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Developing a data mining approach to investigate association between physician prescription and patient outcome – A study on re-hospitalization in Stevens–Johnson Syndrome

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ABSTRACT

Stevens–Johnson syndrome (SJS) is a potentially life-threatening skin reaction. Drugs are the major causes for cases of SJS. While treating patients with SJS, the first and most important step is to identify and discontinue any possible responsible drugs. However, potential drugs that may lead to SJS are many and encompass various therapeutic areas. Very few physicians are familiar with the potential risk of all these drugs. If properly treated, most SJS cases are expected to recover without much sequelae. All drugs that have been associated with SJS should be avoided in these patients to prevent recurrence. If the physicians fail to identify and discontinue the drugs causing SJS, or even adding new drugs related to SJS, the patient may get worse or SJS may recur. These conditions can cause SJS patients to be re-hospitalized. Currently the reasons for re-hospitalization of SJS patients in Taiwan are not known. This study uses Taiwan National Health Insurance Research Database to analyze the causes of re-hospitalization for cases of SJS. First, we classified prescription history of re-hospitalized patients through the rule-based classification method. Secondly, by using the basic prescription actions, we identified drug association patterns. Then, by employing A-priori algorithm, pairs of drugs with relatively higher frequency of appearance were identified and their degrees of association were measured by using selected symmetric and asymmetric association mining methods. Finally, by listing and ranking up these pairs of drugs according to the value of support based on their degrees of association, we provide prescribing physicians with possible means of increasing the awareness and reducing re-hospitalization of SJS patients.

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1. Background

Serious adverse drug reactions (ADRs) are common in hospitalized patients and occur in 6.7% of all inpatients. The incidence of fatal ADRs is reported to be 0.32% in the United States, and they are estimated to be between the fourth and sixth leading cause of death in inpatients [1]. Steven–Johnson syndrome is a life-threatening skin reaction to medication, and is characterized by mucocutaneous tenderness and typically hemorrhagic erosions, erythema and less severe epidermal detachment presenting as blisters and areas of denuded skin [2]. Severe cutaneous ADRs, such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been estimated to occur in one out of every 1000 hospitalized patients and are associated with significant morbidity and mortality. The mortality rate of SJS is around 5% [3].

More than 100 drugs have been implicated as causes of SJS. The drugs most frequently associated with SJS are antibacterial sulfonamides, anticonvulsants, nonsteroidal anti-inflammatory drugs, and allopurinol [4]. The treatment of SJS requires hospitalization, usually in an intensive care unit. Early diagnosis with prompt recognition and withdrawal of all potential causative drugs is essential for a favorable outcome. Morbidity and mortality would decrease if the responsible drug is withdrawn no later than the day when blisters and erosions first occur [5]. The first and most important step in treating SJS is to discontinue any possible causative agents. However, if physicians fail to identify and discontinue the drugs causing SJS, or even adding new drugs related to SJS, the patient may get worse or SJS may recur. Subsequent re-hospitalization will unnecessarily increase risk for the patient and medical costs. We think the occurrence of this kind of adverse drug events (ADEs) should be prevented.

The occurrence of SJS is associated with an interaction between genetic predisposition and pharmacological action of drugs. It is well known that many drugs can cause SJS, especially in certain populations. For example, strong associations between HLA-B*1502 and carbamazepine- or lamotrigine-induced SJS/TEN had been identified in Chinese and Thai [6–8]. Since there are many potential drugs related to SJS that encompass a wide range of therapeutic areas, few physicians are familiar with all these drugs. That allows room for mistakes. The patterns of changes of prescription behaviors of physicians before and after their patients developed SJS have not been investigated. It would be useful to know which prescription behaviors are associated with re-hospitalization of SJS patients, in order to develop means to avoid such occurrences.

There have been a growing number of applications of data mining in healthcare [9]. For instance, A-priori algorithm has been used to detect ADE in health care data. The association rules are generated to identify the combination of medications and patient characteristics lead to ADEs [10]. In another work, decision tree technique has been used to mine the electronic health records and to identify ADEs alert rules in the field of vitamin K antagonists [11].

Association mining is one of the techniques used to unearth hidden relationships among attributes. It has been applied to identify relationships between a specific drug and other drugs, or relationships a specific disease and other diseases. Taking examples in Taiwan, association mining was implemented in several studies in the National Health Insurance Research Database managed by Taiwan National Health Insurance such as to analyze co-prescribing pattern of antacids drug [12], to explore the co-morbidity of Attention Deficit/Hyperactivity Disorder, ADHD (the most prevalent chronic behavior condition in childhood) [13].

The Taiwan National Health Insurance Research Database contains all the prescription information for outpatients and hospitalized patients by all physicians in Taiwan [14,15]. In this study, we investigated re-hospitalized SJS cases in a year of National Health Insurance Database. The classification of prescription behaviors of physicians treating hospitalized SJS patients leading to re-hospitalization can help physicians to understand the causes associated with of SJS re-hospitalization.

2. Methodology

2.1. *Patients and drugs*

We used Taiwan National Health Insurance Research Database in the year of 2004 to extract patient and prescription data of all re-hospitalized SJS patients of that year. The purpose of this study is to analyze patterns of prescription behaviors that may lead to re-hospitalization of SJS patients. We found a total of 554 hospitalized SJS patients during that year. Among these patients, there was a total of 86 patients that was re-hospitalized. They included 52 males and 34 females, with a mean age of 54 years. Prescription records within 2 months before each hospitalization were reviewed. Most patients received prescriptions containing multiple drugs. Prescribed drugs that have been known to cause SJS were listed as the drugs possibly causing their hospitalization. The frequency of drugs used associated with hospitalization of the 554 patients, the first hospitalizations of the 86 patients, and the second hospitalization of the 86 patients is listed in Table 1.

2.2. *Classifying prescription behavior*

In this study, Taiwan National Health Insurance Research Database in the year of 2004 is used in data pre-processing to obtain prescription records for patients who were re-hospitalized because of SJS, and to encode which drugs were prescribed. This study uses rule-based classification to classify the prescription behaviors that were performed by physician before each hospitalization for patients who were re-hospitalized for SJS treatment. Following is the definition of patient prescription actions.

Definition

f_XY stands for prescription actions where:

f: the drug.

X: whether patient used that drug before first hospitalization, if yes fill '1', otherwise fill '0'.

Y: whether patient used that drug after first hospitalization, if yes fill '1', otherwise fill '0'.

By this definition, there are three basic prescription actions: