Outcome of a patient-specific overruling algorithm to reduce drug-drug-interaction alerts

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Abstract

Drug-drug interactions are frequent and over-alerting in clinical decision support systems is a major area of concern. Efforts to achieve a better fit between decision support and the clinical workflow are being undertaken. One possibility is to reduce DDI alerts by taking into account clinical information available in an electronic patient record, e.g. laboratory values. The present article describes the method and outcome of a patient-specific overruling algorithm using serum potassium levels to decide if DDI alerts should be overruled in circumstances where two drugs induce interactions that could lead to hyperkalaemia.

Key words: drug-drug interaction, decision support, CPOE, alert

Introduction

Especially in elderly people and hospitalised patients, drug-drug interactions (DDIs) are considered important with regard to patient safety and adverse events [1, 2]. Polypharmacy and multimorbidity increase the risk of potentially dangerous drug combinations. Most often, physicians cannot be aware of all DDIs possible in a given setting, and thus computerised support in terms of alerts has been proposed for years. However, most alerts are insufficiently specific or sensitive to achieve a high acceptance by physicians, and overriding of alerts as well as alert fatigue are very frequent [3–5]. Attempts are being undertaken to reduce over-alerting [6]. In our hospital, former studies found that the frequency and nature of DDIs was very steady over years [7]. The current study investigated an attempt to reduce the most frequent false-positive DDI alerts by implementing an overruling algorithm that was active during the prescription process.

Methods

The prospective study was performed in a publicly owned primary and secondary acute-care hospital in Thun, Switzerland. The hospital cares for approximately 16,000 inpatients and 55,000 outpatients per year. A fully electronic, interdisciplinary patient record (ePR) including computerised physician order entry (CPOE) and clinical decision support (CDS) has been in place since 2004. Prior to the start of study, all newly added prescriptions were checked for possible DDIs, based on the official Swiss Drug Database HOSPINDEX and its DDI definitions. Depending on the maximum level of DDI, the prescriber was either forced to read the interaction alert (DDI level 1), received an interruptive alert with the possibility to override it (DDI level 2 and 3) or did not receive a DDI alert at all (DDI levels 4 and 5). A manual DDI check including all DDI levels was always possible regardless of whether or not the prescription was new. For this study, changes in the alerting algorithm were regularly programmed into the ePR. The algorithm focused on distinct ATC (international Anatomical Therapeutical Chemical classification) codes that had been identified in a former analysis of the frequency of DDIs (potassium sparing agents, angiotensin converting enzyme inhibitors (ACE-I), angiotensin II blocking agents, aldosterone antagonists, potassium supplements). DDIs resulting in level 1 or level 3 alerts were predefined as being dependent on measured serum potassium levels (there was no relevant number of DDI alerts in levels 2, 4, 5 involving these ATC codes and laboratory values). The adapted CDS algorithm was activated during each new prescription and checked for DDI alerts including a combination involving the above-mentioned ATC groups. Given a positive match involving these ATC pairs (between the newly added drug and existing prescriptions or between existing prescriptions only), the defined laboratory cut-off (potassium level 4.3 mmol/l, the reference range being 3.4–4.6 mmol/l) was compared with the most recent serum potassium level (no older than 72 hours) was identified. If the measured serum potassium level was lower than the cut-off level, an overriding algorithm suppressed the automatic DDI alert and registered the overruled combination in a separate table for statistical analysis. No changes in the overruling algorithms were made after the study start in 2012.

Results

In 2012, 348,631 drugs were prescribed for 29,847 patients. Out of these prescriptions, 40,837 (12%) for 5,547 patients involved DDIs (level 1: 3,324; level 2: 1,162; level 3: 6,037; level 4: 6,999; level 5: 23,315). Forty-three percent of all level 1 alerts (1,422/3,324) and 42% of all level 3 alerts (2,532/6,037) were overruled by the defined algorithm. Overall, 38% of all interruptive DDI
alerts were automatically overruled and thus not presented to the prescribing physicians at all. Out of the 643 patients where the overruling algorithm was active, only 8 developed hyperkalaemia (potassium level >4.6 mmol/l) during the hospital stay. In only one of these eight cases was prescription of two drugs in the above-mentioned ATC groups still active when hyperkalaemia occurred.

**Discussion**

Drug-drug interactions are considered important in terms of medication safety as well as problematic in terms of over-alerting. Official drug databases (at least in Switzerland) do not take into account clinical situations nor do they include structured data (such as cut-off levels) as a basis for clinical decision support. Efforts to increase the positive predicted value of DDIs, i.e. to reduce over-alerting, are necessary for most electronic patient records. In a former analysis of the DDIs registered in our hospital, DDIs concerning hyperkalaemia alerts emerged as the most prominent single group of DDIs. In most cases, potassium supplements are prescribed intentionally with drugs like ACE-I or aldosterone antagonists, as these are drugs of choice for the underlying conditions (e.g. chronic heart failure). Furthermore, these diseases are physiologically accompanied by low potassium levels. Thus, combination treatment is most often made by intention and not by accident, leading to a low yield from standard alerts. With this typical clinical situation in mind, in the current study we tried to reduce over-alerting by taking into account current potassium levels in a given patient. Depending of the potassium level, certain DDIs were overruled by the electronic patient record. With this approach, 42% of all level 1 alerts as well as 43% of all level 3 alerts could be eliminated without creating adverse events in terms of unintended hyperkalaemia episodes. As these DDI levels are presented in an interruptive manner, the perceived alert frequency could be reduced significantly.

Measuring serum potassium levels is the easiest way to take into account clinical circumstances in the given setting. Others have shown even better outcomes when further clinical data are considered. The sample size of the study is sufficient, but adverse events could be missed owing to no measurement of serum potassium levels or early discharge of a patient.

Most often, official databases (e.g. drug databases) or pathways are too little tailored to the clinical situation to allow efficient decision support. The described intervention is one of many options to achieve better a fit of CDS in the electronic patient record, measures desperately needed to improve computerised support.

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**References**