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# Enhancing Safe Usage of Nonsteroidal Anti-inflammatory Drugs

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## Abstract

**Objective:** Assessing the Impact of Audit/Feedback and Educational Resources on Adherence to Monitoring Recommendations for Nonsteroidal Anti-inflammatory Drug (NSAID) Safety.

**Study Design:** A retrospective study

**Methods:** Physicians commonly prescribing NSAIDs within a large managed care organization were selected into either a control or intervention group (receiving audit/feedback with peer-derived benchmarks and continuing medical education). Medical records were reviewed before and after a 10-month intervention period to evaluate adherence to laboratory monitoring and cytoprotective agent recommendations. General estimating equations were employed to adjust for patient clustering.

**Results:** Among the initially selected 101 physicians, 85 remained eligible post-intervention (comprising 38 internists, 36 family physicians, and 11 rheumatologists). The mean percent change in performance between participants regarding complete blood count (CBC) monitoring was 16% versus 10%, for creatinine monitoring was 0% versus 17%, and for the use of cytoprotective agents was -3% versus -1%. However, these changes were not statistically significant.

Factors such as rheumatology specialty, number of NSAID prescriptions and physician visits, and patient risk factors for NSAID-related toxicity exhibited stronger associations with improved safety practices compared to the intervention itself.

**Conclusions:** Audit/feedback and educational materials did not demonstrate a significant impact on improving NSAID-related safety practices. Potential contributing factors include high baseline performance, dilution of intervention effects by case mix and provider factors, nonreceipt of intervention materials, and diverse indications for laboratory tests.

**Introduction:**

Nonsteroidal anti-inflammatory drugs (NSAIDs) rank among the most widely prescribed medications worldwide. Their extensive usage, however, comes with significant risks, as chronic NSAID administration is frequently associated with adverse events leading to substantial morbidity and mortality. Such events encompass serious gastrointestinal (GI) complications, with approximately 0.5% of arthritis patients using NSAIDs regularly being hospitalized annually due to these issues. Moreover, NSAID utilization is linked to hypertension, exacerbation of congestive heart failure, and various forms of renal injury. Notably, inappropriate NSAID prescription, particularly among older adults with comorbid conditions predisposing them to NSAID-related toxicity, remains a prevalent concern. (Fries et al., 2004)

In response to the widespread use of NSAIDs and the attendant risks, several medical organizations have issued guidelines advocating for NSAID safety monitoring practices. These guidelines emphasize the identification of high-risk NSAID users, regular monitoring utilizing complete blood count (CBC) and creatinine testing to detect early GI and renal toxicity, and consideration of cyclooxygenase-2 (COX-2) selective NSAIDs or cytoprotective agents for high-risk patients. However, adherence to these recommendations among physicians is suboptimal. (Hanlon et al., 2002)

Despite concerted efforts, including guideline formulation and educational initiatives, historical attempts to influence physician behavior toward better

adherence to NSAID safety recommendations have yielded limited success. Notably, audit and feedback strategies have demonstrated promise in effecting changes in provider practice patterns. (Patino et al., 2003)

In light of these challenges and with the objective of enhancing the quality of care for chronic NSAID users, we conducted a group selected study to evaluate a multimodal intervention aimed at improving safety practices associated with NSAID prescribing. We hypothesized that physicians receiving the intervention would exhibit greater improvement in three key NSAID-prescribing process measures compared to those in the control group during the baseline and follow-up periods. (Hulscher et al., 2004)

**Methods:**

**Baseline Cohort:**

Following approval by the institutional review board, all adult patients with pharmacy benefits within a large regional managed care organization (MCO) who received one or more prescriptions for nonsteroidal anti-inflammatory drugs (NSAIDs) during a 7-month period were identified. Utilizing National Drug Codes from pharmacy claims, from medical records patients were selected retrospectively, focusing on those under providers more likely to prescribe and follow up with long-term NSAID users, namely family or general practitioners, internists, and rheumatologists. Rheumatologists were intentionally oversampled. A total of 2334 eligible patients were identified, from which 680 (29%) patients and their corresponding 136 providers (5 patients per provider) were retrospectively chosen, with preference given to those with three or more NSAID prescriptions. A response rate of 66% was obtained, resulting in 452 records (from 103 physicians, including 43 internists, 44 general practitioners, and 16 rheumatologists).

**Baseline Medical Record Abstraction:**

Chart documentation and laboratory data were reviewed for the 10-month period , ensuring a minimum of 90 days follow-up past the last NSAID prescription identified. Using a customized version of MedQuest software, trained abstractors achieved 97% interrater reliability for all main variables, with process measures for safe NSAID prescribing developed based on published literature.

**Multimodal Intervention to Improve NSAID Safety:**

Physicians were stratified by specialty and selected Two physicians involved in study design were excluded from randomization. Physicians received a mailed twice, focusing on "Safer Use of NSAIDs." This packet included a brochure providing provider-specific audit and feedback on safe NSAID practices, key literature citations with CME credits, and a hyperlink to a case-based educational website on safe NSAID prescribing. Feedback was sought via a faxed questionnaire distributed weeks after the initial mailing, broadcasted weekly for 5 consecutive weeks.

**NSAID Safety Quality Indicators:**

Performance feedback for three process-of-care measures (CBC testing, creatinine testing, and cytoprotective agent prescription) was provided based on data from the 10-month observation period.

**Follow-up Cohort:**

Approximately 6 months after distribution, all NSAID prescriptions were identified. Patients receiving one or more NSAID prescriptions were included in the follow-up cohort. Records were reviewed by trained abstractors over a similar 10-month period for the same three primary processes of care.

**Statistical Analyses:**

Statistical analyses were conducted using SAS software, with adjustments made for baseline performance and cluster randomization.

**Results:**

**Patient Selection and Chart Requests:**

Following our selection process and subsequent request for medical records, we received 66% of the requested medical charts (n = 312). No significant differences were noted in sex and age between patients whose records were reviewed and those whose records were not sent for review. A total of 101 physicians were selected

Six months after our intervention, we received 83% of the requested medical records from 85 of the 96 physicians (n = 421). Characteristics of the participants and their associated NSAID-treated patients are described. Only minimal differences were observed between the demographics and patient case mix of intervention physicians compared with control physicians. Fewer than 5% of the patients in the baseline cohort were represented in the follow-up cohort.

**Response to Intervention Targeted at Improving NSAID Safety:**

After the mailed intervention, 20 of the 50 intervention physicians responded (40%) via the Web site (n =1), postcard (n = 14), or fax (n = 11) (numbers include multiple responses from individual physicians). Continuing medical education (CME) was awarded to 15 physicians.

**Primary and Secondary Analyses:**

Performance rates for the three main process measures including CBC testing, creatinine testing, and cytoprotective use for the pre-intervention and post-intervention time periods were similar at baseline between the participants group physicians. In secondary analyses, no differences in performance between the participants groups were observed when all cohort physicians were included, when the analysis was restricted to high-risk patients only, or when the cytoprotective process measure included COX-2-selective NSAID use.

**Multivariable Analysis:**

Factors associated with improvement in NSAID safety practices were examined. A greater number of patient office visits, more NSAID prescriptions, and higher-risk patients were associated with an increased likelihood of adherence to NSAID safety-monitoring guidelines. Rheumatologists were also more likely than family practice physicians to increase their rate of toxicity monitoring. However, neither analysis showed significant differences in the likelihood for improvement in performance compared with control physicians. Nonetheless, when absolute performance was examined, the performance of physicians who confirmed receipt of the intervention materials and/or engaged in the optional CME activities showed a higher but nonsignificant trend compared with both the remaining intervention physicians and the control physicians.

**Discussion:**

In pursuit of enhancing NSAID safety practices, we conducted a group selected study employing a multimodal intervention, incorporating audit and feedback alongside comparison with the top 10% of cohort physicians. Our study encompassed physicians prescribing NSAIDs across both primary care and specialty settings within a diverse managed care environment. Despite utilizing methodologies previously effective in altering practice patterns for chronic diseases, we did not observe significant differences in NSAID safety-monitoring practices. Instead, provider and patient factors, as well as health services utilization, were found to be more strongly associated with adherence to NSAID safety-monitoring guidelines. (Thomson O'Brien et al., 2004)

Various methodologies have demonstrated varying degrees of success in changing physician practice and improving adherence to evidence-based clinical guidelines. Traditional CME activities and passively consumed written materials have shown limited benefits, while electronic reminder systems, local opinion leaders, and academic detailing have exhibited more promise. In our study, we utilized audit and feedback, previously shown to be efficacious in various chronic diseases. However, the effects observed were modest at best, consistent with findings from other interventions targeting physician behavior. (Jamtvedt et al., 2004)

Despite incorporating recognized elements of successful audit and feedback interventions, our study faced several limitations. Laboratory tests, used as process measures for toxicity monitoring, are ordered for diverse indications, potentially reducing the "signal-to-noise" ratio in our outcomes. Additionally, greater-than-expected attrition among study physicians and variability in process-of-care measures may have impacted our results. Post-hoc power calculations indicated that our study may have been underpowered to detect smaller differences in performance between participants groups. (National Committee for Quality Assurance, 2004)

The presence of a ceiling effect among physicians with 100% adherence to NSAID safety guidelines limited the detectable improvement in performance. Difficulties in engaging busy physicians and challenges in capturing their attention despite repeated mailings likely contributed to our negative results. However, a trend toward higher

performance was noted among physicians who confirmed receipt of intervention materials and engaged in CME activities. (Kiefe et al., 2001)

Our study's negative results contrast with our previous success in using audit and feedback to improve care for diabetic patients. This disparity may be attributed to the less widely known or accepted quality measures for NSAID monitoring compared to diabetes care. Furthermore, the peer-derived Achievable Benchmark of Care for NSAID monitoring measures may have lacked face validity due to near-perfect benchmarks, potentially diminishing the intervention's impact. (Wolfe et al., 1999)

Our findings underscore the complexities inherent in interventions aimed at improving adherence to NSAID safety guidelines. Challenges in engaging physicians, a ceiling effect in baseline performance, and nonspecific indications for processes of care were significant factors contributing to the intervention's limited effectiveness. Moving forward, a deeper understanding of clinical and methodological insights gained from this study will inform future interventions, fostering greater success in improving physician adherence to evidence-based practice guidelines. (MacLean et al., 2000)

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