection (positive throat culture and increased anti streptolysin O titre) support probability of ARF] is the gold standard guideline for the diagnosis of ARF.

When Jones criteria are strictly followed, there are some chances of unnecessary long term treatment by over diagnosis or lacks of treatment due to under diagnosis, that’s why, 1992 updated guideline suggest these 3 condition, patients with chorea, indolent carditis and previous history of rheumatic fever or RHD in which ARF can be diagnosed without adherence of Jones criteria.

In the same way in 2006 and 2012 National Heart Foundation of New Zealand, Cardiac Society of Australia and New Zealand introduced Australian guideline for diagnosis of acute rheumatic fever in new and recurrence cases.

ARF is among one of the main cause of morbidity and mortality in developing countries and major cause of aquired cause of rheumatic heart disease (RHD) worldwide. Long term secondary prophylaxis therapy (3-weekly intramuscular benzathine penicillin (BPG), or oral penicillin V or erythromycin allergic to penicillin) is the key method to prevent recurrence and cardiac complications. Secondary prophylaxis should be continued up to 10 years since the last attack or 21 years of age, which will be long. In case of severe to carditis, heart failure, or valve surgery duration should be prolonged 35 - 40 years.

In developing countries, low socioeconomic status, poor hygiene, poor immunization status and inappropriate medical care are the main cause of Burden of ARF. The graph of ARF in developed countries is decreased dramatically during the 20th century due to standard medical care, broad economic package and health education from governments and partners. ARF is still a great public health problem in developing countries and the most common cause of aquired heart disease worldwide.

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