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Original Research

Toward safer prescribing: evaluation of a prospective drug utilization review system on inappropriate prescriptions, prescribing patterns, and adverse drug events and related health expenditure in South Korea

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ABSTRACT

Objectives: This study aimed to evaluate the effect of the prospective drug utilization review (DUR) system introduced in Korea in December 2010 as a real-time method to improve patient safety, in terms of changes in prescribing practices, adverse drug events (ADEs), and ADE-related healthcare expenditure, using non-steroidal anti-inflammatory drugs (NSAIDs) and their common ADEs as a guide.

Study design: We used an interrupted time-series study design using generalized estimating equations to evaluate changes in prescription rate and ADE-related healthcare expenditure. Cox regression analysis was used to evaluate the probability of NSAID-associated ADEs.

Methods: A total of 154,585 outpatients with musculoskeletal or connective tissue disorders, without pre-existing gastric bleeding or ulcers were included in this study. The primary outcome was the level and trend change in prescription rate, drug–drug interactions, coprescribed gastro-protective drugs, and defined daily dose (DDD) of NSAIDs. The secondary outcome was the probability of ADEs and changes in ADE-related healthcare expenditure.

Results: There was a significant trend change after introducing the DUR system in terms of drug–drug interactions (−3.6%) and coprescribed gastro-protective drugs (+0.6%). The mean DDD of NSAIDs increased by 0.2. The probability of ADEs decreased overall (−1.7%) and in the high-risk group (age ≥65 years; −9.6%); however, only the latter was significant. There was no significant trend or level change in ADE-related health expenditure.

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Conclusions: The introduction of the DUR system was associated with more efficient prescribing, including a reduction in drug–drug interactions and an increase in the use of gastro-protective drugs. The system had a positive effect on patient outcome but was not associated with reduced ADE-related costs. Further studies are needed to evaluate the long-term effects of the DUR system in Korea.

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Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications in many countries. They are considered effective for the treatment of chronic conditions of pain and inflammation.^{1–3} However, NSAIDs are associated with many adverse drug events (ADEs), including gastrointestinal (GI) bleeding and the risk of cardiovascular disease.^{4–6} Approximately 18% of patients using NSAIDs experience ADEs, either due to overutilization or inappropriate use.^{7,8} Prescribing drugs involves weighing up the benefits and risks; careful decision-making is needed to improve their safe use. Thus, many countries have focused on preventing potential ADEs associated with medical errors and have adopted systems that monitor the prescription of the drugs (drug utilization review [DUR] systems) to reduce ADEs and improve patient safety. DUR is defined as an ongoing systematic approach to review drug prescription and utilization.^{9–11} The DUR system operates prospectively (detecting inappropriate prescription) and retrospectively (providing feedback to the provider, including preventable drug-related morbidity and specific drug utilization). Many countries, including the US, have adopted this system to improve patient outcomes.¹²

In Korea, the need for a DUR system was raised in 2003. In response, in 2004, the Ministry of Food and Drug Administration announced a list of age-related drug contraindications and drug–drug interactions.¹³ The list of registered drugs has increased annually to reduce inappropriate prescriptions, but there has been no integrated approach to improving patient safety because the list was adopted separately through a different claim submission system. Hence, the government decided to introduce a DUR system in Korea. Starting in April 2008, a DUR system was piloted in one city. This provided useful information, including information on drug–drug interactions and the duplication of ingredients.^{13,14} After this pilot test, the DUR system was rolled out nationwide in December 2010. To improve patient safety and reduce pharmaceutical expenditure, this system provides information on drugs that were previously prescribed or prescribed by different hospitals and checks whether the prescriptions are inappropriate in real time.

According to previous studies, DUR systems have reduced inappropriate drug prescription and drug–drug interactions.^{15–18} In addition, actionable drug information of DUR systems has reduced healthcare expenditure and controlled drug utilization, particularly of frequently associated with the risk of ADEs.^{19,20} Some researchers have suggested that a DUR

system alone is insufficient to change prescribing patterns and that such change depends on physicians' drug-prescribing choices.^{12,21} In Korea, many researches have suggested that the DUR system has improved prescribing and reduced pharmaceutical expenditure.^{13,14,22,23} These studies focused on actual change in prescribing as a result of the DUR and its operating system and evaluated overall prescribing changes. In addition, most of these studies focused on the changes in utilization of antibiotic agents. There was a lack of evidence of changes in the prescription of NSAIDs, the most commonly used prescription drugs in Korea.

We investigated whether the introduction of a DUR system would result in a change in prescription patterns and in quality of care. First, we hypothesized that drug information provided by the DUR system would change prescription patterns and drug utilization. As the introduction of the DUR system could impact drug choices, we studied whether there was any change in drug–drug interactions involving NSAIDs. In addition, as the information provided could also influence physicians' use and choice of gastro-protective drugs to reduce NSAID-related ADEs, we evaluated changes in the prescription of proton-pump inhibitors (PPIs) and H₂ receptor antagonists (H₂RA). Furthermore, it could influence the utilization of NSAIDs; hence, we evaluated changes in defined daily dose (DDD) prescribed. Second, a change in prescription patterns may impact patient outcome; we examined NSAID-related ADEs (GI ulcer or bleeding) after prescription of NSAIDs. Finally, ADE-related health expenditure may also decrease after the introduction of a DUR system; thus, we evaluated changes in healthcare expenditure due to ADEs.

Methods

Database and data collection

We used National Health Insurance Services (NHIS) sampling cohort data from 2002 to 2013. Using NHIS sampling cohort data, we selected outpatients who had musculoskeletal or connective tissue disorders based on the International Classification of Disease (ICD)-10 codes (M00–M99) during the period 2008–2013. First, we considered conditions that may mimic NSAID-related ADEs (GI bleeding or ulcer) as these may have created noise in our outcome variable. Thus, we excluded patients who attended hospital services with GI disease as a major diagnosis (ICD-10 codes: K226, K228, K25–K29) during the period 2002–2007. Second, we excluded patients who were not prescribed NSAIDs based on

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