Practices for managing a flare of long-standing rheumatoid arthritis: Survey among French rheumatologists

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Abstract

Objective

To describe the practices of rheumatologists in France for managing a flare in a patient being treated for long-standing rheumatoid arthritis (RA) and to estimate the corresponding costs.

Methods

A survey questionnaire was sent to the 2485 practicing rheumatologists in France; 917 completed questionnaires were returned (37% response rate). The questionnaire collected information on the respondents and on their recommendations for managing a fictional patient with a 10-year history of RA in flare, with a recent episode of neck pain, despite prednisone and methotrexate therapy. Investigational and treatment (first month) costs were estimated from the perspective of society in 2001 Euros (€).

Results

Over 80% of the respondents recommended measuring laboratory inflammation parameters, complete blood cell counts, liver enzymes, serum creatinine, and radiographs (hands, anteroposterior cervical spine view, wrists, knees); 50-70% recommended additional cervical spine incidences, elbow and chest radiographs, and bone absorptiometry. Adding anti-TNF therapy (24%) or another DMARD (10%), increasing the methotrexate dosage (24%), and substituting leflunomide for methotrexate were the main recommended treatments. Most respondents suggested continuing the glucocorticoid in the same dosage (61%) or a higher dosage (36%). Analgesics and non-steroidal anti-inflammatory drugs were recommended by 65% and 41% of respondents and rehabilitation therapy by 83%. The median cost was €500 (mean €1,105; range €80-4,089).

Conclusion

We found a high level of agreement among French rheumatologists regarding the evaluation of established RA. Marked variations in recommended treatments were observed and translated into major cost differences.

Key words

Rheumatoid arthritis, evaluation, drug prescription, survey.

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This work was supported by research funds from the Education Ministry. An educational grant was received from Wyeth-France.

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Received on April 13, 2004; accepted in revised form on September 17, 2004.

Introduction

The chronic fluctuating course of rheumatoid arthritis (RA) can lead to progressive joint destruction and disability despite treatment. The treatment should be adjusted periodically to the individual patient's disease and expectations. The prognosis of RA changed with the availability of new therapies, such anti-TNF therapy (1-3). Guidelines for rheumatologists regarding the management of RA have been proposed (4) and are important to minimize variability in clinical practice (5).

To collect data on the practices of rheumatologists in France regarding the management of RA, we conducted a questionnaire survey focusing on the management of a patient with a 10-year history of RA and a current flare despite glucocorticoid and methotrexate therapy.

Participants and methods

Rheumatologists and respondents

To draw up the list of all rheumatologists practicing in France, we reviewed the 2001 yearbook published by the French Society for Rheumatology and the web-based yellow-pages directory. Of the 2559 rheumatologists thus identified, 74 were excluded for the following reasons: wrong address (n = 53), retired (n = 13), deceased (n = 5), or not rheumatologists (n=3). This population of rheumatologists has been described in detail elsewhere (6).

Questionnaire

We designed a questionnaire that had two parts, one for collecting information on the respondent and the other for evaluating how the respondent would manage a patient with a flare of long-standing RA.

The following data on the respondent were collected: gender, time in practice (in years, from the year of the doctoral dissertation to 2001, with three categories: 10 years or less, 11 to 21 years, and more than 21 years), type of practice (hospital-based, office-based, both, or other), and geographic area (Paris and the surrounding urban area, northwest, northeast, southeast, and southwest and overseas districts of France).

The second part of the questionnaire presented the (fictional) clinical vignette of a 60-year-old woman who had experienced RAat cessation of menses 10 years earlier; she had received intramuscular gold and sulfasalazine and was currently on oral prednisone (10 mg/day) and intramuscular methotrexate (15 mg/week). Total hip arthroplasty had been performed on the right hip. She had been on disability for the last 9 years because of her RA. A transient episode of neck pain had occurred 2 months earlier. Her current symptoms indicated a flare: diffuse joint pain with a visual analogue scale (VAS) pain score of 60/100; a score of 1.5 on the HAQ; synovitis of the metacarpophalangeal joints, wrists, right elbow and left knee; and motion-range limitation at wrists.

The respondents were asked to complete two items describing their recommendations for this fictional patient. In the first item, the respondents selected investigations from the list shown in Table I. In the second item, the respondents indicated their treatment choices among suggestions in a list of medications (Table II) and another list of non-pharmacological treatments (intra-articular injections [glucocorticoid injections, isotopic synovectomy, or chemical synovectomy]); rehabilitation therapy [physical therapy, occupational therapy, or orthoses]; and surgical procedures). A question about the type of diet recommended was asked of the rheumatologists.

Costs

Only investigational (laboratory tests and other examinations) and treatment costs were evaluated, from the perspective of society, in 2001 Euros (€). The cost of each investigation was estimated based on the price lists established by the French national health insurance system. The costs of medications were calculated from retail prices, by multiplying the price of each treatment unit (e.g., tablet) by the number of units prescribed per day. Because some respondents failed to indicate the treatment duration, we calculated the cost for 1 month of treatment. We did not calculate the costs of rheumatologist visits, since data on the number of

these visits could not be derived from the questionnaire.

Conduct of the study

In compliance with French regulations, we used the names of the rheumatologists only to draw up the initial list of rheumatologists who were mailed the questionnaire and the list of those who were sent a second questionnaire because they had not answered the first one. In November 2001, the questionnaire was sent to the 2,559 rheumatologists identified initially. Only 594 completed questionnaires were returned. As explained above, 74 rheumatologists, all non-respondents, were excluded, leaving 2,485 potential respondents. The remaining 1,891 non-respondents were sent the questionnaire again, in mid-December 2001; this produced 323 additional completed questionnaires. Our final response rate was 917 of the 2485 included rheumatologists (37%).

Statistical analysis

All statistical tests were carried out using SAS and BMDP software.

Comparison of respondents and non-respondents. For the overall population of rheumatologists (respondents and non-respondents), we determined the number and percentage with each of the characteristics studied. Respondents and non-respondents were compared by univariate analyses using chi-square tests for the categorical variables (geographical area, gender, and type of practice) and Kruskal-Wallis tests for the time in practice, handled as a continuous variable. Multivariate logistic regression was then performed using the above-described categories for each study variable. In our model, we used hospital-based practice (code 1), 11-20 years in practice (code 2), and Paris area (geographical area) as the reference values. Global P values smaller than 0.05 were considered statistically significant.

Analysis of questionnaire data. Descriptive statistics (numbers and percentages) were calculated for the investigations and treatments. Costs for each category were described by determining the mean, standard deviation, range, and quartiles.

Comparison of responses according to respondent characteristics. For this analysis, characteristics were entered as explanatory variables into a logistic regression analysis to evaluate differences in practice (type of investigation, treatment and corresponding costs).

Results

Respondents' profile

The characteristics of the respondents and non-respondents are reported in Table I. The male-to-female ratio was 2.3 for respondents and 2.6 for non-respondents. In the univariate analysis, differences between respondents and non-respondents were significant for geographical area, type of practice, and time in practice (data not shown). In the logistic regression analysis, response rates were lower in the Paris area than in other geographical areas ($p = 0.0365$ to 0.0026), higher in women than in men ($p = 0.0033$), lower among office-based than hospital-based rheumatologists ($p < 0.0001$), higher among rheumatologists in a mixed office and hospital practice or in other types of practice than among rheumatologists in hospital practice only ($p < 0.001$ and $p = 0.0063$, respectively), and higher among rheumatologists with 11-20 years of practice than in those with fewer or more years in practice ($p < 0.0001$).

Recommended investigations

Table II shows the investigations recommended for evaluating the patient with a flare 10 years into the history of her RA. Nearly 90% of respondents checked inflammation parameters (erythrocyte sedimentation rate and C-reactive protein), tests for monitoring treatment safety (complete blood cell counts, liver enzymes, and serum creatinine), and radiographs (hands, cervical spine, wrists, and knee, anteroposterior incidence).

Investigation of the episode of neck pain 2 months before presentation was recommended by 70% of respondents, among whom 88% suggested anteroposterior radiographs and 70% lateral radiographs in the neutral position and with the neck flexed and extended. Magnetic resonance imaging was not on the response options list but was recommended by 3% of the respondents.

Answers varied substantially regarding bone status evaluation in this 10-year postmenopausal woman with RA and

Table I. Characteristics of the source population of rheumatologists and of the respondents.

No. (%)	Source population 2485 (100)	Respondents 917 (37)
Geographical area	no.	no. (%)
Paris metropolis	643	222 (35)
Northwest of France	401	164 (41)
Northeast of France	425	183 (43)
Southeast of France	687	234 (34)
Southwest and overseas districts of France	329	114 (35)
Gender	no.	no. (%)
Female	679	274 (40)
Male	1294	640 (38)
Male-to-female ratio	2.5	2.3
Unknown	112	3 (3)
Type of practice	n.	n. (%)
Hospital	487	205 (42)
Office	1682	487 (29)
Hospital and office	261	197 (75)
Other	37	27 (73)
Unknown	18	1 (6)
Time in practice	no.	no. (%)
0-10 years	974	225 (23)
11-20 years	764	360 (47)
> 20 years	714	316 (44)
Unknown	36	16 (44)

Table II. Laboratory and non-laboratory investigations recommended by rheumatologists (n = 917) for a fictional patient with a 10-year history of rheumatoid arthritis and a current flare.

Laboratory tests	*%*	*Radiographs*	*%*
Erythrocyte sedimentation rate	95	Hands: anteroposterior	90
Complete blood cell counts	93	Cervical spine: anteroposterior	88
C-reactive protein	88	Wrists: anteroposterior	85
Liver enzymes (ASAT, ALAT)	86	Knees: anteroposterior	80
Creatinine	84	Cervical spine: lateral	70
Calcium	46	Cervical spine: lateral in flexion and extension	70
Rheumatoid factor	45	Elbows: anteroposterior	65
Alkaline phosphatase	41	Cervical spine: anteroposterior mouth open	64
Gamma-glutamyl-transpeptidase	40	Feet: anteroposterior	54
Serum electrolytes	35	Chest: anteroposterior	53
Proteinuria	35	Knees: lateral	46
Antinuclear antibody	34	Elbow: lateral	39
Serum protein electrophoresis	32	Wrists: lateral	26
Serum phosphate	31	Feet: lateral	18
Serum albumin	26	Feet: oblique	10
Urine dipsticks	25	Chest: lateral	10
Serum vitamin D	18	Others	< 2
Antikeratin antibody and related	16		
Uric acid	11	*Other investigations*	*%*
Urine culture*	8		
Hepatitis C serology	6	Bone absorptiometry	63
Hepatitis B serology	5	MRI: cervical spine (C1-C2) *	3
Complement	5	Radionuclide bone scan	2
Cryoglobulin	4	Others	< 1
HLAclass II	3		
HLAclass I	2		
Others	< 1		

HLA: human leukocyte antigens; MRI: magnetic resonance imaging; *items recommended by the respondents but not on the response option list.

Table III. Drugs recommended by rheumatologists (n = 917) for a fictional patient with a 10-year history of rheumatoid arthritis and a current flare.

Drugs	% (n.)	Class	%
Disease-modifying antirheumatic drugs	99 (912)	Methotrexate alone or in combination	58.2
		• Methotrexate + etanercept or infliximab	24
		• Methotrexate alone	23.7
		• Other combination with methotrexate	10.5
		Leflunomide	37.6
		Not specified	3
		Cyclosporine	0.6
		Tiopronin	0.3
		Sulfasalazine	0.2
		Hydroxychloroquine	0.1
Glucocorticoids	99 (910)	Prednisone	94
		Others	6
Analgesics°	65 (600)	Level II	57.2
		Level I	39.2
		Level III	1.8
		Combination of analgesics	1.5
		Not specified	0.3
Antiinflammatory drugs	41 (372)	Cox-2 inhibitor	47
		Conventional NSAIDs	46.6
		Not specified	6.4
Other treatments*	24 (219)	Treatment for osteoporosis	69
		Gastroprotective drugs	15
		Folic acid	11
		Others	5

NSAIDs: nonsteroidal antiinflammatory drugs; °World Health Organization classification; *treatments recommended spontaneously by the respondents but not on the response option list.

glucocorticoid treatment. Bone absorptiometry was the most commonly recommended exam (63% of respondents), followed by serum assays of calcium (46%), phosphate (31%), and vitamin D (18%).

Recommended treatments

Table III shows the treatments recommended by the respondents. A variety of regimens of disease-modifying antirheumatic drugs (DMARDs) were proposed. Methotrexate alone or in combination with another DMARD was recommended by 58.2% of respondents. The mean recommended methotrexate dosage was 16.7±2.8 mg/week, and the DMARD most often used in combination with methotrexate was infliximab (24%). Leflunomide was selected by 37.6% of respondents.

All the respondents recommended continuing the glucocorticoid therapy; 61% suggested using the same dosage, 36% a higher dosage, and 3% a lower dosage. Among the respondents in favour of a higher dosage, 14% suggested switching from prednisone to methylprednisone; the higher dosages suggested by the respondents in this group were 13.4 ±9.3 mg/d for prednisone and 320 ± 218 mg/day for methylprednisone, the corresponding durations being 28 ± 20 days and 3 ± 5 days, respectively.

Secondary prophylaxis for osteoporosis was felt to be appropriate by 16.5% of respondents, among whom 55% suggested combining a bisphosphonate with calcium and vitamin D supplementation.

Analgesics were recommended by 65% of respondents, with a preference for step II drugs. Non-steroidal anti-inflammatory drugs (NSAIDs) were deemed necessary by only 41% of respondents, with an even distribution between Cox-2 inhibitors (47%) and conventional NSAIDs. Gastroprotective drugs were rarely recommended as a prophylaxis for NSAID side effects; in 91% of cases, the recommended drug was a proton-pump inhibitor.

Local treatments chosen by the respondents were as follows: intra-articular glucocorticoid injection (61%), surgery (26%), and chemical or radiation syn-

Table IV. Costs of investigations and treatments recommended by rheumatologists (n = 917) for a fictional patient with a 10-year history of rheumatoid arthritis and a current flare (2001 Euros).

	Mean	Mode	Minimum	1st quartile	Median	3rd quartile	Maximum
Diagnostic investigations							
Laboratory tests (n = 908)	80	653	3	45	64	94	519
Other tests (n = 913)	276	328	23	205	261	319	964
Total 1	356	412	47	255	326	415	1460
Treatment for one month							
DMARDs (n = 884)	724	113	4	19	113	226	2757
Glucocorticoids (n = 901)	11	7	4	7	7	11	142
Analgesics (n = 588)	17	0	0	0	19	27	473
Anti-inflammatory drugs (n = 348)	14	0	0	0	0	21	124
Other treatments (n = 130)	6	0	0	0	0	0	109
Total 2	746	2761	7	76	146	264	3234
Total costs (1 + 2)	1105	2962	80	387	500	1054	4089

DMARDs: Disease-modifying antirheumatic drugs.
Costs were calculated based on brand names and dosages reported by the respondents.

ovectomy (11%). The joint most often selected for injection was the knee (46%), followed by the elbow and wrist (24%); for surgery, the selected joints were the wrist (47%), knee (22%), and cervical spine (21%). Three types of surgery were recommended by similar proportions of respondents, namely, prosthetic joint replacement, arthrodesis, and surgical synovectomy.

Rehabilitation measures were recommended by 83.5% of respondents, among whom 94% suggested medical devices, 37% physical therapy, 37% occupational therapy, and 4% cervical orthoses. Patient education about RA was recommended by only 0.5% of respondents.

A normal diet was considered appropriate by 88% of the respondents, whereas a low-salt low-carbohydrate diet was deemed necessary by 9% of respondents.

Costs

The median total cost for management of the flare in this patient with RAof 10 years' duration was €500 (mean €1105, range €80-4089) (Table IV). The median cost of non-laboratory investigations was 4-fold that of laboratory investigations, this difference being ascribable to the cost of radiographs. DMARD therapy was the treatment with the highest median cost, the reason being that 24% of respondents recommended the costly methotrexate + infliximab regimen.

Comparison of responses according to the characteristics of respondents

Responses regarding investigations showed no significant differences according to the respondent characteristics. The recommended management was associated with significantly higher median costs in the group of hospital-based respondents than in the groups of office-based or hospital- and office-based respondents (respectively, $p = 0.008$ and $p = 0.0077$, respectively). Furthermore, median costs were significantly higher in the northwest of France than in each of the other geographic areas except the southwest of France (p values, 0.0031 to 0.0125).

Discussion

Our survey among rheumatologists in France showed that 80% of respondents would use investigations to assess inflammation, treatment safety, and radiographic damage (particularly at the cervical spine in our fictional patient with a history of neck pain). In contrast, few respondents would investigate osteoporosis. Although all respondents recognised a need for adjusting the treatment, the suggested modalities varied widely. Non-laboratory tests and DMARD treatment were the most burdensome interventions from the perspective of the cost to society.

We furnished the rheumatologists with the clinical vignette of a patient experiencing a flare of long-standing RAdespite glucocorticoid and methotrexate therapy. To provide a basis for making management decisions, the vignette included details on pain severity, disability, and joint status, including VAS and HAQ scores. In practice, VAS scores are easy to obtain during physician visits. The HAQ is a valuable predictor of long-term outcomes and costs in RA (7-9). Guidelines recommend HAQ score determination at presentation to serve as a point of reference for monitoring the patient (4, 10). In addition, HAQ score determination benefits the evaluation of RA by giving the patient an opportunity to express his or her own opinion on the disease. The rheumatologist calculates and interprets the global score, and then explains it to the patient.

The clinical vignette in our questionnaire gave information at a single point in time. Furthermore, results of laboratory tests for inflammation and radiographs were not described. However, the existence of a flare despite treatment indicated severe disease and therefore the need for aggressive management.

Many respondents in our study recommended radiographic evaluation, including radiographs of the cervical spine to evaluate the recent episode of neck pain. However, weak correlations have been found between neck symptoms and cervical spine radiographic abnormalities (11). MRI provides more accurate information on vertebral and spinal cord lesions, but plain flexion radi-

ographs of the neck are superior to MRI for the identification of anterior atlantoaxial subluxations (12). Few respondents recommended MRI, possible explanations for this being the absence of MRI on the list of response options and the limited availability of MRI. American guidelines recommend that the progression of radiographic joint damage be monitored periodically (4). It has been documented that early erosive disease in peripheral joints is strongly associated with atlantoaxial subluxations (13).

The possibility of bone loss in the fictional patient does not seem to have generated an appropriate level of concern among our respondents: only 63% recommended absorptiometry; and 46%, 31%, and 18% recommended serum assays of calcium, phosphate, and vitamin D, respectively. Both RA and glucocorticoid therapy are established risk factors for osteoporosis (14-15), and the patient was 10 years postmenopausal. Although evaluation of practices regarding bone loss was not the primary objective of our study, the detection and treatment of bone loss are important components of the management of RA. Guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis are available (16). Inadequate attention to bone status evaluation in glucocorticoid-treated patients has been reported previously (17).

Non-laboratory tests contributed a greater proportion of the cost of RA evaluation than did laboratory tests. This was ascribable to the high cost of radiographs. In an earlier study (6), we found similar median costs for the non-laboratory and laboratory tests recommended by the same respondents to evaluate a patient with early typical RA.

The respondents suggested a variety of treatments for controlling the flare in the fictional patient: increasing the prednisone dosage and/or switching to methylprednisolone, increasing the methotrexate dosage or adding another DMARD, substituting another DMARD for the methotrexate, and/or adding local treatment (intra-articular glucocorticoid treatment, chemical or radiation synovectomy, or surgery). Methotrexate is one of the reference treatments for RA and its efficacy has been extensively documented (18, 19). Substituting leflunomide for methotrexate was recommended by 38% of respondents. It is worth noting that leflunomide was introduced on the French market shortly before our survey. The drug most often suggested for use as an add-on therapy to methotrexate was the anti-TNF agent infliximab, which was recommended by 24% of the respondents, probably because of the rapid efficacy of anti-TNF agents (20-22)

Infliximab, however, is an expensive agent that contributed a large proportion to the cost of treatment in our survey. Available surveys of DMARD prescribing practices in RA have focused on trends over time (23-25). Their results should be interpreted in the light of the drugs available on the market at the time of data collection. These surveys did not produce information on DMARD selection according to the clinical status of the patients. In our survey, DMARDs contributed the largest portion of the cost of the first month of treatment. In contrast, in a survey of practices in patients with early RA, median costs were equally distributed between DMARDs and analgesics (6). Differences in treatment practices influence the cost of treatment, particularly in hospital practice where newer and costlier treatments are more likely to be available.

When interpreting our data, the differences between respondents and non-respondents must be borne in mind. However, when we looked at investigations and treatments, we found no differences in prescribing patterns based on the characteristics of the respondents. This strongly supports the validity of our results. We have no explanation for the higher median costs for rheumatologists in hospital practice.

Regular follow-up, with treatment adjustments as needed, is crucial to improve the outcome of this disabling disease. We focused on just one aspect of management, namely, the prescription of investigations and treatments. We did not evaluate the social and economic situation of the patients, their health insurance coverage, or the availability of new treatments such as anti-TNF agents in the health care system.

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