General Principles of Treatment of Rheumatoid Arthritis

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INTRODUCTION

Over the past 10 years or so there has occurred a 'quiet' revolution in the approach to treatment of rheumatoid arthritis. However the majority of the practitioners of modern scientific medicine seem to be unaware of this. The pessimism that 'there is no treatment of rheumatoid arthritis' still persists. The fact, however, is that upto 95% of the patients can be given remission with the judicious use of the "anti-rheumatoid" drugs which seem to be specific for rheumatoid arthritis.

In this short review I shall outline the general principles of the management of rheumatoid arthritis in the light of the present day knowledge.

Five Components of the Management of Rheumatoid Arthritis (RA)

Huskisson (1984) has simplified the management of RA by outlining its 5 major components. These include :—

1. Correct diagnosis.
2. Relief of symptoms.
3. Slow acting disease modifying anti-rheumatoid drugs. (DMARD)
4. Surgical intervention.
5. Physical therapy and rehabilitation.

It must be mentioned that these modalities of treatment are not mutually exclusive and they must be carried out as and when required, simultaneously.

1. Correct diagnosis

Till recently there has been widespread controversy with regard to the diagnosis of RA. The criteria of American Rheumatism Association have been mentioned for diagnosis without going in their depth and without careful attention to the 'exclusions'. Moreover, it is now realized that the histopathology of synovium is really not always specific for rheumatoid arthritis. Therefore, the recent trend is to narrow down the clinical entity of rheumatoid arthritis using the following RESTRICTIVE definition (Bitter, 1984) :—

PERSISTENT SYMMETRICAL, EROSIVE AND/OR SEROPOSITIVE POLYARTHRITIS MEANS RA

Any other clinical presentation would not qualify for the inclusion in the category of rheumatoid arthritis.

Special attention must be given to these differential diagnoses which closely mimic rheumatoid arthritis :—

a. Primary generalized osteoarthritis.
b. Psoriatic arthritis.
c. Different diseases within the category of seronegative spondarthritis including enterocolitic and unclassifiable varieties.
d. Collagen diseases in early stages.
e. Several rare conditions (sarcoidosis, multicentric reticulohistiocytosis, hyperlipidemia type II and IV etc.).

Making a correct diagnosis of RA is essential because the drug treatment of rheumatoid arthritis may not be effective in other varieties of arthritides.

2. Relief of symptoms

A. Non-steroidal anti-inflammatory drugs (NSAIDs)

The pain in RA joints is due to the presence of inflammation. Therefore, suppressing inflam-

mation by using NSAIDs is a main symptomatic treatment. There are 7 major classes of these drugs :—

1. Aspirin and its modified forms.
2. Propionic acid derivatives (e.g. ibuprofen and naproxen).
3. Mefanamic acid and derivatives (e.g. enfenemic acid).
4. Acetic acid derivatives (e.g. diclofenac).
5. Indane-indene derivatives (e.g. indomethacin, sulindac).
6.* Pyrazolone derivatives (e.g. phenylbutazone).
7. Oxicans (e.g. piroxicam).

(* This group of drugs are not used in RA any more.)

All of these drugs are potentially harmful where upto 30% patients show side-effects. Therefore, they must be given cautiously to elderly persons and children and they must be avoided in early pregnancy. Irrespective of their category, all of them have irritant action on gut mucosa causing peptic ulceration. Therefore, they must be given with meals and adequately covered with antacid therapy.

These drugs have several important drug interactions including those with oral anticoagulants, antidiabetic drugs, methotrexate, etc. and these combinations, therefore, must be avoided as far as possible.

The following points are therapeutically important in the use of these drugs:—

1. Which of these medicines will be optimally effective in a given patient CANNOT BE PREDICTED before hand. Therefore, a trial-and-error method is used where each of the above group of medicines can be used for 3-4 days by turn and then the most effective one for a given patient is found out.

2. The use of more than 1 NSAIDs does not add to their efficacy. Therefore, it is preferable to use one NSAID at a time. Sometimes, however, a long acting drug can be given in larger doses at bed-time to cover the 8 hrs. period of the night.

3. Due to reasons not clear, a major proportion of the total dose of the NSAID given at bed-time seems to work better than in equally divided doses given round-the-clock (except in Piroxicam, where it is effective when given at any time of the day).

4. All the NSAIDs cause fluid and sodium retention to a varying extent. Therefore, their use in cardiac failure and renal diseases with fluid and sodium retention must be avoided (the exception is sulindac which does not have this problem). Diuretics are usually ineffective in controlling this problem.

B. Local corticosteroids

For acute symptoms in one or a few joints, injection of local corticosteroids could be extremely useful and highly recommended. However, a maximum of 3 injections can be given in a joint. Repeated injections must be avoided as it can lead to weakness of joint ligaments and produce secondary osteoarthritis. Use of disposables has markedly reduced the danger of local infection.

C. Anti-depressants/muscle relaxents

One of the reasons for morning stiffness in RA is pain-spasm-pain-spasm cycle in the muscles. It has been found that antidepressant drugs like amitriptyline, doxepin or imipramine can be extremely useful in relieving the morning stiffness. An additional benefit in its use is in the relief of depression, which is present in a majority of the patients of RA. Antidepressant drugs thus work as an important adjunct to NSAIDs in the control of symptoms in RA and they must be used regularly in this disease.

D. Other measures

(i) *Local heat or cold :* Relief of symptoms can be obtained sometimes by cold compression of the joints if the local inflammation is

very acute. On the other hand chronic inflammation with marked stiffness may be relieved by slow heat (like wax-bath).

(ii) *Rest and exercise :* In acute stage of RA, complete rest can be very beneficial. On the other hand adequate exercise intersperced with optimum rest would be ideal for a chronic case.

(iii) *Diet :* Most of the patients with RA have poor appetite and do not eat well. Therefore, properly balanced and paltable diet with adequate vitamin and mineral supplementation is essential.

3. Disease modifying anti-rheumatoid drugs (DMARDs)

This category consists of a diverse group of drugs which are not anti-inflammatory. They belong to wide groups of compounds several of them having a thiol ring, others may have cytotoxic property while still others may have some other property. They seem to work in RA, but not in several other chronic inflammatory polyarthritides. Their exact mode of action is not known. These drugs can be classified into 3 categories :—

Group-I

Drug of proven value and widely used (in developed countries as well as in advanced centres in India):—

1. Gold salts (sodium thioauromalate and thioauroglucose, Auranofin)
2. D-Penicillamine
3. Chloroquine
4. Cyclophosphamide
5. Methotrexate
6. Azathioprine
7. Sulphasalazine

Group-II

Clinically active drugs under continuing investigation :—

1. Combinations of the above drugs
2. Levamisole
3. Captopril and other thiols compounds
4. Dapsone
5. Fenclofenac
6. Thymopoetin
7. Zinc
8. Cyclosporin-A

Group-III

Treatment modalities still at experimental stage :—

1. Plasmapheresis
2. Selective cellular centrifugation
3. Thoracic duct drainage
4. Total lymphoid irradiation (TLI)
5. Antilymphocyte globulin
6. Methylprednisolone pulsing
7. Interferon

Increasing knowledge about the use and the effect of these DMARDs in RA has been a major advance in the over all management of RA over the last 10 years. These drugs act slowly and show their effect only after 12 weeks or so and in case of one drug (chloroquine) only after 24 weeks or so. However, sulfasalazine may show its effect in as short a period as 8-10 weeks. These drugs modify the course and induce remissions in RA. Even the healing of bony erosions have been shown to occur with the use of gold and cyclophosphamide.

There are a few important points with regard to the use of DMARDs. Firstly, most of them are potentially toxic drugs requiring careful monitoring. These drugs must be used with extreme caution and by those who are experienced in their use. One must know their side effects and the way to manage them. Secondly, one can neither predict the effectiveness of any of the DMARDs nor their side effects in a given patient. Therefore, like NSAIDs, one has to do trial-and-error to find the optimal DMARD for a given patient. Such a DMARD would not produce any side effect and yet, lead to remission of RA. Obvi-

ously, because of the slow onset of their action, it may take several months to years before the suitable DMARD can be found for a given RA patient. This is a CRUCIAL POINT FOR THE UNDERSTANDING OF THE DRUG TREATMENT OF RA. This prolonged period when the DMARD has yet to start its effect must be adequately covered with symptom relieving agents. This is the period when some patients may loose hope of recovery and leave the treatment half-way. Reassurance and patient education helps in persuading the patients to continue the treatment till adequate trial of DMARDs has been given.

Till recently it was widely believed that DMARDs cannot and must not be used in any combination. The principle still holds true in most of the situations. However, recent work suggests (Bitter, 1984) that in extremely resistent RA cases some combinations of RA like gold plus chloroquine, gold plus D-penicillamine, gold and methotrexate, or cyclophosphamide, azathioprine and chloroquine may induce remission without any undue toxic effects. But this approach must still be considered experimental.

The other important points to keep note of are, first that till the disease goes in remission all the drugs i.e. NSAIDs, anti-depressants and DMARD must continue simultaneously. The second point is with regard to the maintenance therapy with DMARDs. Once remission is achieved, most of the symptom controlling drugs are discontinued, but DMARDs are continued for a long period of time usually, in a reduced dose. But, the question is to how long their maintenance dose should be given, remains unresolved.

4. Surgical Intervention

Minor or major surgical interventions are often needed simultaneously with the drug treatment. Surgical help may be needed even in the early stages of the disease e.g. minor excision of the lower end of ulna to help the free movement of involved wrist. Persistent single joint involvement may require synovectomy. Snapped tendons may need repair or deformed joints may need corrective surgery. The most important point to remember is that the surgical colleagues must be involved in the total management of the case right from the beginning. This would definitely avoid the undue delay in surgery when it is required.

5. Physical Therapy

Like surgery, physical therapy also plays its role right from the beginning of the management of RA. Local cold compress or heat, rest and exercise have already been mentioned earlier. It is important to remember that exercise may not be good for an acutely inflammed joint. But, proper splinting of the joints at night in acute stage of the disease may go a long way in preventing contractures and deformities. Regarding exercise in general, non-weight bearing isometric contraction exercises are most suitable for RA joints. For optimal result and prevention of deformities involvement of physiotherapist from the start of the management is essential.

SUGGESTED FURTHER READING

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