Perioperative Medication Management in the Rheumatic Diseases

C. Ronald MacKenzie¹

Published online: 23 August 2017
© Springer Science+Business Media, LLC 2017

Despite major advances in therapy, patients with chronic rheumatic diseases continue to require surgery to address pain and functional incapacity [1–3]. Most often of an orthopedic nature, particularly total joint arthroplasty, rheumatologists and increasingly specialists in hospital-based medicine are asked to evaluate and care for such patients in the perioperative setting. As modern day rheumatic disease therapy is a complex and rapidly evolving domain, perioperative management in this clinical context may seem challenging particularly to physicians less familiar with these therapies. This commentary presents a succinct summary of the relevant pharmacological considerations emphasizing the results of a recently published collaboration of American College of Rheumatology (ACR) and the American Association of Hip and Knee Surgeons (AAHKS) from which evidence-based guidelines for the perioperative management of anti-rheumatic drug therapy have been developed [4]. Owing to their anti-inflammatory and immunosuppressive nature, concerns regarding the risk of postoperative infection as well as impaired wound healing have long encircled the use of these medications in the surgical setting. Given the high prevalence of their usage, decision-making is a frequently encountered conundrum and one that provides an opportunity for the mitigation of important postoperative risks.

By way of background, the anti-rheumatic disease medications are categorized as agents believed to modify disease activity (DMARDs) or as *biologics*, agents that target specific mediators (cytokines) of the inflammatory response.

Corticosteroids as well as other agents of uncertain mechanism of action are also included in this review due to their long-standing usage and recognized efficacy in the therapy of rheumatic disease. On a practical level, the principle management questions are when a given medication should have been stopped preoperatively and in order to avoid postoperative disease flares, how soon can it be restarted afterward? In the case of the former, decisions are based on a medication's half-life and with respect to the latter on the patient's postoperative course. The literature upon which treatment considerations can be based is nonetheless sparse with no reported randomized controlled trials concerning this clinical problem. As such consensus-based approaches to guideline development are necessary.

Current Guidelines

As referenced above, the efforts of a panel of experts (rheumatologists, orthopedic surgeons, an infectious disease specialist and a methodologist) represents the most current and authoritative statement concerning this perioperative challenge. The methodology employed is summarized herein [4]. After convening to construct the key clinical questions to be addressed in a relevant guideline, a systematic literature review pertaining to the continuing versus withholding of anti-rheumatic therapy was conducted. Patient values and preferences were then considered and the quality of evidence and strength of recommendations evaluated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology [5, 6]. Group consensus was then reached by a voting panel of participating rheumatologists and orthopedic surgeons. Recommendation strength reflects the panel's degree of certainty that the benefits of a given recommendation outweigh the potential harms

✉ C. Ronald MacKenzie
MackenzieR@HSS.edu

¹ Hospital for Special Surgery, 535 East 70th St., New York, NY 10021, USA

Table 1 General Principles^a

1. Patients with rheumatic disease undergoing total hip and total knee arthroplasty are at increased risk for postoperative wound breakdown and periprosthetic infection.
2. Appropriate management of anti-rheumatic medication in the perioperative period may provide an opportunity to mitigate risk.
3. Nonbiologic disease-modifying anti-rheumatic drugs may be continued throughout the perioperative period in patients who are undergoing total hip and knee replacement surgery.
4. Biologic medication should be withheld as close to one dosing cycle as scheduling permits prior to elective total hip and knee replacement and restarted after evidence of wound healing (typically 14 days).

^a Adapted from reference 4

vis-à-vis the quality of the supporting evidence and patient preferences.

Table 1 presents the principles underlying the medication recommendations summarized in Table 2. Further, but not included in the figure, glucocorticoid dosing in the perioperative setting was also addressed. Challenging the traditional, virtually rote application of a “stress-dose” paradigm, the continuance of the patient’s usual daily dose of glucocorticoid is thought to be, with few exceptions, sufficient [7].

These recommendations are intended to guide, not mandate, treatment, and it is recognized that not all perioperative scenarios are covered. While developed for total joint arthroplasty, these guidelines represent the best available

Table 2 Medications included in the 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the perioperative management of anti-rheumatic medication in patients with rheumatic diseases undergoing elective total hip or total knee arthroplasty. Reprinted with permission from [4]

DMARDs: CONTINUE these medications through surgery	Dosing interval	Continue/withhold
Methotrexate	Weekly	Continue
Sulfasalazine	Once twice daily	Continue
Hydroxychloroquine	Once twice daily	Continue
Leflunomide (avara)	Daily	Continue
Doxycycline	Daily	Continue
BIOLOGIC AGENTS: STOP these medications prior to surgery and schedule surgery at the end of the dosing cycle. RESUME medications at minimum 14 days after surgery in the absence of wound healing problems, surgical site infection, or systemic infection	Dosing interval	Schedule surgery (relative to last biologic agent dose administered) during
Adalimumab (Humira)	Weekly or every 2 weeks	Week 2 or 3
Etanercept (enbrel)	Weekly or twice weekly	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4–6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2
Anakinra (Kineret)	Daily	Day 2
Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Belimumab (Benlysta)	Every 4 weeks	Week 5
Tofacitinib (Xeljanz): STOP this medication 7 days prior to surgery	Daily or twice daily	7 days after last dose
SEVERE SLE-SPECIFIC MEDICATIONS: CONTINUE these medications in the perioperative period	Dosing interval	Continue/withhold
Mycophenolate mofetil	Twice daily	Continue
Azathioprine	Daily or twice daily	Continue
Cyclosporine	Twice daily	Continue
Tacrolimus	Twice daily (IV and PO)	Continue
NOT-SEVERE SLE: DISCONTINUE these medications 1 week prior to surgery	Dosing Interval	Continue/withhold
Mycophenolate mofetil	Twice daily	Withhold
Azathioprine	Daily or twice daily	Withhold
Cyclosporine	Twice daily	Withhold
Tacrolimus	Twice daily (IV and PO)	Withhold

A summation of effort organized according to the medication class

evidence concerning the perioperative management of anti-rheumatic medication. As such, they can be extrapolated to other orthopedic settings including the spine, hand and foot, and to general surgical procedures.

References

1. Mertelmann-Voss C, Lyman S, Pan TH, et al. US trends in rates of arthroplasty for inflammatory arthritis including rheumatoid arthritis, juvenile idiopathic arthritis, and spondyloarthritis. *Arthritis Rheum.* 2014;66(6):1432–9.
2. Nikiphorou E, Carpenter L, Morris S, et al. Hand and foot surgery rates in rheumatoid arthritis have declined from 1986 to 2011, but large-joint replacement rates remain unchanged: results from two UK inception cohorts. *Arthritis Rheum.* 2014;66(5):1081–9.
3. Mertelmann-Voss C, Lyman S, Pan TJ, et al. Arthroplasty rates are increased among US patients with systemic lupus erythematosus: 1991–2005. *J Rheumatol.* 2014;41(5):867–74.
4. Goodman SM, Spinger B, Guyatt G, et al. 2016 American College of Rheumatology/American Association of Hip and Knee Surgeons Guidelines for the perioperative management of anti-rheumatic medication in patients with rheumatic diseases undergoing elective total hip and knee arthroplasty. *Arthritis Rheum.* 2017.
5. Neumann I, Santesso N, Aki EA, et al. A guide for health professionals to interpret and use recommendations in guidelines developed with the GRADE approach. *J Clin Epidemiol.* 2016;72:45–55.
6. Andrews J, Guyatt G, Oxman AD, et al. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol.* 2013;66(7):719–25.
7. MacKenzie CR, Goodman S. Stress dose steroids: myth and perioperative medicine.