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Effect of Blood Loss on Physical Function in Arthritis Patients: A Pooled Analysis

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ABSTRACT

BACKGROUND AND OBJECTIVES: The clinical consequences of lower gastrointestinal bleeding resulting from nonselective nonsteroidal anti-inflammatory drug (NSAID) use are less well documented than upper gastrointestinal bleeding. The aim of this study was to assess the effect of clinically significant gastrointestinal blood loss on health-related quality of life (HRQoL) using the SF-36 in a large arthritis population.

STUDY DESIGN: To compare treatment-associated changes in HRQoL, data from 14 multinational randomized controlled trials (2–52 weeks' duration) involving 14,173 subjects with osteoarthritis/rheumatoid arthritis, treated with celecoxib versus placebo or active comparator NSAIDs or both, were pooled. Clinically significant blood loss was defined as hemoglobin decreases ≥2 g/dL from baseline versus no change (from −1 to +1 g/dL).

RESULTS: Subjects with no change in hemoglobin reported statistically significant and clinically meaningful improvements in all SF-36 domains. In those with clinically significant blood loss, improvements were reported in bodily pain (both females and males), and role physical and vitality domains (females) only. Change scores in SF-36 between subjects with significant blood loss and those with no changes in hemoglobin demonstrated statistically significant and clinically meaningful differences in physical function (both females and males) and role physical (males) domains—more pronounced in women and men with baseline hemoglobin values ≤14 and ≤15 g/dL, respectively.

CONCLUSIONS: Treatment-associated improvements in physical function reported by subjects with no blood loss were not evident in those with significant blood loss. Differences between groups were statistically and clinically meaningful, and more pronounced when baseline hemoglobin levels were ≤14 g/dL for females and ≤15 g/dL for males. Use of medications with lower incidence of significant blood loss should be warranted in patients with arthritis.

See funding, conflict of interest, and authorship disclosures at the end of this article.

KEYWORDS: Cyclo-oxygenase 2; Gastrointestinal bleeding; Health-related quality of life; Nonsteroidal anti-inflammatory drugs

Arthritis is a painful condition that can greatly impact an individual's physical function and health-related quality of life (HRQoL). Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed for management of arthritic pain. It is well recognized that the use of NSAIDs is associated with an increased risk of upper gastrointestinal bleeding, which can be serious and life-threatening, and can cause considerable damage to the small intestine.[1] Lower gastrointestinal tract perforations, ulcers, strictures, and inflammation can result in chronic blood and protein loss, potentially leading to anemia and iron deficiency, and may in fact be more common than gastropathy associated with NSAID use.[2]

The clinical consequences of upper gastrointestinal perforations and hemorrhage have been well documented, whereas those of noncatastrophic gastrointestinal blood loss are less well understood.[2] In patients with arthritis, the potential impact of gastrointestinal blood loss on physical function and other aspects of HRQoL due to the use of NSAIDs has not been well characterized.

Previous studies have consistently and independently documented an association between low hemoglobin levels or anemia with adverse functional outcomes.[3-7] In a prospective cohort study, Penninx et al[6] found that participants with anemia had a greater mean decrease in physical performance over a 4-year period than those without anemia, even after adjustment for baseline characteristics. These authors also conducted a cross-sectional study in which anemia was associated with poorer physical performance, lower muscle strength, and disability in the elderly.[4] Han et al[7] evaluated the relationship between hemoglobin concentration and physical disability in a pooled analysis of patients with rheumatoid arthritis. Relative to patients with baseline hemoglobin levels >14 g/dL, men and women with anemia had more severe baseline disability. At week 22, improvement of >1 g/dL in hemoglobin levels was associated with clinically significant improvement in functional ability.[7] These published data prompted us to hypothesize that clinically significant blood loss may lead to anemia and consequently impact patients' physical function and HRQoL.

In this study, we conducted longitudinal analyses to assess the effect of clinically significant blood loss on physical function and HRQoL in subjects with osteoarthritis or rheumatoid arthritis.

METHODS

Source of Data and Study Sample

We collected data derived from all randomized controlled trials conducted by Pfizer in which subjects with osteoarthritis or rheumatoid arthritis were treated with celecoxib and either placebo or active comparator nonselective NSAIDs (or both) for subjects who also had both hemoglobin and Medical Outcomes Survey Short Form-36 (SF-36) data available. We applied no additional exclusion criteria (Appendix A). Table 1 presents the following characteristics of each trial included in this study: Number of study subjects and their age range, comparator treatment, disease indication, HRQoL and physical function assessments, and duration of trial.

Blood Loss and Outcomes Measures

Predefined Blood Loss: The change in hemoglobin from baseline was used to define blood loss. Some trials used only 2 measurements per subject (one at baseline and one at follow-up), while others used up to 3 assessments per subject. "Clinically significant blood loss" was defined as decreases in hemoglobin