

Balancing gastrointestinal benefit–risk in individuals who are prescribed NSAIDs for arthritis

Musculoskeletal problems and conditions are widespread and their impact is pervasive. They are the most common cause of severe long-term pain and physical disability, affecting hundreds of millions of people around the world [1]. Those predominantly affecting joints are collectively called arthritis. Arthritis is quite common: one in four Europeans has some form of arthritis or rheumatism and one in five is under long-term treatment for it [2]. As our population ages, these numbers are unlikely to go down. The burden of rheumatic diseases may not be heavy in terms of mortality but the effect on daily life is significant. In fact, it has been reported that musculoskeletal conditions have the greatest impact on quality of life compared with other diseases [3, 4]. One UK report found that when their arthritis is bad, 69% of people have difficulty in carrying out daily tasks and 54% even struggle to get out of bed [5].

Our primary aim in treating someone with any form of arthritis is to stop the progression of the disease and to help the patient to live as active and pain free a life as possible. Medical professionals have a range of treatments to offer people with arthritis or other forms of rheumatism. In the treatment of RA and SpA, major progress has been made in the last decade and NSAIDs are now used less in these patients. However, the number of patients with OA is increasing and NSAIDs are now used extensively by these (often elderly) patients, who quite frequently also have one or more comorbidities. As the European League Against Rheumatism (EULAR) guidelines on the treatment of OA clearly state, a combination of non-pharmacological and pharmacological treatment modalities is needed for optimal management [6]. Our first port of call is lifestyle changes with exercise and weight loss where appropriate, in addition to other non-pharmacological options including physiotherapy, education and coping programmes. The effect sizes (ESs) of these interventions may be limited (ES often in the range of 0.20) and partly due to placebo effects [7]. Where these need to be supplemented, there is a range of pharmacological treatments from local glucocorticoid injections to topical creams as well as oral pain relief [6, 8]. Paracetamol (acetaminophen) is the first oral analgesic to try. When this is not effective, we have the option of NSAIDs, with opioids as an alternative in those patients who are unresponsive to NSAIDs or intolerant of them [6]. The ESs of these NSAIDs are moderate ($ES \geq 0.50$) and they are preferred by many patients. It is the decision about when to use NSAIDs—with the benefit of efficacy and the risks for some patients—that is the focus of this supplement.

Samuel Johnson, the 18th-century English essayist, said judgement is forced upon us by experience. In fact, he implies that without experience we prefer not to make judgements. As physicians, we have to make judgements every day. Our judgements are often a question of assessing benefit vs risk. In some situations, it is clear what treatment or advice should be given. In others, a careful analysis of the benefits and risks by both physician and patient is needed to decide on the best course of action. As physicians, our judgements are based not only on our own experience by what we find out through our own practice, but also on other people's experience and on what we read in journals and discuss with our colleagues. As research and experience constantly expand, then although the objective of our judgement remains the same—achieving the best outcome for the patient—our knowledge base offers us an increasing amount of information to help us make this judgement.

This is certainly true of NSAIDs—both non-selective and Cox-2-selective inhibitors. Choosing whether to treat a patient with an anti-inflammatory drug and deciding which one will suit a patient best, is a decision that requires us to consider several aspects of a patient's health. From the early use of salicin in the 5th-century BC, it was noted that the anti-inflammatory aspirin had gastrointestinal (GI) side effects. The same phenomenon was reported in the 1980s when ibuprofen began to be sold over the counter. Then, in the 1990s, the issue of cardiovascular (CV) risk appeared and now we have a picture of both non-selective NSAIDs and Cox-2-selective inhibitors having CV risk that varies from agent to agent and which is often dose related.

In the three papers that comprise this supplement, we look at the benefit–risk judgements that we make about non-selective NSAIDs and Cox-2s when we are treating a patient with arthritis. How do we weigh up all the different factors in order to give a patient as much benefit as possible while minimizing risk?

Professor Lanus examines new data on the increase in numbers of lower GI events and illustrates how serious lower GI complications can be. He considers how this fits into the context of assessing GI risk in the entire GI tract and looks at a new end-point for establishing whether our arthritis patients are experiencing lower GI events. This may enable assessment of GI health without sophisticated techniques such as balloon endoscopy. There is a dearth of studies with lower GI events as their primary end-point to aid with this difficult issue and it is hoped that the outcome of the celecoxib or diclofenac and omeprazole for gastrointestinal safety in high

gastrointestinal risk patients with arthritis (CONDOR) study will add valuable evidence to enable improved patient outcomes.

In the second paper in the supplement, I review the evidence for the degree of CV and GI risk across the range of anti-inflammatory treatments and consider how we decide which treatment will give the most benefit and minimize risk in this population of patients who often present with increased risk of a cardiac event, GI risk factors or both. The cases where a Cox-2 may be more suitable than a non-selective NSAID with or without gastroprotection are considered.

Dr Richard Ward, a Canadian family physician, asks how we manage the kind of cases often seen in primary care, where older individuals present with a range of comorbidities and complex polypharmacy. He focuses particularly on the evidence for the efficacy of NSAIDs when given with frequently used concomitant medication, such as aspirin, ACE-inhibitor or selective serotonin re-uptake inhibitors (SSRIs).

I hope that considering all these aspects of using both non-selective NSAIDs and Cox-2s in individuals with arthritis will give you a clear idea of the evidence we currently have based on our study and personal experiences. This experience should facilitate well-informed judgments about what treatment we prescribe for the patients in our care.

Acknowledgements

Medical writing assistance was provided by Just: Health PR Ltd, with financial support from Pfizer Inc. The author was fully involved in all stages of the preparation of the manuscript, which was based on a round table conference under the chairmanship of Professor Lanias and the author. A medical writer assisted with searches of the literature and collation of data and supported the author in the drafting of the text.

Supplement: This paper forms a part of the supplement entitled 'Balancing gastrointestinal benefit–risk in individuals who are prescribed NSAIDs for arthritis'. This

supplement was supported by an unrestricted grant from Pfizer Inc.

Disclosure statement: J.W.J.B. is an advisor to Pfizer and has received honoraria as a speaker from Pfizer and MSD.

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Accepted 29 January 2010

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