Variation in the Initial Treatment of Knee Monoarthritis in Juvenile Idiopathic Arthritis: A Survey of Pediatric Rheumatologists in the United States and Canada

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ABSTRACT. ***Objective.*** To characterize variations in initial treatment for knee monoarthritis in the oligoarthritis subtype of juvenile idiopathic arthritis (OJIA) by pediatric rheumatologists and to identify patient, physician, and practice-specific characteristics that are associated with treatment decisions.

Methods. We mailed a 32-item questionnaire to pediatric rheumatologists in the United States and Canada (n = 201). This questionnaire contained clinical vignettes describing recent-onset chronic monoarthritis of the knee and assessed physicians' treatment preferences, perceptions of the effectiveness and disadvantages of nonsteroidal antiinflammatory drugs (NSAID) and intraarticular corticosteroid injections (IACI), proficiency with IACI, and demographic and office characteristics.

Results. One hundred twenty-nine (64%) questionnaires were completed and returned. Eighty-three percent of respondents were board certified pediatric rheumatologists. Respondents' treatment strategies for uncomplicated knee monoarthritis were broadly categorized: initial IACI at presentation (27%), initial NSAID with contingent IACI (63%), and initial NSAID with contingent methotrexate or sulfasalazine (without IACI) (10%). Significant independent predictors for initial IACI were believing that IACI is more effective than NSAID, having performed > 10 IACI in a single patient at one time, and initiating methotrexate via the subcutaneous route for OJIA. Predictors for not recommending initial or contingent IACI were believing that the infection risk of IACI is significant and lacking comfort with performing IACI.

Conclusion. There is considerable variation in pediatric rheumatologists' initial treatment strategies for knee monoarthritis in OJIA. This variation is primarily associated with perceptions of medication effectiveness and proficiency with IACI. Further studies are warranted to clarify the optimal treatment of OJIA. (J Rheumatol 2007;34:1918–24)

Key Indexing Terms:
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The oligoarthritis subtype of juvenile idiopathic arthritis (OJIA) is defined as arthritis of unknown etiology that begins before age 16 years, persists for at least 6 weeks, and affects fewer than 5 joints in the first 6 months of disease[1]. OJIA is the most common subtype of JIA[2,3]. Consequently, OJIA is one of the most common conditions treated by pediatric rheumatologists, accounting for up to 20% of all new rheumatic diagnoses[4]. Although it affects few joints, OJIA is recognized as a chronic and potentially disabling condition. For example, chronic OJIA involving the knee or ankle frequently results in a leg-length discrepancy that is often permanent and may require the use of a shoe-lift[5-7]. Radiographic evidence of erosive joint changes may be seen in as few as 2 years in up to 10% of children with OJIA[8,9], and up to 40% of children with OJIA will have active arthritis for more than 10 years[10]. Accordingly, the early management of OJIA may be crucial to prevent future morbidity.

Despite the prevalence and morbidity of OJIA, the optimal treatment strategy for OJIA is not known. Nonsteroidal antiinflammatory drugs (NSAID) and intraarticular corticosteroid injections (IACI) have been shown to be effective in the treatment of OJIA, with an apparently higher response rate for IACI[11]. Although no clinical trials of the relative efficacy of

these medications or treatment strategies for OJIA have been reported, some authors recommend a trial of NSAID for uncomplicated OJIA, followed by IACI if satisfactory clinical improvement does not occur[3,11]. Given the lack of available evidence, wide variations in clinical practice likely exist, and the relative frequencies of different treatment strategies have not been described.

To further investigate the treatment of OJIA, we developed and distributed a physician questionnaire. This questionnaire surveyed the current variation in treatment strategies for the initial pharmacologic management of monoarthritis of the knee in OJIA by pediatric rheumatologists and identified patient, physician, and practice-specific characteristics that are associated with these treatment decisions. Our study therefore outlines the pertinent treatment strategies and influential factors to be considered in future studies of the treatment of OJIA.

MATERIALS AND METHODS

Subjects. Subjects were identified from a 2006 list of physician Fellow Members of the Section of Pediatric Rheumatology of the American College of Rheumatology in the United States (n = 187) and Canada (n = 14). The Section of Pediatric Rheumatology comprises individuals who designate that they spend the majority of their time caring for children with rheumatic disease. Subjects were mailed questionnaires and a small financial reimbursement as compensation for their time. Questionnaires were given unique identifiers to facilitate response tracking. Subjects who had not returned the questionnaire within 6 weeks were mailed a second questionnaire. All identifying information was deleted prior to the analysis of the data. A formal exemption was granted by the Institutional Review Board prior to distribution of the questionnaire.

Questionnaire design. A 32-item self-administered questionnaire was developed for this study following a thorough review of the relevant literature regarding the pharmacologic management of OJIA. The questionnaire was critically evaluated for content by all authors and was pilot-tested for clarity by 3 additional pediatric rheumatologists. A copy of the questionnaire is available from the authors upon request.

Subjects' treatment strategies were evaluated utilizing clinical vignettes of chronic monoarthritis of the knee in a 2-year-old Caucasian girl with recent onset OJIA. Vignettes were developed to represent a typical and standardized clinical presentation of OJIA[8,12-16] and allowed comparison of treatment approaches among respondents. For each vignette, respondents were asked to indicate all of the medications that they would recommend at this time from an exhaustive list, and to indicate the likelihood that they would recommend IACI on the following 6-point Likert scale: no chance (< 5% chance), very unlikely (5–25% chance), unlikely (26–50% chance), likely (51–75% chance), very likely (76–95% chance), always (> 95% chance). In the first vignette, the patient presented for initial evaluation and treatment following 6 weeks of untreated knee swelling with associated morning stiffness and a minor gait abnormality. Her examination revealed a moderate-sized, warm effusion without joint contracture or leg-length discrepancy. Respondents were also asked their likelihood of recommending IACI if this patient presented with the additional findings of a significant knee joint contracture or leg-length discrepancy or was 8 years old instead of 2 years old. The second vignette was the same patient with OJIA and monoarthritis of the knee who had been treated with NSAID for 2 months by another pediatric rheumatologist, with only minimal improvement in her symptoms and no change in her physical examination. She was now presenting for initial evaluation and treatment. The third vignette was the same patient with OJIA and monoarthritis of the knee who had been treated with 3 different NSAID over a total of 6 months by another pediatric rheumatologist, with only minimal improvement in her symptoms and no change in her examination. She was now presenting for initial evaluation and treatment. Respondents were asked separately about their perceptions of the effectiveness and relative disadvantages of NSAID and IACI in the treatment of OJIA. Physicians' proficiency with the IACI procedure, utilization of IACI in clinical practice, and perceived obstacles to performing IACI were assessed. Basic demographic information was obtained.

Outcomes. Questionnaire responses were entered into a Microsoft Access 2003 database (Microsoft Corp., Redmond, WA, USA). Less than 2% of the total questionnaire responses were omitted by respondents, and missing values were not imputed. The main outcome of interest was the recommendation for IACI, since this is the most commonly reported second-line treatment for OJIA[17,18]. Because subjects were asked explicitly about their likelihood of recommending IACI, we wished to identify subjects who felt strongly about their recommendations. Therefore, responses of "very likely (76–95% chance)" or "always (> 95% chance)" for the likelihood of recommending IACI for each of the vignettes were considered positive recommendations. The "likely (51–75% chance)" response was not considered a positive recommendation, because all subjects who responded "likely" to the initial vignette increased the likelihood of their recommendation to "very likely" or "always" for the vignette describing 2 months of failed NSAID therapy, indicating responsiveness to the new vignette with a stronger conviction toward the recommendation for IACI. Three treatment groups were then determined based on the timing of the recommendation for IACI: initial IACI, IACI contingent upon NSAID failure, and no recommendation for IACI in the first 6 months of monoarthritis of the knee.

Analysis. Statistical analysis was performed using Stata 9.0 (Stata Corp., College Station, TX, USA). Descriptive statistics, including means, medians, and frequencies, were obtained. Simple comparisons of frequencies were made using the chi-square and Fisher's exact tests, where appropriate. Logistic regression models were developed to determine predictors of the treatment groups. More than 30 physician and practice-specific characteristics were first analyzed in univariate logistic regression models to evaluate associations with the treatment groups. Covariates tested included the perceived efficacy of IACI versus NSAID for the treatment of monoarthritis in OJIA, the preferred dosing and route of administration of methotrexate (MTX) for the treatment of OJIA (not restricted to monoarthritis), the perceived duration of an adequate trial of a single NSAID in the treatment of OJIA, the perceived most significant disadvantages of the use of NSAID in OJIA, the perceived most significant disadvantages of the use of IACI in OJIA, the number of specific joints that a respondent would personally inject and would refer to another physician for injection, the largest number of IACI performed in a single patient at one time, the number of pediatric IACI performed during fellowship training, access to a sedation unit that can facilitate IACI, the perceived most significant procedural obstacles to performing IACI, medical practice setting, number of patients seen per week, years in practice, completion of fellowship training in pediatric rheumatology, board certification status, and sex. Ordinal covariates were dichotomized based on the distribution of responses for ease of interpretation of the model results. Two separate regression models were used: one compared the respondents who recommended initial IACI to those who recommended IACI contingent upon NSAID failure, and the other compared the respondents who recommended IACI in the first 6 months to those who did not. Covariates that were associated with treatment group assignment ($p < 0.10$) were entered into multivariable logistic regression models. There was no colinearity between the selected covariates. A backward-stepwise procedure was then performed to determine the most parsimonious model. Covariates were removed from the full model until the likelihood ratio test indicated that the nested model was significantly different from the full model ($p < 0.05$). Interaction terms were not fitted into the model, because the strong predictive value of the covariates produced zero cell counts (perfect predictions) for many of the interaction terms. A polytomous (multinomial) prediction model that included all 3 treatment strategy groups in the outcome was also fitted. The results were similar, and only the results of the multivariable logistic regression models are presented for ease of interpretation.

RESULTS

One hundred thirty-eight (69%) questionnaires were returned. Nine respondents declined to participate, because they no longer participate in patient care. This left 129 (64%) questionnaires for analysis.

Demographics. The basic demographic characteristics of respondents are shown in Table 1. In general, the respondents were experienced pediatric rheumatologists; 75% had pediatric rheumatology fellowship training, 83% were board certified in pediatric rheumatology, and 81% were in practice for more than 10 years. Three-quarters of respondents had another physician in their office or division who treats pediatric rheumatology patients. About 60% of respondents saw more than 20 pediatric rheumatology clinic patients per week. About one-third of respondents routinely saw patients outside of pediatric rheumatology. Subjects from Canada had a higher response rate than those from the US (93% vs 61%; p = 0.02, Fisher's exact test). Subjects who did not respond to the questionnaire were less likely to be based in children's hospitals (48% vs 76%; p = 0.0001, chi-square test).

Treatment preferences. Responses to the clinical vignettes were grouped into 3 broad treatment strategies as shown in Table 2. About one-quarter of respondents recommended IACI as initial therapy for uncomplicated monoarthritis of the knee at the time of patient presentation. The remainder of respondents recommended initial treatment with NSAID. The overall majority of respondents recommended IACI contingent upon failure to improve with NSAID. The remaining minority of physicians recommended MTX or sulfasalazine (SSZ) in response to NSAID failure. These physicians who did not recommend IACI for any of the vignettes presented were considered together in further analysis. Of the respondents who recommended contingent IACI, 58 (46% of all respondents) made this recommendation for the vignette describing 2 months of failed NSAID. Seven (21%) of the respondents who recommended initial IACI and 11 (14%) of the respondents who recommended contingent IACI also recommended concurrent MTX or SSZ with IACI for the vignette depicting uncomplicated monoarthritis of the knee that is unresponsive to 6 months of NSAID therapy.

In the clinical vignettes of uncomplicated monoarthritis of the knee that was unresponsive to NSAID therapy, IACI was recommended by 90% of respondents in at least one vignette. MTX was recommended by 19% and SSZ by 10%. Infrequently recommended medications were hydroxychloroquine (5%), oral corticosteroids (4%), and tumor necrosis factor-α inhibitors (2%). In a separate question regarding the dosing of MTX, 14% of respondents indicated that they do not use MTX to treat any patients with OJIA.

Respondents varied in the duration of NSAID failure prior to recommending an increase in therapy by initiating IACI, MTX, or SSZ. As mentioned, 27% recommended IACI at initial presentation. No respondent recommended MTX or SSZ at initial presentation. Seventy-nine percent recommended increasing therapy in response to 2 months of failed NSAID therapy. In considering monoarthritis of the knee unresponsive to NSAID for 6 months, all respondents (100%) recommended increasing treatment with IACI, MTX, or SSZ.

Recommendations for IACI were associated with patient factors. A few respondents were influenced by the patient's age; 9 respondents (11%) who recommended contingent IACI for the 2-year-old girl recommended initial IACI for an 8-year-old girl. All respondents who recommended initial IACI for the 2-year-old girl recommended the same treatment for the 8-year-old. Signs of complications of arthritis on examination resulted in recommendations for initial IACI from 81 (64%) of all respondents and 49 (61%) of the respondents who recommended contingent IACI for uncomplicated monoarthritis of the knee. Thirty-eight (48%) of those who recommended contingent IACI for uncomplicated knee arthritis recommended initial IACI for a patient with a knee joint contracture, and 45 (57%) recommended initial IACI for a patient with a leg-length discrepancy. In contrast, 2 months of failed NSAID therapy for uncomplicated knee monoarthritis resulted in the recommendation for IACI by 58 (73%) of those in the contingent IACI treatment group. Therefore, within the contingent IACI group, the presence of joint contracture or

Table 1. Demographic characteristics of the respondents (n = 129). Missing data were excluded when calculating percentages.

Characteristic	
Female sex, n (%)	63 (50)
Pediatric rheumatology board certified, n (%)	106 (83)
Pediatric rheumatology fellowship trained, n (%)	95 (75)
Years practicing pediatric rheumatology, median (range)	17 (1–47)
Country of practice	
United States, n (%)	115 (90)
Canada, n (%)	13 (10)
Children's hospital based, n (%)	97 (76)
No. other pediatric rheumatologists in practice, median (range)	1 (0–8)
Pediatric rheumatology clinic patients seen/wk, median (range)	22.5 (0–100)
Total clinic patients seen/wk, median (range)	30 (0–125)

Table 2. Treatment strategy groups for uncomplicated monoarthritis of the knee in OJIA based on responses to clinical vignettes (n = 127).

Treatment	No. Respondents (%)
Initial IACI	34 (27)
Initial NSAID with contingent* IACI	80 (63)
Initial NSAID with contingent* MTX (without IACI)	11 (9)
Initial NSAID with contingent* SSZ (without IACI or MTX)	2 (2)

* Contingent upon failure to improve with NSAID therapy. IACI: intra-articular corticosteroid injection; NSAID: nonsteroidal antiinflammatory drug; MTX: methotrexate; SSZ: sulfasalazine.

leg-length discrepancy at initial presentation prompted fewer respondents to recommend IACI at that time than did failure to respond to NSAID treatment for 2 months ($p = 0.001$ and $p = 0.03$, respectively, chi-square test).

Perceptions of medication effectiveness. Respondents differed in their perception of the relative effectiveness of NSAID and IACI in the treatment of OJIA. In 2 separate questions, respondents estimated the likelihood of resolution of monoarthritis of the knee for the patient in the initial vignette evaluated 6 months after presentation if she were given 2 different treatments: scheduled NSAID or a single IACI at presentation. Overall, respondents believed that IACI was more effective. Seventy-two percent of respondents estimated a greater than 50% chance of resolution of uncomplicated knee monoarthritis 6 months after a single IACI, while 33% of respondents estimated a greater than 50% chance of resolution given 6 months of scheduled NSAID ($p < 0.0001$, chi-square test). However, when viewed at the individual level, there were differences in opinion. Sixty-two percent of respondents felt that a single IACI at presentation was more likely to result in resolution than scheduled NSAID. Sixteen percent believed that scheduled NSAID was more likely than a single IACI to result in resolution at 6 months. The remaining 22% felt that a single IACI and scheduled NSAID were about equally effective when considering 6-month outcomes.

Respondents generally agreed in their perception of the duration of time without clinical improvement that indicates failure for a particular NSAID in the treatment of OJIA. The mean response (± standard deviation) was 7.5 (± 3.1) weeks. The median (range) was 8.0 (2–16) weeks, and the mode was 8 weeks, with 27% of respondents offering this answer.

Predictors of treatment preferences. Ten covariates were found to have significant association with the initial IACI treatment group versus the contingent IACI group in univariate analysis. These covariates were entered in a multivariable logistic regression model as described. The independent predictors of initial versus contingent IACI treatment strategy from the resultant parsimonious model are shown in Table 3. Those that believe IACI is more effective than NSAID, those that have performed more than 10 IACI in a single patient at one time, and those that initiate MTX for OJIA via the subcutaneous rather than the oral route were all more likely to recommend initial IACI versus contingent IACI. This parsimonious model showed excellent discrimination between those who recommended initial versus contingent IACI, with an area under the receiver-operating characteristic (ROC) curve of 0.82.

Multivariable logistic regression was also used to compare respondents who recommended IACI versus the respondents that recommended MTX or SSZ instead of IACI for 6 months of uncomplicated knee arthritis that is not responsive to NSAID. Six covariates were found to have significant association with the any-IACI group versus the no-IACI group in univariate analysis. These covariates were entered in a multivariable logistic regression model as described. The independent predictors from the resultant parsimonious model are shown in Table 4. Those that believe IACI are more effective than NSAID were much more likely to recommend IACI. Respondents who believe the risk of infection from IACI has a significant negative effect on its utility in OJIA and those who believe that their lack of comfort with the IACI procedure is a significant obstacle were less likely to recommend IACI. This parsimonious model demonstrated excellent discrimination between those who recommended IACI versus those who did not, with an area under the ROC curve of 0.90.

Respondents' treatment preferences did not demonstrate an independent association with practice-specific characteristics, such as nursing or other support staff, means for patient sedation, physician time, physician reimbursement, or availability of referral for IACI. Treatment preferences did not have an independent association with basic demographic and education factors, such as sex, years in practice, completion of pediatric rheumatology fellowship training, number of pediatric IACI performed during fellowship, or specialty board certification.

DISCUSSION

Ours is the first study to our knowledge to survey pediatric rheumatologists in detail regarding their treatment of monoarthritis in OJIA. We report considerable variation in the current initial treatment of monoarthritis of the knee. This result is not surprising, given that there are no published studies of comparative efficacy for these various treatment approaches and similar variation has been reported in the treatment of rheumatoid arthritis[19-24]. For uncomplicated monoarthritis of the knee, most respondents recommended a

Table 3. Independent predictors of recommending initial IACI at patient presentation versus IACI contingent upon NSAID failure for uncomplicated monoarthritis of the knee in OJIA.

Respondent Variable	No. (%) Giving Response	Odds Ratio (95% CI)
Believe IACI more effective than NSAID	72 (70)	6.91 (1.69–28.3)
Perform > 10 IACI in single patient at one time	18 (17)	10.8 (2.83–41.5)
Initiate MTX via subcutaneous route	19 (18)	4.11 (1.21–14.0)

Odds ratios are the result of a multivariable logistic regression model using a backward-stepwise procedure. OR greater than 1 indicates association with the recommendation for initial IACI. IACI: intraarticular corticosteroid injection; NSAID: nonsteroidal antiinflammatory drug; MTX: methotrexate

Table 4. Independent predictors of recommending IACI versus not recommending IACI in the treatment of uncomplicated monoarthritis of the knee in OJIA that is unresponsive to NSAID for 6 months.

Respondent Variable	No. (%) Giving Response	Odds Ratio (95% CI)
Believe IACI more effective than NSAID	76 (63)	38.1 (3.51–413)
Believe infection risk of IACI significant	9 (8)	0.08 (0.01–0.58)
Lack comfort with performing IACI procedure	15 (13)	0.08 (0.02–0.44)

Odds ratios are the result of a multivariable logistic regression model using a backward-stepwise procedure. OR greater than 1 indicates association with the recommendation for initial IACI. IACI: intraarticular corticosteroid injection; NSAID: nonsteroidal antiinflammatory drug.

trial of NSAID, followed by IACI in cases of NSAID failure. A significant minority of respondents recommended IACI at initial presentation, while the remainder recommended initial NSAID, followed by MTX or SSZ instead of IACI.

In the analysis of this questionnaire, respondents' treatment decisions were strongly associated with differences in the perceived effectiveness of IACI and proficiency and enthusiasm in performing IACI. Clearly, physicians typically recommend therapies in accordance with their beliefs and comfort. However, the heterogeneity of beliefs and comfort in this sample deserves further exploration.

The efficacy of NSAID in juvenile arthritis has been shown in many clinical trials[11]. However, none of these studies specifically addresses the clinical vignette presented in this questionnaire, namely monoarthritis of the knee secondary to OJIA. It is therefore unclear how such patients will respond to NSAID therapy. In a cohort of 207 patients with OJIA who were treated with NSAID initially, more than 90% of them required at least one IACI over their disease course[8]. In a small prospective study of patients with OJIA, only 10% demonstrated a clinical response to 6–12 weeks of NSAID[25]. Even in the presence of a clinical response, it is unclear if NSAID sufficiently extinguish synovitis, as one cross-sectional study[5] demonstrated that IACI is superior to NSAID in preventing the leg-length discrepancy presumably caused by persistent inflammatory hyperemia[26].

The efficacy of IACI in juvenile arthritis has been shown in many observational studies, as well as a few clinical trials[11,27]. One apparent advantage of treatment with IACI is the rapidity of response, as demonstrated in a retrospective series of 61 children with juvenile rheumatoid arthritis, all of whom experienced resolution of arthritis within a few days following IACI[28]. However, treatment with IACI is invasive, is not universally or indefinitely effective, and has potential complications[27]. These uncertainties regarding response to treatment understandably lead to variation in treatment practices.

Additionally, many other factors relevant to these treatment decisions have not been quantified. One rationale for a NSAID trial is to avoid unnecessary IACI. However, the cost of ongoing arthritis during an NSAID trial in terms of patient pain, disability, and longterm outcome is unknown. Conversely, the costs associated with IACI in terms of patient discomfort during the procedure and potential benefit in longterm outcome are also unknown. Other poorly quantified factors include the relative benefit of a one-time procedure versus a daily chronic oral medication and the potential for longterm cardiovascular adverse effects of NSAID. Studies to date have primarily utilized simple outcome measures that do not incorporate any of these other relevant factors. The knowledge gap and resultant uncertainty created by a lack of comparative treatment studies with comprehensive outcome measures is common in medicine[29].

Patient-specific factors influence physicians' treatment decisions, although perhaps not as expected. Because IACI is beneficial in the treatment of joint contractures and the prevention of leg-length discrepancies[5,28,30], we anticipated the recommendation for IACI in these instances to be higher than was observed. Instead, only about 60% of respondents who recommended treatment with contingent IACI would be at least very likely to recommend IACI for a patient with knee monoarthritis and either joint contracture or leg-length discrepancy on initial physical examination. Viewed slightly differently, complicated arthritis prompted 64% of all respondents to recommend initial IACI versus 27% for uncomplicated arthritis. These results may reflect physicians' desire to establish a rapport with the child and family before recommending IACI, although this was not assessed by this questionnaire. Alternatively, some respondents may believe that knee joint contractures respond well to NSAID. Patient age appeared to be less of a factor in treatment; 27% of all respondents recommended initial IACI for a 2-year-old patient, while 34% recommended initial IACI for an 8-year-old patient. The higher rate of recommendation for IACI for the older patient was surprising, as leg-length discrepancies are more common in younger children[6,7] and as such, these patients may receive even greater potential benefit from early IACI[5]. The reasons for this unexpected result were not assessed by this questionnaire, but may reflect a belief that the IACI procedure is better tolerated by older children. For the sake of brevity, treatment recommendations for complicated arthritis were assessed using one-sentence questions following the initial vignette instead of separate dedicated vignettes; this may have affected the results.

The recommendations for MTX therapy for OJIA in this questionnaire were wide-ranging. MTX is effective in extended-course OJIA[31], but has not been studied in a clinical trial

for monoarthritis of the knee. One study suggests effectiveness for patients with persistent-course OJIA[25], and its use for these patients is seemingly justified. Indeed, one may suggest that MTX could act prophylactically to prevent uveitis or arthritis of other joints, although this is speculation and has not been studied. Those respondents that would initiate MTX for the treatment of OJIA via the subcutaneous route were more likely to recommend initial IACI for the treatment of monoarthritis. These physicians may believe in the concept of early, decisive treatment[32] or may simply have less aversion to the use of needles. Interestingly, 9% of respondents recommended MTX preferentially over IACI for the treatment of monoarthritis, while 14% indicated that they would not use MTX to treat any patients with OJIA. Clearly, the use of MTX in OJIA is in need of further evaluation.

Our study design has limitations. Not all pediatric rheumatologists in the US and Canada were surveyed. Subjects were thought to represent those most active in the pediatric rheumatology academic community due to their membership in the Section of Pediatric Rheumatology of the American College of Rheumatology. There are about 215 board-certified pediatric rheumatologists in the US[33], similar to the number included in the questionnaire mailing. Subjects who did not respond to the questionnaire were less likely to practice in children's hospitals, but this characteristic was not found to be associated with treatment decisions among the responders. This study's response rate of 69% is higher than that reported for other mailed physician questionnaires[34]. However, it is not known how the treatment strategies of those who were not included as subjects or chose not to respond differ from those of the respondents.

Physicians' treatment strategies for OJIA were not derived from actual clinical practice, but rather through clinical vignettes in a questionnaire survey. However, clinical vignette-based surveys are a well-validated approach to characterizing physicians' practice variation[35]. Indeed, the results may more closely represent physicians' personal recommendations for treatment, as they are not subject to external influences, such as parents' and patients' preferences. A social desirability bias, whereby subjects alter their responses in order to be viewed favorably by others, is unlikely given that the optimal treatment for OJIA is not known[36].

The format of the questionnaire resulted in limitations, as well. Physicians were only asked about their treatment recommendations at initial presentation and after 2 and 6 months of failed NSAID therapy, but these appear to be significant timepoints in the decision process. The vignette inquiring about treatment recommendations after 2 months of unsuccessful NSAID therapy was meant to identify physicians' choices following an adequate trial of a single NSAID. This was likely accomplished, as evidenced by the fact that the mean, median, and mode response to a separate question about adequate NSAID trial duration in OJIA were about 8 weeks. The vignette inquiring about treatment recommendations after 6 months of unsuccessful NSAID therapy was meant to determine physicians' second-line choices following failure of the NSAID class of medications. This was likely accomplished, as all respondents recommended at least one other medication in response to this scenario.

The clinical vignettes were presented chronologically and their order was not varied among respondents. Although the order of the vignettes may have influenced respondents' recommendations, there was an insufficient number of pediatric rheumatologists available to administer multiple versions of the questionnaire to test this hypothesis.

To simplify the administration and analysis of the questionnaire, respondents were only asked their treatment recommendations for case vignettes involving monoarthritis of the knee. This was a reasonable choice, as this is the most common presentation of OJIA[8,12,13,16]. However, the frequency of recommendations for IACI may be expected to decrease for joints other than the knee, due to less physician comfort with injecting other joints. Additionally, some physicians in our study were more likely to recommend IACI for an older patient. Although not assessed by this questionnaire, other subtypes of JIA, such as psoriatic arthritis, enthesitis related arthritis, and undifferentiated arthritis, may present similarly with monoarthritis of the knee. Therefore, our findings may not generalize to all patients with OJIA or all patients with JIA and knee monoarthritis.

In assessing the outcomes of the questionnaire, the decision to dichotomize recommendations for IACI at the "very likely" level was based on the distribution of responses and the responsiveness of the likelihood scale. This subjective decision obviously influenced the results. However, if the responses were instead dichotomized at the "likely" level, the distribution of treatment strategies would not change significantly: 39% initial IACI, 54% contingent IACI, and 7% MTX or SSZ without IACI ($p = 0.12$, chi-square test).

Most pediatric rheumatologists recommend IACI in the treatment of monoarthritis of the knee in OJIA. The presence and timing of this recommendation vary among individuals and are associated with differences in the perception of medication efficacy and IACI proficiency. Clinical trials to date are limited and do not adequately assess all of the relevant treatment strategies or outcomes. Further investigation into the treatment of OJIA is warranted in order to optimize the care of the most common condition in pediatric rheumatology.

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REFERENCES

1. Petty RE, Southwood TR, Manners P, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 2004;31:390-2.

2. Oen KG, Cheang M. Epidemiology of chronic arthritis in childhood. Semin Arthritis Rheum 1996;26:575-91.
3. Cassidy JT, Petty RE. Oligoarthritis. In: Cassidy JT, Petty RE, editors. Textbook of pediatric rheumatology. 5th ed. Philadelphia: WB Saunders; 2005:274-90.
4. Bowyer S, Roettcher P. Pediatric rheumatology clinic populations in the United States: results of a 3 year survey. Pediatric Rheumatology Database Research Group. J Rheumatol 1996;23:1968-74.
5. Sherry DD, Stein LD, Reed AM, Schanberg LE, Kredich DW. Prevention of leg length discrepancy in young children with pauciarticular juvenile rheumatoid arthritis by treatment with intraarticular steroids. Arthritis Rheum 1999;42:2330-4.
6. Vostrejs M, Hollister JR. Muscle atrophy and leg length discrepancies in pauciarticular juvenile rheumatoid arthritis. Am J Dis Child 1988;142:343-5.
7. Simon S, Whiffen J, Shapiro F. Leg-length discrepancies in monoarticular and pauciarticular juvenile rheumatoid arthritis. J Bone Joint Surg Am 1981;63:209-15.
8. Guillaume S, Prieur AM, Coste J, Job-Deslandre C. Long-term outcome and prognosis in oligoarticular-onset juvenile idiopathic arthritis. Arthritis Rheum 2000;43:1858-65.
9. Selvaag AM, Flato B, Dale K, et al. Radiographic and clinical outcome in early juvenile rheumatoid arthritis and juvenile spondyloarthropathy: a 3-year prospective study. J Rheumatol 2006;33:1382-91.
10. Minden K, Kiessling U, Listing J, et al. Prognosis of patients with juvenile chronic arthritis and juvenile spondyloarthropathy. J Rheumatol 2000;27:2256-63.
11. Hashkes PJ, Laxer RM. Medical treatment of juvenile idiopathic arthritis. JAMA 2005;294:1671-84.
12. Sharma S, Sherry DD. Joint distribution at presentation in children with pauciarticular arthritis. J Pediatr 1999;134:642-3.
13. Al-Matar MJ, Petty RE, Tucker LB, Malleson PN, Schroeder ML, Cabral DA. The early pattern of joint involvement predicts disease progression in children with oligoarticular (pauciarticular) juvenile rheumatoid arthritis. Arthritis Rheum 2002;46:2708-15.
14. Huemer C, Malleson PN, Cabral DA, et al. Patterns of joint involvement at onset differentiate oligoarticular juvenile psoriatic arthritis from pauciarticular juvenile rheumatoid arthritis. J Rheumatol 2002;29:1531-5.
15. Sullivan DB, Cassidy JT, Petty RE. Pathogenic implications of age of onset in juvenile rheumatoid arthritis. Arthritis Rheum 1975;18:251-5.
16. Cassidy JT, Brody GL, Martel W. Monarticular juvenile rheumatoid arthritis. J Pediatr 1967;70:867-75.
17. Cron RQ, Sharma S, Sherry DD. Current treatment by United States and Canadian pediatric rheumatologists. J Rheumatol 1999;26:2036-8.
18. Brunner HI, Kim KN, Ballinger SH, et al. Current medication choices in juvenile rheumatoid arthritis II — Update of a survey performed in 1993. J Clin Rheumatol 2001;7:295-300.
19. Criswell LA, Henke CJ. What explains the variation among rheumatologists in their use of prednisone and second-line agents for the treatment of rheumatoid arthritis? J Rheumatol 1995;22:829-35.
20. Maetzel A, Bombardier C, Strand V, Tugwell P, Wells G. How Canadian and US rheumatologists treat moderate or aggressive rheumatoid arthritis: a survey. J Rheumatol 1998;25:2331-8.
21. Zink A, Listing J, Ziemer S, Zeidler H. Practice variation in the treatment of rheumatoid arthritis among German rheumatologists. J Rheumatol 2001;28:2201-8.
22. Pope JE, Hong P, Koehler BE. Prescribing trends in disease modifying antirheumatic drugs for rheumatoid arthritis: a survey of practicing Canadian rheumatologists. J Rheumatol 2002;29:255-60.
23. Jobanputra P, Wilson J, Douglas K, Burls A. A survey of British rheumatologists' DMARD preferences for rheumatoid arthritis. Rheumatology Oxford 2004;43:206-10.
24. Maravic M, Berge C, Daures JP, Boissier MC. Practices for managing a flare of long-standing rheumatoid arthritis: survey among French rheumatologists. Clin Exp Rheumatol 2005; 23:36-42.
25. Brik R, Gepstein V, Berkovitz D. Low-dose methotrexate treatment for oligoarticular juvenile idiopathic arthritis nonresponsive to intra-articular corticosteroids. Clin Rheumatol 2005;24:612-4.
26. MacRae VE, Farquharson C, Ahmed SF. The pathophysiology of the growth plate in juvenile idiopathic arthritis. Rheumatology Oxford 2006;45:11-9.
27. Cleary AG, Murphy HD, Davidson JE. Intra-articular corticosteroid injections in juvenile idiopathic arthritis. Arch Dis Child 2003;88:192-6.
28. Padeh S, Passwell JH. Intraarticular corticosteroid injection in the management of children with chronic arthritis. Arthritis Rheum 1998;41:1210-4.
29. Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. JAMA 2003;290:1624-32.
30. Allen RC, Gross KR, Laxer RM, Malleson PN, Beauchamp RD, Petty RE. Intraarticular triamcinolone hexacetonide in the management of chronic arthritis in children. Arthritis Rheum 1986;29:997-1001.
31. Woo P, Southwood TR, Prieur AM, et al. Randomized, placebo-controlled, crossover trial of low-dose oral methotrexate in children with extended oligoarticular or systemic arthritis. Arthritis Rheum 2000;43:1849-57.
32. Levinson JE, Wallace CA. Dismantling the pyramid. J Rheumatol Suppl 1992;33:6-10.
33. Althouse LA, Stockman JA 3rd. Pediatric workforce: a look at pediatric rheumatology data from the American Board of Pediatrics. J Pediatr 2006;149:869-70.
34. Cummings SM, Savitz LA, Konrad TR. Reported response rates to mailed physician questionnaires. Health Serv Res 2001;35:1347-55.
35. Veloski J, Tai S, Evans AS, Nash DB. Clinical vignette-based surveys: a tool for assessing physician practice variation. Am J Med Qual 2005;20:151-7.
36. Phillips DL, Clancy KJ. Some effects of "social desirability" in survey studies. Am J Sociology 1972;77:921-38.