Emerging Issues in Pharmacological Management of Rheumatoid Arthritis: Results of a National Needs Assessment Survey Identifying Practice Variations for the Development of Canadian Rheumatology Association Clinical Practice Recommendations

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ABSTRACT. ***Objective.*** To describe Canadian clinical practice patterns in the pharmacological management of rheumatoid arthritis (RA) and identify practice variations.

Methods. A 44-item pre-guideline needs assessment survey was sent to all members of the Canadian Rheumatology Association (CRA). Descriptive statistics were used to summarize respondent characteristics and practice patterns.

Results. Survey respondents (n = 164) reported variations in practice regarding assessment strategies, treatment with disease-modifying antirheumatic drug monotherapy versus combination therapy, methotrexate dosing and escalation, corticosteroid strategies, and optimal use of biologics.

Conclusions. Practice variations identified in this pre-guideline needs assessment survey were used to formulate key treatment questions for the development of CRA recommendations. (J Rheumatol First Release Sept 1 2011; doi:10.3899/jrheum.110208)

Key Indexing Terms:
RHEUMATOID ARTHRITIS PHYSICIAN PRACTICE PATTERNS ANTIRHEUMATIC AGENTS

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Development of the survey was supported by funds from the Canadian Rheumatology Association. O. Schieir is supported by a Fonds de la Recherche en Santé de Québec (FRSQ) Doctoral Research Award. Dr. Akhavan is supported by a UCB/CRA/TAS Post-Graduate Rheumatology Fellowship. Dr. Hazlewood is supported by a UCB/CRA/TAS Post-Graduate Rheumatology Fellowship and an Alberta Heritage Foundation for Medical Research Clinical Fellowship. Dr. Bombardier holds a Pfizer Chair and a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care.

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Accepted for publication June 28, 2011.

The last decade has brought significant changes in the management of rheumatoid arthritis (RA) that have improved the prognosis for many adults living with RA[1,2]. For patients this means symptom control, performing activities of daily living, remaining in the workforce, and improving overall quality of life[3]. Rheumatology healthcare professionals, however, are faced with the challenge of keeping up with the large volume of research studies pertaining to common as well as new therapeutic agents that continue to emerge to treat RA. High quality clinical practice guidelines can be useful for synthesizing and transmitting evidence-based healthcare to appropriate knowledge users[4]. However, practice recommendations regarding the pharmacological management of RA developed for the Canadian cultural and organizational healthcare context are lacking[5].

The objectives of this pre-guideline needs assessment survey were to: (1) describe current practice patterns regarding the pharmacological management of RA in a sample of Canadian rheumatology professionals; and (2) identify practice variations to formulate potential key treatment questions for the development of clinical practice recommendations.

MATERIALS AND METHODS

A questionnaire including demographic/practice characteristics, general treatment questions, and clinical case scenarios related to RA assessment strategies and treatment with corticosteroids and traditional and biologic disease-modifying antirheumatic drugs (DMARD) was developed by the Canadian Rheumatology Association (CRA) Therapeutics Committee, pilot tested with

12 rheumatologists and fellows, and refined to 44 items. In the summer of 2007, the questionnaire was sent to all members of the CRA anonymously, a convenience sample of rheumatology healthcare professionals across Canada. Data were collected using Survey Monkey (www.surveymonkey.com) and exported to Excel for descriptive analysis. The CRA Therapeutics Committee reviewed results of each survey question at a face-to-face meeting and identified practice variations for the purpose of formulating key treatment questions to be addressed through the development of clinical practice recommendations.

RESULTS

One hundred sixty-four members of the CRA completed the questionnaire. Sixty-two percent were male and 60% had been in practice for 10+ years. The greatest proportion of respondents resided in Ontario (43%) followed by the western provinces (British Columbia, Alberta, Saskatchewan, Manitoba; 30%), Quebec (19%), and the eastern provinces (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland; 8%). Just over half of respondents (51%) reported practicing in academic or teaching hospitals and 73% reported that at least one-quarter of their patients were seen for RA.

Initial DMARD treatment strategies for patients with moderate to severe RA were about evenly split between methotrexate (MTX) monotherapy (up to 20–25 mg per week) and MTX combination therapy. Frequency of radiographs varied from every 6 to 12 months, with annual radiographs most commonly reported (49%), and 12%–14% of respondents were unsure if they would obtain magnetic resonance imaging/or ultrasound in new patients with normal radiographs. The most common use of corticosteroids was as temporary bridge therapy (63%), with intramuscular or intraarticular (44%) and oral prednisone 5–10 mg or 10 mg (46%) as the most commonly reported treatment strategies. Most starting doses for MTX ranged from 10 mg to 20 mg per week, with 15 mg most commonly reported (51%), and 25 mg was the most common maximum dose (84%), with only 1% that reported using > 30 mg. Timing for escalation mostly varied between 4 and 12 weeks, with 10–12 weeks most commonly reported (25%). Fifty-six percent used subcutaneous MTX frequently, and only 1% reported never using it (Table 1).

Patterns for initiating biologic therapy varied greatly. Provided that there was unrestricted access, 57% reported that they would start tumor necrosis factor inhibitor (anti-TNF) after 3–6 months of combination therapy [MTX + leflunomide (LEF) = 14%; MTX + hydroxychloroquine (HCQ) + sulfasalazine (SSZ) = 33%], 31% after 3–6 months on MTX monotherapy 20–25 mg per week, and 16% immediately in patients with moderate to severe RA. After failure of 1 anti-TNF, 68% reported they would switch to a second anti-TNF, and 32% reported they would switch to another mechanism of action [MTX + abatacept (ABAT) = 21%; MTX + rituximab (RTX) = 16%]. There were multiple reasons for switching biologics, with swollen joint count > 5 (70%) and radiographic progression (45%) most commonly reported (Table 1).

The most common safety issues that patients were warned about prior to starting all biologics were pneumonia or serious infections (98%), tuberculosis (96%), injection site reactions (90%), and malignancy (82%). Two-thirds of respondents reported that it was important to ensure vaccines were up to date prior to treatment with anti-TNF or abatacept and 82% prior to RTX. Roughly 50% reported that they would stop MTX prior to surgery, while 90% reported that they would stop biologics (except RTX), with great variability in the timing for suspension. Forty percent believed that treatment with anti-TNF therapy was associated with an increased risk of lymphoma over and above the risk attributable to RA, and 25% and 11% reported that anti-TNF or ABAT and RTX, respectively, were associated with an increased risk of solid tumors.

DISCUSSION

Through this pre-guideline needs assessment survey of 164 Canadian rheumatology healthcare professionals, practice variations were observed regarding RA assessment strategies; treatment with DMARD monotherapy versus combination therapy; MTX dosing and escalation, appropriate corticosteroid strategies, defining treatment responses; and optimal use of biologics (when to start, when to change, what to change to, safety and monitoring).

Our study had certain limitations. The needs assessment survey may have failed to identify all practice strategies considered by Canadian rheumatology professionals. However, survey questions were pilot-tested with a panel of rheumatology experts and trainees, and included multiple response options and an open-ended "other" category in an effort to increase response sensitivity. Second, our study was based on a convenience sample of members of the CRA who responded to the needs assessment survey. Although respondents may not be representative of the opinions of all Canadian rheumatology professionals, demographic distributions were similar to those of the 2007 CRA membership as a whole (n = 445) with respect to gender (male = 61% vs 60%), province (western provinces = 29% vs 30%, Ontario = 41% vs 43%, Quebec = 21% vs 19%, eastern provinces = 9% vs 8%), and practice setting (academic/teaching hospitals = 59% vs 51%). Last, we cannot rule out the possibility that individual practice strategies may have changed since 2007; however, notable system changes are limited to the very recent approval in Canada of 2 new anti-TNF agents and an interleukin 6 inhibitor with indications similar to those of other biologic agents.

In conclusion, practice variations identified in this pre-guideline needs assessment survey were used to formulate key treatment questions for the development of 2011 CRA recommendations for the pharmacologic management of RA[6,7].

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Table 1. 2007 Canadian practice patterns for pharmacological management of RA (N = 164).

Questionnaire Items	Mode (%)	Commonly Reported Strategies (%)	Comments
General			
Targets/outcomes used to guide treatment decisions	Swollen joint count (94)	Morning stiffness (81), radiographs (80), tender joint count (80), ESR/CRP (76), patient global (65), HAQ (52)	42% use gestalt; 28% use DAS28: < 5% use other composite measures such as ACR score, CDAI, or SDAI
Starting therapy*			
Scenario: New DMARD-naive patient (RF+, 6 SJC, 9 TJC)	MTX up to 20–25 mg (53)	HCQ + MTX (45), HCQ + SSZ + MTX (21)	5% start HCQ alone; < 5% start MTX + LEF; < 3% start MTX + biologic; < 2.5% start SSZ alone
Frequency of radiographs	Annual (49)	Every 6 mo 1 st yr then annual (16); annual until progression stops (11)	5% obtain only if treatment changed; < 5% obtain every 6 mo until progression stops; 14% reported "other"
Obtain MRI/US			
Scenario: New RA patient with normal radiographs	MRI: No (49); US: No (64)	MRI: Yes (37); US: Yes (24)	MRI: 14% reported "unsure"; US: 12% reported "unsure"
Treatment with corticosteroids			
a. Situations in which believe prednisone should be used in RA	Temporary bridge for ≤ 12 wks (63)	In whom no other options exists; longterm at lowest possible dose (23)	6% considered as a DMARD; 5% hardly use due to risk/benefit ratio; 3% only use with systemic features
b. Treatment strategy Scenario: New RA patient 7–10 SJC	IM or IA (44)	Start prednisone 10 mg daily (30); start prednisone 5–10 mg daily (16)	5% don't use prednisone; 5% use 10 mg daily > 6 mo
Treatment with MTX			
a. Starting dose (per wk)	15 mg (51)	10 mg (30); 20 mg (9)	< 5% start with dose < 10 mg; 3% start with dose > 20 mg
b. Maximum dose (per wk)	25 mg (84)	20 mg (9)	6% reported max dose of 30 mg; 1% reported max dose > 30 mg
c. Timing for escalation	10–12 wks (25)	5/6 wks (22); 4 wks (17); 7/8 wks (16)	10% escalate within < 4 wks; 10% escalate within 13–26 wks
d. Use of subcutaneous (sc) MTX	Frequently (56)	Occasionally (26); if dose > 15 mg (18)	1% reported "never". Reasons for using sc MTX: to improve absorption, reduce side effects, and better effectiveness. Reasons for NOT using sc MTX: patient refusal and no time to teach it
e. Investigations prior to starting*	CBC (100); creatinine (99); ALT (96) AST (91); ESR (90)	CRP (84); albumin (82); ALP (76); hepatitis B/C serology (69); chest radiograph (60)	43% would order a pregnancy test; 38% would order bilirubin; 10% would order TB skin
f. Investigations for monitoring*	CBC (99); ALT (93); AST (86)	Creatinine (79); Alb (65); ALP (54)	48% would order ESR; 38% would order CRP
g. Frequency of monitoring	Every 4 wks (52)	Every 6 or 8 wks (41)	Every 12 wks (6%)
h. Situations to suspend therapy*	Female attempting conception (98)	Bacterial infection requiring antibiotics (78); zoster (71)	81% suspend > 3 mo prior to female attempting conception; 76% suspend in male with partner attempting conception; 40% do NOT suspend prior to surgery
i. MTX combinations agreed are safe and effective to use*	MTX + ETN (90); MTX + ADA (88); MTX + INF (87)	MTX + SSZ + HCQ (83); MTX + ABAT (62); MTX + RTX (56)	37% agree that MTX + LEF is safe and effective to use
Treatment with biologics			
a. When to start anti-TNF Scenario: Patient with moderate to severe RA (assuming no access issues)	After failure 3-6 mo MTX + HCQ + SSZ (33)	After failure 3-6 mo MTX 20-25 mg (31)	16% start immediately; 14% start after failure of MTX + LEF; 6% reported "other"
b. Factors rated as somewhat and very important when initiating a biologic*	Effectiveness (99); safety (98); halt radiographic progression (96)	Patient preference (87); reimbursement (86)	54% rated mechanism of action
c. Biologic side effects warn patients about*	Pneumonia or serious infections (98); TB (96); site reactions (90)	Lymphoma (82); opportunistic infections (72); demyelinating disease (61); congestive heart failure (36); lupus-like reactions (34); solid malignancies (34); traveling to TB endemic area (23)	After an initial discussion, 30%, 66% and 4% always, occasionally, and never warn patients about biologic side effects, respectively

Table 1. Continued.

Questionnaire Items	Mode (5)	Commonly Reported Strategies (%)	Comments
d. Strategy after failure of anti-TNF* Scenario 1: Failure of anti-TNF+ MTX and flare of 4+ joints after 2 visits (assuming no access issues)	2nd anti-TNF + MTX (68)	ABAT + MTX (21); RTX + MTX (16)	5% reported "other"
e. Treatment with RTX When to provide next set of 3 infusions	Beginning to flare (73)	After 6 mo (15); after 9 mo (10)	2% provide next infusions at full flare; 43% would retreat with a minimal first response to get a better response
F. Reason to switch biologics*	SJC > 5 (70)	Radiographic progression (45); SJC > 10 (36); DAS28 (36); patient decides therapy is not effective (33)	Switches based on response with composite measures: DAS28 > 3.2 (21%); DAS28 > 2.6 (15%); SDAI > 11 or CDAI > 10 (< 5%); 29% would not switch therapy if patient is substantially better than when they first started the biologic regardless of disease activity

* Can provide more than 1 answer. ACR: American College of Rheumatology; CDAI: Clinical Disease3 Activity Index; SDAI: Simplified Disease Activity Index; HAQ: Stanford Health Assessment Questionnaire; SJC: swollen joint count; TJC: tender joint count; MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; LEF: leflunomide; CBC: complete blood cell count; ALT: alanine aminotransferase; ALP: alkaline phosphatase; AST: aspartate aminotransferase; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ETN: etanercept; ADA: adalimumab; ABAT: abatacept; IM: intramuscular; IA: intraarticular; TB: tuberculosis.

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