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Procedures on Rheumatoid Arthritis Management by Rheumatologists in Morocco

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Original Research Article

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Abstract: This work aim is to assess procedures used by Moroccan rheumatologists in managing rheumatoid arthritis in order to check levels of adherence to the recommendations put forth by the Moroccan Rheumatology Association (SMR). A questionnaire was developed, validated by a committee of experts and then sent to all Moroccan rheumatologists. The questionnaire was produced in Google forms and e-mailed to them on three occasions between October and November 2015. The questionnaire included a set of multiple choice questions as well as clinical cases reviewing the various items of the recommendations of SMR. The degree of adherence to recommendations is rated on an assessment scale. Amongst the 300 rheumatologists practicing in Morocco, only 235 had a valid email address. The participation rate was 32.3%. The proportion of patients consulting for early RA (less than 3 months) was 26%. Basic treatment was started by 96% of the rheumatologists. Methotrexate (MTX) was used in 94.4% of the cases in combination with oral corticosteroid therapy in half of the patients involved. Half of rheumatologists ensured follow-up in a systematic fashion using baseline DAS 28. If therapeutic failure of seronegative non erosive RA due to inadequate response to MTX occures, 92.8% of the physicians optimized the MTX dose up to 25 mg per day and 64.2% proposed a combination of (MTX+Sulafasalzin+Hydroxychloroquin).However, in case of therapeutic failure of a severely active, seropositive erosive RA treated with MTX, 67.6% offered biotherapy. The proportion of patients with RA who received biotherapy treatment was 24%. In 64.3% of the cases, Rituximab was used as first-line therapy. In patients who have failed a first anti-TNF therapy, 52.6% of rheumatologists proposed another anti-TNF agent. Only 37% of rheumatologists were able to stop corticosteroid, 81.3% continued prescribing substantive treatment while 60% managed to stop biological therapy. Only 38.2% routinely vaccinated their patients.
Keywords: Rheumatoid Arthritis (RA), Recommendations, Survey, Rhuematologists.

INTRODUCTION

Rheumatoid arthritis is a chronic disease, which eventually progresses to a severe disability in the event of lack of optimal proper care [1]. With a view to standardizing and homogenizing RA management in Morocco, the Moroccan Rheumatology Association (SMR) prepared recommendations on good medical practices in 2011 -subsequently updated in 2014[2]. These recommendations provide frames of reference for evaluation of practices. This post-evaluation involves gauging any variance between the current practice and these recommendations.

The goal pursued by our study was to assess RA management in Morocco. This is the first experiment of its kind, which seeks to assess the arrangements for practical RA management by rheumatologists in Morocco and to check the level of their adherence to the SMR's recommendations.

MATERIALS AND METHODS

A questionnaire survey was conducted targeting the community of Moroccan rheumatologists to assess arrangements for practical RA management. The questionnaire was prepared and validated by a committee of experts and emailed to all Moroccan rheumatologists. It included multiple-choice questions, in addition to clinical cases developed in close connection with the 2014 Moroccan Rheumatology Association's recommendations. It is comprised of four parts:

-The first part aims at collecting information

on the rheumatologist in relation to his/her area of endeavor, seniority, title), the number of patients seen within a month, the patient's specific disease characteristics(date of diagnosis and pace of surveillance);

- The second part contains 13 multiple-choice questions: the 1st item lists the additional examinations requested to be performed to determine RA diagnosis. The 2, 3 and 4th items aim at determining the terms and conditions governing substantive treatment. Questions from the 5th to the 9th item specify procedures for steroid therapy prescription (administration route, therapeutic dose and withdrawal). The 10th, 11th and 12th questions assess monitoring of patients (i.e. the evaluation method, monitoring done by a general practitioner). The final question specifies the proportion of remission in rheumatoid arthritis (RA);

- The third segment is in the form of a clinical case, which includes two items on the therapeutic treatment approach to be used when facing a significant episode of rheumatoid arthritis (RA);

The fourth and final part includes 11 multiple-choice questions: the first nine questions put emphasis on biotherapy (i.e. selection criteria, side-effects, length of treatment and alternative therapeutic strategy in case of inadequate response). The 10th item outlines the therapeutic procedure to follow to cope with a persistent remission. The final question seeks to determine the vaccination status of patients receiving biotherapy.

The survey was conducted using Google forms. It was a simple opinion poll. Indeed, physicians responded without reviewing the medical records of their patients with regard to their daily practice in connection with RA management. The survey was conducted between October and November 2015. The first electronic filing of the questionnaire was sent on 14 October 2015, followed by three follow-up reminders: on 24 October, 8 and 24 November. The survey was completed on 29 November 2015. Appropriate measures were taken to preserve the anonymity of participants.

RESULTS

Close to 300 rheumatologists are currently serving in Morocco, of which around 46 could not be reached by email. Over the 254 sent mails, 235 were received and 19 displayed non valid email addresses. Seventy six rheumatologists responded to the questionnaire, representing a participation rate of 32.3%. Responses to the questions were analyzed. Results are expressed as a proportion. Incomplete answers were excluded from the study.

The majority of respondents (41.7%) practiced their activity in the private sector, 33.3% in hospital settings and 25%in the public sector. As regards findings in connection with years of experience, 31% of rheumatologists asserted having had less than five years of experience in the field and 28.2% more than twenty years. Furthermore, the participants were overwhelmingly specialists (71.4%), while 15.7% were academics and 12.9% medical residents.The number of patients with RA, examined monthly, ranged between 10 and 20 for 44.4% of the physicians, <10 for 26.4%, between 20 to 30for 20.8% while 8.3% of rheumatologists were receiving more than 30 RA patients per month. On the other hand, the proportion of patients who consult their doctor at an early stage of the RA amounted to 26 %(RA evolving for less than three months)

95.8% of rheumatologists started basic treatment regimen immediately after establishing RA diagnosis. Treatment consisted basically of MTX in 94.4%of the cases. The proportion of patients receiving MTX orally amounted to 48% in the private sector and 38% in the public sector, respectively.

Oral corticosteroid therapy was prescribed for more than 50% of patients afflicted with recent RA. On average, 71% of rheumatologists prescribed a dose equal to or less than 7.5 mg per day. In mature RA cases, the proportion of patients undergoing long- term corticosteroid therapy (under 7.5 mg per day for most cases) was 66%. To avoid prescription of systematic oral corticosteroid therapy at the time of early management of RA, 29% of rheumatologists preferred resorting to an overdue single corticosteroid injection using intramuscular injection (IM), whereas 51% selected the option of corticosteroid first-line attack.

Among the 94.4% of rheumatologists who ensured monitoring of patients once every three months, half of them did it in a systematic way, using baseline DAS28. On the whole of the rheumatologists sampled in the survey, 74% did not have a referring GP, tasked with ensuring the monitoring of patients (i.e. remoteness and geographical isolation problems and/or prescription renewal).

On average, the proportion of patients in RA remission monitored in consultation stood at 39% (Table1). In the event of therapeutic failure of seropositive and non erosive RA treated with MTX, 92.8 % of practitioners titrated the MTX dose to at least 25 mg per day, 64.2% proposed a combination of Methotrexate/ Sulfasalazine/ Synthesis Antimalarial Drugs) (MTX/SLZ/APS). However, in the event of therapeutic failure of a severely active, seropositive and erosive RA treated with MTX, 67.6% of physicians offered medical biotherapy.

Rituximab was prescribed as first intention biotherapy in 64.3% of cases, while the prescription proportion of Etanercept, Adalimumabet and Tocilizumab stood at 15.3%, 8.6% and 1.4%,

respectively. Other DMARDs are not yet marketed in Morocco.

The selection of biotherapy was guided in 80% of the cases by the existence or non-existence of health insurance coverage and secondly, by better tolerance to the treatment, treatment pricing, ease of the route of administration and greater treatment efficiency. The majority of rheumatologists (63%) ensured medical follow-up to less than 25% of patients with RA receiving biotherapy. 19.4% cases of tuberculosis were reported in patients receiving biotherapy and 85.7% in patients on infliximab.

The vast majority of patients received biotherapy for an average duration of two years (Table2). In the event of response failure or escape of first anti-TNF therapy, 52.6%of rheumatologists proposed an alternative anti-TNF and 36.8% would choose to use another biological treatment other than anti-TNF. In the event of response failure or escape of a first anti-TNF therapy, the neutralizing, anti-drug antibodies (ADAs) were requested by only 25% of the rheumatologists.

However, in the case of persistent remissions, only 37% of rheumatologists managed to stop corticosteroid therapy, 81.3% continued prescribing first-line drug treatment and 60% were able to stop biological therapy. Only 38.2% systematically vaccinated patients on biotherapies. It was a flu vaccination in 90% of the cases and a pneumococcus vaccine for 70%.

Table-1: The proportion of patients with RA in remission monitored in consultation

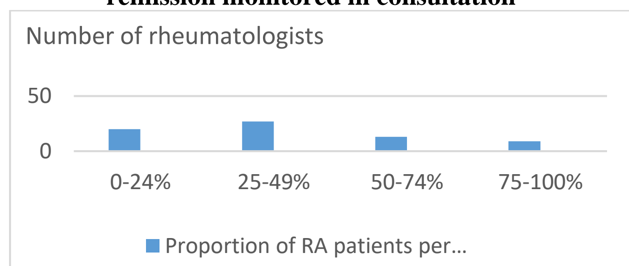
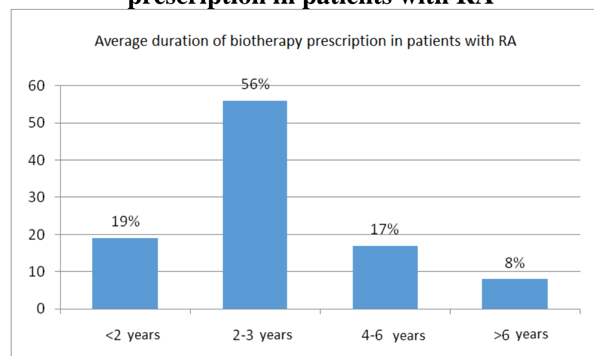


Table-2: Average duration of biotherapy prescription in patients with RA



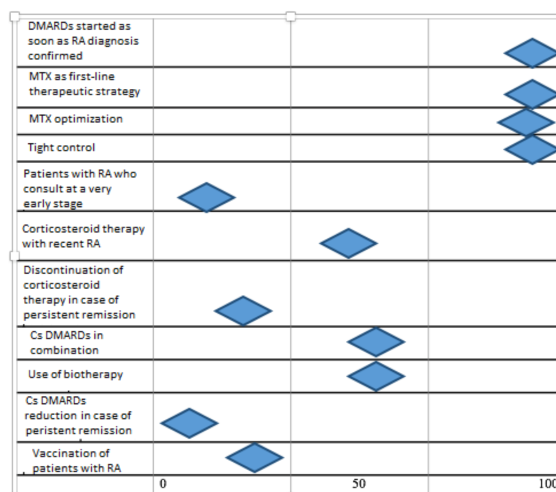


Fig-1: Degree of consistency with the SMR's recommendations relating to RA management

DISCUSSION

RA is the most frequent chronic inflammatory disease of the joints in adult patients. Its prevalence rate is estimated to lie somewhere between0.3 and 1% of the adult general population (approximately around 200.000 patients in Morocco) [3]. It has both a functional impact and is life-threatening [1]. Overall, the main findings arising from the study objectively highlight a fair degree of consistency with the recommendations of the Moroccan Rheumatology Association in RA management Figure 1.

The highest level of consistency with the recommendations (>90%) was found with several items: i.e. initiating treatment of RA, using Traditional Disease Modifying Anti-Rheumatic Drugs (DMARDs) as close to diagnosis as possible, use of MTX as a first-line therapy strategy by Moroccan rheumatologists in patients with active RA, increase of MTX dose up to 25 mg per day in the event of a therapeutic failure of a seropositive and non erosive RA on MTX, as well as the tight control of the disease including a dynamic therapeutic strategy together with an explicitly stated objective« Treat to Target »[5-6].Figure 1 However, there are some sticking points, which are still at odds with the recommendations on RA management.

The proportion of patients, who made out-patient visits at a very early stage of RA, stood at 26%. This seems to be due to geographical distance, the absence of a family physician, the use of non-medical therapy, i.e. traditional medicine, in this case. A study on the use of medicinal plants in rheumatology has shown that 39%of patients rely on traditional herbal remedies before they are able to access treatment [14].

According to the recommendations of the Moroccan Rheumatology Association, low doses of

steroids can be considered to be part of the initial therapeutic strategy (in combination with DMARDs), for at least a period of 6 months maximum but they have to be stopped at the earliest possible date [2-8]. Nonetheless, based on our survey, oral corticosteroids therapy was prescribed for more than 50% for patients with recent RA and at a mature stage in the development of the pathology, the proportion of patients receiving long term corticosteroid therapy was 66%. For this purpose, the Moroccan Rheumatology Association (SMR) recommended using an alternative therapy to daily oral corticosteroids using Methylprednisolone from 80 to 120mg, administered by intravenous route to avoid withdrawal effects [2-13].

In case of persistent remission, only 37%of Moroccan rheumatologists managed to stop corticosteroids. This item is the most controversial one. In fact, in the literature, almost one patient out of three with RA is treated with long-term corticosteroids [12]. Similarly, in the 2013 EULAR recommendations, the binding power of the recommendation for stopping corticosteroids reached 8.9±1.2 level of agreement and a vote proportion of 37% [7].

For patients who responded inadequately or were intolerant to MTX treatment and in the absence of poor prognostic factors, a combination of first-line-attack treatment was recommended to be used, such as the triple combination of MTX/SLZ/APS [2]. Biotherapy would be prescribed as a second option if triple therapy failed to deliver. This would ultimately result in reducing the cost burden of RA management in our context, while keeping focus on treatment goals. However, this recommendation was not broadly followed by Moroccan rheumatologists. Only 64% proposed this combination. This was probably due to the fears of having to cope with the potential harmful side effects increased by both triple therapy and the non-availability of folic acid, which can help decrease side effects and not on hydroxychloroquine, known for ensuring greater tolerance than chloroquine currently marketed in Morocco [9-10].

In the event of failure of MTX as monotherapy in patients with active RA, several scholarly studies have shown greater effectiveness of triple therapy compared to biotherapy (MTX/SLZ or MTX/APS) and to monotherapy(MTX or SLZ alone) with a good safety profile[15].In clinical trials, the retention rate of triple therapy was good , reaching up to 62% in 5 years[11].Also, in a multi-centre non-inferiority study, the authors concluded the non-inferiority of the triple therapy in comparison with the combination of MTX and Etanercept [9].

Also, in the event of therapeutic failure of a severe, active, seropositive and erosive RA on MTX, only 2/3 of the rheumatologists proposed biotherapy regimen. This can be possibly explained by the low level of health insurance coverage rate, which made up only 33.7% of the total population in 2010, according to the Moroccan National Health Insurance Agency. Ongoing developments were made to extend the coverage rate to 62% in 2014.

In our study, Rituximab was prescribed as a first-line attack biotherapy in 64.3% cases. As a matter of fact SMR proposes Rituximab as a frontline regimen in its RA management strategy, mainly for its high efficiency in csDMARDs -naive patients, as well as those with a poor response to csDMARDs, for its less exorbitant cost at the moment and compared with other therapies, less problems in connection with tuberculosis reactivation.

In the event of long-lasting persistent remission, it is specified that cautious reduction of csDMARDs can be viewed as an appropriate path to follow [2], while 81.3% of rheumatologists continued prescription of substantive treatment.

Indeed, the discontinuation of csDMARDs by patients with deep RA remission is followed by relapses in almost 70% of the patients [4]. Hence, this recommendation highlights the importance of reducing csDEMARDS rather than discontinuing them.

In the event of inadequate response or escape of first anti-TNF antagonists, the neutralizing, anti-drug antibodies (ADAs) were requested by only 25% of rheumatologists, in view of their recent introduction into Morocco and high cost.

Finally, vaccination of patients receiving treatment with biotherapy should be systematically embedded in the monitoring procedures. However, only38.2% of rheumatologists routinely vaccinated their patients receiving biological treatment. In the literature and in accordance with the new CDC (Center for Disease Control) guidelines, patients with RA should get a flu shot every year as well as a pneumococcal vaccine (PNC vaccine) [16].

A major limitation of the study is that the participation rate was only 32%. It should also be noted that, since this is a review investigation, the results may differ materially from actual practice. However, data collected provide us at least with the participants' points of views and can, therefore, act as a reference point on arrangements for the management of patients with RA in routine clinical practice. In addition to this, the data provide a reflective sampling of some the comments made by the survey participants and do not necessarily reflect the views of all rheumatologists.

CONCLUSION

Management of patients with RA is indeed an uphill difficulty and the recommendations help in the process of standardizing it. In Morocco, arrangements

for RA management denote a fair degree of closeness with the SMR's recommendations. Nevertheless, there are still some sticking points which are inconsistent with the recommendations. In fact, corticosteroid therapy remains widely prescribed, whereas it should be part and parcel of the initial therapeutic strategy (in combination with DMARDs), lasting for a period of 6 months maximum and should be stopped at the earliest stage possible. In the absence of poor prognosis factors, use of the triple association MTX/SLZ/APS is highly recommended, except that its adoption by Moroccan rheumatologists is not widespread. This attitude will certainly be instrumental in alleviating the cost burden of RA management, while maintaining the treatment objectives. Finally, access to biotherapy is still quite limited, due to low rates of medical coverage.

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