

Medication Adherence of Patients with Selected Rheumatic Conditions: A Systematic Review of the Literature

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Objective: Nonadherence with medication treatment has been found to occur in large proportions of patients with a broad range of chronic conditions. Our aim was to perform a systematic review of the literature examining adherence with treatments for inflammatory rheumatic conditions to assess the magnitude of the problem in this patient population.

Methods: A MEDLINE search of English language literature was performed to identify studies published between January 1, 1985 and November 30, 2007 that evaluated adherence with chronic medications needed in the treatment of rheumatic conditions.

Results: A total of 20 articles met the criteria for evaluation, the majority of which focused on the treatment of rheumatoid arthritis. Most of the studies examined the use of nonsteroidal anti-inflammatory medications and disease-modifying antirheumatic drugs. Adherence was assessed based on self-report, pill counts, pharmacy dispensings, openings of pill containers using electronic devices, laboratory assays, and physician assessment. Adherence varied greatly based on the adherence measure used, arthritic condition evaluated, and medication under study. Overall, the highest rates of adherence were based on self-reports for a wide variety of medications and conditions (range of persons reporting adherence was 30 to 99%), while the lowest adherence rates were for allopurinol based on pharmacy dispensings (18-26%).

Conclusions: Adherence has not been widely examined for most chronic inflammatory rheumatic conditions and the few studies that exist used different definitions and populations, thus limiting any conclusions. However, the current literature does suggest that nonadherence is a substantial problem.

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Estimates suggest that at least 50% of adults prescribed pharmacological therapy for chronic conditions will have difficulty adhering to their regimen after 6 months (1,2). Adherence (or compliance) with a medication regimen generally refers to whether a patient takes a prescribed medication according to the provider's instructions (3). Poor adherence contributes to worse clinical outcomes and increased health care utilization and cost (4,5). While

providers assume patients with rheumatic conditions take their medications since nonadherence may result in increased joint pain and functional impairment, this in fact is not necessarily the case (6,7). While the magnitude and determinants of adherence have been well examined in patients with a variety of conditions, such as cardiovascular disease and hypertension, it has not been greatly explored in arthritis and musculoskeletal conditions (8).

The last reviews of arthritis medication adherence were performed approximately 20 years ago and focused solely on the treatment of rheumatoid arthritis (6,9). Therefore we undertook a comprehensive critical appraisal of the literature regarding adherence as it related to the treatment of selected chronic rheumatic conditions since that last review.

METHODS

Identification and Selection of Articles

A MEDLINE search of English language literature was performed to identify studies published between January

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1, 1985 and November 30, 2007 that evaluated adherence, compliance, or persistence of medications for the treatment of rheumatic conditions. The following key words were used as search terms: (patient compliance or adherence or persistence or discontinuation or switching) and (ankylosing spondylitis, or arthritis, or gout, or psoriatic arthritis, or polymyalgia rheumatica, or rheumatoid arthritis, or systemic lupus erythematosus, or vasculitis, or anti-inflammatory agents, or etanercept, or infliximab, or adalimumab, or prednisone, or methotrexate, or hydroxychloroquine, or azathioprine, or sulfasalazine, or anti-rheumatic agents, or allopurinol, or uricosuric agents, or probenecid, or gold sodium thiomalate, or gold compounds, or gold sodium thiosulfate, or cyclophosphamide). We then limited the search to those articles published in English and work involving humans. A total of 2916 articles were identified. Each article abstract was reviewed to identify potentially relevant articles for retrieval, selecting studies that included original data and examined adherence or persistence with medications in the treatment of chronic inflammatory rheumatic conditions. We excluded studies that examined the use of medications for the treatment of osteoarthritis ($n = 3$), as patients may not require chronic therapy, meaning they only take their medications as needed when they have pain, and thus adherence is difficult to assess. We also excluded studies when the type of arthritis was not specified ($n = 4$), since some forms of arthritis do not require continuous therapy with medications (for example, infrequent gout attacks). The majority of articles were unrelated to adherence or the treatment of chronic rheumatic conditions.

A total of 70 original studies were identified as well as 9 review articles (9-17) and 6 editorials and/or commentaries (18-23), which were retrieved for full text review. The references lists for all the articles were reviewed for additional relevant studies. There were 11 additional articles identified from the reference lists, 4 of which were review articles and thus not included. After review of the full-text papers, an additional 57 articles were excluded for the following reasons:

1. discontinuation of medications due to ineffectiveness and/or adverse effects ($n = 25$)
2. interventions to improve adherence ($n = 10$)
3. patient beliefs and attitudes regarding medications ($n = 5$)
4. development or validation of instruments to measure adherence ($n = 7$)
5. treatment guideline adherence ($n = 3$)
6. case reports of individual patients ($n = 1$)
7. physician prescribing patterns ($n = 4$)
8. adherence is evaluated for the same study population as an earlier study by the same investigator ($n = 2$)

Based on the results of this final stage of assessment, 20 articles are included in this review (16 identified from the

Table 1 Characteristics of the Studies ($N = 20$)
Evaluating Drug Adherence in Rheumatic Conditions

Condition	Frequency of Articles
Rheumatoid arthritis	11
Systemic lupus erythematosus	4
Gout	3
Juvenile idiopathic arthritis	2
Polymyalgia rheumatic	1
Multiple inflammatory arthropathies	1
Medications	
DMARDs	9
NSAIDs and salicylates	7
Arthritis medications or medications in general	6
Glucocorticoids	4
Urate-lowering medications	3
Biologic agents	2
Colchicine	1
Adherence evaluation	
Patient interview/questionnaire	9
Pharmacy records	4
Electronic device	3
Laboratory assay	3
Chart review	2
Pill counts	1
Physician assessment	1
Population size	
<50	7
50 to 200	10
200 to 1000	2
>1000	3
Duration of monitoring	
≤1 month	3
1 to 6 months	1
6 months to 1 year	3
>1 year	6

original MEDLINE search and 4 identified from the review of reference lists).

RESULTS

Characteristics of the Studies

The majority of studies focused on the treatment of rheumatoid arthritis (Table 1). There were 4 or fewer studies examining adherence in conditions including juvenile idiopathic arthritis (14,24), polymyalgia rheumatica (25), systemic lupus erythematosus (26-29), and gout (7,25,30). The most common medications studied were nonsteroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic agents (DMARDs). These studies employed a variety of study designs to assess adherence including chart review, analysis of pharmacy records, patient interviews, self-administered questionnaires, pill counts, electronic devices to measure openings of pill containers, laboratory assays to measure metabolites, and assessments by treating physicians. Sample sizes ranged from 12 to almost 5600.

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