Rheumatoid Arthritis: acquired experience in an Internal Medicine outpatient clinic of a Regional Hospital

Helena Brito*, Augusta Pereira**, Eurico Gomes***

Abstract

The authors made a retrospective study of rheumatoid arthritis files from the outpatient clinic of Internal Medicine of Faro District Hospital, from 1991 to 1994. The assessed parameters were: gender, age, clinical manifestations, medical treatment and clinical course.

The female gender was predominant (73.3%), and the average age of the group was 56 years of age. All the patients presented articular manifestations and in 40% of the cases revealed extra--articular manifestations.

The assessment of the therapy performed (gold compounds, methotrexate, d – penicillamine) allowed to conclude that methotrexate was the drug with a better clinical response and less toxicity.

From the review of literature about RA the authors point out the need of the earlier use of more aggressive drugs, probably in combination, which can prevent eventual loss of joint structure and function increasing the patient life span.

Keywords: rheumatoid arthritis, methotrexate, gold compounds, d – penicillamine.

Introduction

Rheumatoid arthritis is a chronic systemic disease of unknown aetiology featured by a persistent inflammatory synovitis leading to the joints progressive destruction, with different rates of deformation and functional disability. [1]

It reaches at least 1% of the global population and happens in all racial and ethnic groups. Women are affected around three times more often than men, although the difference between genders tends to reduce with age. [1]

The etiopathology is not quite clear. However it is thought that this can be triggered by the exposure to an immunologically susceptible host to an antigen (endogenous or exogenous) and this interaction is responsible for an immunologic deregulation process and of auto- immunity leading to chronic synovitis and the articular destruction. [1,2,3]

Rheumatoid arthritis can reach any peripheral joint and usually presents a symmetric joint involvement. Extra-articular manifestations are more frequent in patients with serious articular disease, high titles of rheumatoid factor and rheumatoid nodes. [1,2]

The diagnosis is made on the basis of clinical criteria with support of laboratory and radiology tests, using at present the Rheumatoid Arthritis Diagnosis Criteria (revised) of the American Rheumatism Association (1988). [2]

The effect of medical therapy in the evolution of the disease is highly variable reason why attempts have been made to identify predictable factors of the bad prognosis, in order to use in such patients more aggressive therapy. [3,4]

Our aim with this study was to evaluate the clinical aspects and the medical therapy of patients with such pathology followed up in the Internal Medicine clinic /Rheumatology of Faro District Hospital, what we think may contribute to the evaluation of the therapeutic efficacy both at short as long-term.

Materials and methods

The clinical files of patients with a diagnosis of rheumatoid arthritis followed up in the Internal Medicine / Rheumatology Clinic of Faro District Hospital from 1991 to 1994 (30 patients) were retrospectively studied.

The diagnosis of rheumatoid arthritis was made based on the Rheumatoid Arthritis Diagnosis Criteria (revised) of the American Rheumatism Association

*Resident to the Supplementary Internal Medicine Internship

**Internal Medicine Senior Hospital Assistant

***Head of the Internal Medicine Service

Internal Medicine Service of Faro District Hospital

TABLE I

Rheumatoid arthritis diagnosed it criteria (revised) of the American Rheumatism Association (1988)*

1. Morning stiffness in the joint and around it lasting at least one hour before reaching a maximum improvement.
2. Tumefaction of soft parts or liquid (not only bone growth) in at least three joints detected by the physician. The 14 articular areas are the proximal inter-phalanges , metacarpal – phalanxes, wrists , elbows, knees, tibial-tarsus and left and right metatarsal-phalanges.
3. Wrists, metacarpal-phalanges joints and proximal inter- phalanges tumefaction.
4. Simultaneous attainment of the same joints in both sides of the body; bilateral attainment of proximal inter-phalanges, metacarpal-phalanxes or metatarsal – phalanxes is acceptable without an absolute asymmetry.
5. Subcutaneous nodes under the bone prominences, extension surfaces or extra joint areas seen by the doctor.
6. Abnormal amounts of rheumatoid factor in the serum, detectable by any methods, with which positivity is less than 5% in normal control individuals.
7. Radiologic changes typical of rheumatoid arthritis in the anterior posterior X-ray of the hands and wrists; they must include unequivocal erosion or bone decalcification, located on or around the involved joints (osteoarthritis changes are not criterion).
*The diagnosis is supported by the presence of at least 4 criteria. Criteria 1 to 4 must be present for at least six weeks. Adapted from Harris E D Jr.

(1988), (*Table I*).

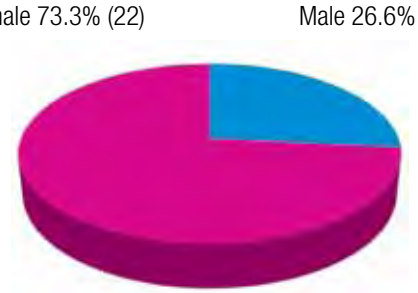
The parameters assessed were gender, age, clinical manifestations, medical therapy and subsequent progression.

Criteria of clinical remission/therapeutic efficacy considered were a reduction on the morning stiffness period, absence of pain on joint mobilization, absence of inflammatory signs in peri-articular regions, reduction in the frequency of crisis (often framed by the clinical condition and a reduction on the need to use anti-inflammatories and /or steroids) and a reduction on the inflammatory laboratorial parameters.

Results

Predominance of the female gender (22 patients – 73.3%) with a ratio women: men of 2.6:1 (*Fig. 1*) was observed.

A higher incidence in patients within the range



Gender Distribution.

FIG. 1

from 40 to 60 years of age, and the general average age was 56 years was observed; 30% of patients were less than 30 years old at the time of the diagnosis (*Fig. 1*).

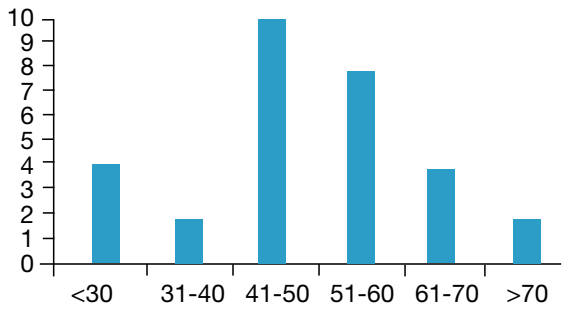
The disease average progression period was 10 years with an interval ranging from 1 to 23 years.

Regarding the clinical manifestations (*Table II*), most patients has shown an insidious onset with symmetric polyarticular involvement, followed by the general symptoms of asthenia, anorexia, weight loss and sometimes fever. All patients had joint involvement, whether at the onset or at the progression the disease, in the hands joints, wrists and knees the most often compromised. In 2 patients it was clear the commitment of the cervical column.

From the studied patients five had rheumatoid

TABLE II

Clinical manifestations	Number of patients	%
Joints	**30**	**100**
Extra – articular	**12**	**40**
Rheumatoid notes	Five	16.6
Vasculitis	–	–
Cardiac	–	–
Pulmonary	1	3.3
Renal	–	–
Neuromuscular	1	3.3
Gastrointestinal	–	–
Ophthalmological	5	16.6



Age Distribution.

FIG. 2

TABLE III

	Clinical remission	Side effects
Methotrexate	60%	13.3%
Gold salts	42%	31.5%
D – penicillamine	20%	20%

nodes, in 4 patients with subcutaneous location (at the hand flexor tendons, elbow and auricular pavilion) and in one case with a location at the level of the cricoarytenoid joint (observed by ENT) with permanent hoarseness symptom.

Only one patient showed manifestations of the Pneumology forum (pleural effusion with exudate features) evolving unfavorably with the administration of non-steroids anti-inflammatory. Another one developed myelopathy with muscle atrophy, 15 years after of disease progression.

The ophthalmological manifestations seen included dry keratoconjunctivitis (3 cases) and anterior uveitis (2 cases).

Around 50% of patients presented, at the time of this study, normochromic normocytic anemia and 16.6% hypochromic microcytic anemia of iron deficiency cause. The average value of the erythrocyte sedimentation rate of this group was 88 mm on the first hour. All patients taking part in the study had a positive rheumatoid factor, but it was not possible for us to co-relate its quantitative value with the severity of the clinical manifestations as not all patients had titles measured.

Initial therapy was, in 19 patients, made by gold salts in parenteral form in one only dose (50 mg/week); from these patients, 9 are still in the same therapy, 8 with clinical remission criteria and 1 who started therapy around one year ago and showed a significant clinical improvement. The causes for withdrawing gold salt therapy include:

- Non-existence of clinical remission criteria – 5 patients;
- Skin rash – 4 patients;
- Kidney failure (creatinine 3.4 mg/dL) - 1 patient;
- Neutropenia and infection by Epstein – Barr virus – 1 patient.

In 15 patients, therapy was started with methotrexate in one only oral those (7.5 mg/week). In 5 patients this was the initial therapy; in the reminder of the patients it was secondary therapy to those which did not succeed with gold salts (seven cases) or d– penicillamine and gold salts (three cases). From the total patients who started methotrexate (average duration of the treatment of 2 ½ years), in 2 it was necessary to withdraw due to toxic hepatitis (proven by laboratorial change of the liver function and hepatic biopsy).

From the 13 patients still in therapy with methotrexate, 9 presented clinical remission criteria, 3 presented a reduction on the crisis frequency, but keeping an increase on the inflammatory laboratorial parameters, and 1 patient who started therapy around one year go keeps an identical clinical situation (without remission criteria).

From the 10 patients who started therapy with d–penicillamine in daily dose (six as initial therapy), [2] suspended the treatment due to an absence of clinical efficacy (around one year after the start) and 2 due to skin rash. From the six still keeping this therapy, 2 showed clinical remission criteria and 4 showed a stabilization of clinical condition around two years after its beginning, keeping morning stiffness for over one hour and an increase of the inflammatory laboratorial endpoints (*Table III*).

From the two patients who are keeping the therapy with non-steroidal anti-inflammatory drugs, one shows a remission of the clinical condition after the first crisis (around one year ago) and the other waits for a normalization of the hemoglobin value to start another therapy. In the studied group, three patients were subject to surgical therapy, namely wrist synovectomy, knee and hip total arthroplasty: for patients

who presented referred to surgical corrections of the knee joints (three cases) and hip (one case) refused the intervention.

Discussion

Rheumatoid arthritis happens more frequently during the fourth and fifth decades of life and it is described with a predominance in the female gender (ratio woman: men of 3.1).[1]

In our sample the distribution by gender and age agreed with the described in the literature.

As it is described for most authors, also in our study the joint commitment was constant, being the peripheral joints the most commonly attained. [2]

Extra-articular manifestations are frequent and may occur practically in any organ and some including cardiopulmonary complications, diffuse vasculitis and infections are potentially lethal. [5] In our casuistry, 40% of patients presented extra-articular manifestations (*Table II*), however none of them leads to death.

The therapeutic approach in patients with rheumatoid arthritis must be made by a multidisciplinary team and must be guided not only to the prevention and treatment of complications (medical therapy, surgery, the physiotherapy), but also if to the inherent psychosocial aspects. [2] The fact the disease evolves for decades, the therapy results are not usually immediately apparent and its course can change spontaneously, contributes to the difficulty of determining the efficacy of the many therapy protocols. The classic pyramidal therapy, initially proposed, has been gradually replaced by other therapeutic regimes with the target not only of pain relief, but also of trying to prevent the eventual loss of the structure and the joint function and increasing the survival. [2, 4]

The therapy with anti-malaria, sulphasalazine line, gold salts, d-penicillamine, methotrexate, azathioprine and cyclosphosphamide. (DMARD – disease modifying antirheumatic drugs) is effective when compared with placebo or non-steroidal anti-inflammatory drugs, to the relief of symptoms and in the improvement of the therapeutic objectives of rheumatoid arthritis. [6] Recent studies have documented the efficacy of methotrexate, presenting this comparing to other DMARD, with a quicker action onset, better clinical response and less toxicity. However, it seldom produces long-term remissions.[7]

In our study, in spite of being made by a sample of only 30 patients and because it is retrospective can offer limitations to appreciate the therapeutic efficacy of different drugs (and the absence of the control group, a variable duration and non-standard of the therapy), enables to state that:

the therapy which has shown less percentage of side effects was the therapy with methotrexate (13.3%) comparatively to side-effects recorded with gold salts (31.5%) d – penicillamine (20%).

regarding the clinical remission criteria recorded in 60% of patients subject to methotrexate therapy and in 42% and 20% of patients undergoing respectively gold salt therapy and d – penicillamine, data which in general agree with those found in literature and drop out of d– penicillamine in the treatment of rheumatoid arthritis.

This assessment, as most published on the literature, is a short term study. At present there is clear evidence that a therapy enabling to prevent the loss of the structure and joint function (around 15 years after the onset of the disease, 60% of patients will be disabled and 30 years after such rate will reach 90%) [6,8] does not exist yet, thus the need of starting more aggressive therapeutic schemes as early as possible. Nowadays, a number of works are ongoing where a variety of combinations of DMARD are being used, but there is the need for long-term controlled clinical trials to assess which combinations, doses and sequences of administration are more beneficial and less toxic.[9, 10]

References

1. Lipsky P E. Rheumatoid arthritis. Harrison's Principles of Internal Medicine 1994: 1648 – 1655.

2. Harris F. D. Jr. Clinical features of rheumatoid arthritis. Kelly textbook of rheumatology 1993:874 – 911.

3. Vikingsson A, Graziano FM. Artrite Reumatóide: a importância do diagnóstico precoce na evolução a longo prazo. Postgraduate Med 1995; 3:38 – 47.

4. Mazières B, Cantegrel A. Rheumatoid arthritis: Modern Treatments. Acta Reumat Port 1995; 72:23 – 29.

5. Fleming A, Crown JM, Corbert M. Early Rheumatoid Disease.I onset. Ann Rheum Dis 1976; 35 (4): 357 – 360.

6. Kushner I. Does aggressive therapy of Rheumatoid Arthritis affect the outcome? J Rheumatology 1989; 16:1 – 4.

7 Shiroky J B, Neville C, Skelton JP. High dose intravenous methotrexate for Refractory Rheumatoid Arthritis. Journal of Rheumatology 1992; 19:247 – 251.

8. Graudal HK, Graudal N, Jurik A G. On the course of seropositive Rheumatoid Arthritis during and after long-term gold therapy. Scand J Rheumat 1994; 23 (5), 223 – 230.

9.Paulus HE. The use of combinations of disease modifying anti-arthritic agents in Rheumatoid Arthritis. Rheumatoid Arthritis 1990; 33:113 – 120.

10. Haagsma CJ et al. Combination of methotrexate and sulphasalazine vs methotrexate alone: a randomized open clinical trial in Rheumatoid Arthritis patients resistant to sulphalazine therapy. Br J Rheumatology 1994; 33 (11): 1049 – 1055.