Sustained Impact of Electronic Alerts on Rate of Prophylaxis Against Venous Thromboembolism

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Summary

Advanced electronic alerts (eAlerts) and computerized physician order entry (CPOE) increase adequate thromboprophylaxis orders among hospitalized medical patients. It remains unclear whether eAlerts maintain their efficacy over time, after withdrawal of continuing medical education (CME) on eAlerts and on thromboprophylaxis indications from the study staff.

We analyzed 5317 hospital cases from the University Hospital Zurich during 2006-2009: 1854 cases from a medical ward with eAlerts (intervention group) and 3463 cases from a surgical ward without eAlerts (control group). In the intervention group, an eAlert with hospital-specific VTE prevention guidelines was issued in the electronic patient chart 6 h after admission if no pharmacological or mechanical thromboprophylaxis had been ordered. Data were analyzed for three phases: pre-implementation (phase 1), eAlert implementation with CME (phase 2), and post-implementation without CME (phase 3).

The rates of thromboprophylaxis in the intervention group were 43.4% in phase 1 and 66.7% in phase 2 (p<0.001), and increased further to 73.6% in phase 3 (p=0.011). Early thromboprophylaxis orders within 12 hours after admission were more often placed in phase 2 and 3 as compared to phase 1 (67.1% vs. 52.1%, p<0.001). In the surgical control group, the thromboprophylaxis rates in the three phases were 88.6%, 90.7%, 90.6% (p=0.16).

Advanced eAlerts may provide sustained efficacy over time, with stable rates of thromboprophylaxis orders among hospitalized medical patients.
Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE) together are referred to as venous thromboembolism (VTE) (1). The DVT attack rate (incidence of first and recurrent DVT) has been estimated for the United States and the European Union at 128/100,000 person-years (2) and 148/100,000 person-years (3), respectively. Approximately one quarter of all VTE events are hospital-related and at least 70% of the VTE-associated deaths occur as a consequence of a hospital-acquired VTE (3, 4). The case fatality rate of PE approximates 7-11% (5, 6).

Appropriate use of prophylaxis to prevent VTE is an important strategy for improving safety among hospitalized patients (7, 8). A recent meta-analysis found significant reductions in any PE (relative risk 0.43) and fatal PE (relative risk 0.38) due to thromboprophylaxis without a significant increase in major bleeding complications (9).

The American College of Chest Physicians (ACCP) has established evidence-based guidelines for the prevention of VTE, including pharmacologic treatment with anticoagulants and mechanical prophylaxis (e.g. compression stockings) (10). Nevertheless, many patients at risk do not receive prophylaxis, as evidenced by three large studies (11-13). The ACCP suggests the use of various strategies for increasing thromboprophylaxis adherence, explicitly including the use of computer decision support systems (CDSS). Some studies investigated computerized reminders of prophylaxis and found substantially higher thromboprophylaxis rates due to electronic alerts (eAlert) (14-16). However, lack of physician compliance with electronically generated suggestions is a well-known problem called ‘alert fatigue’ or ‘overriding’ (17).

Research on VTE prevention has been a focus at the University Hospital Zurich in recent years in the context of an ongoing quality assurance program which also covered multicenter studies (18, 19). In 2007, an advanced eAlert module was developed and implemented into the clinical information system (KISIM, Cistec AG, Zurich, Switzerland) of a medical ward. An eAlert was issued in the electronic chart six hours after the patient was admitted to the ward if no pharmacologic or mechanical prophylaxis had been
ordered. All healthcare professionals involved in the patient care were reminded by a highlighted alert button to consider thromboprophylaxis, but only the physician was enabled to respond to the eAlert. When the physician clicked on the eAlert button, an information screen displayed hospital-specific guidelines on VTE prevention in medical patients.

Physician compliance with the VTE eAlerts was evaluated in a pilot study (16). During this period, continuing medical education (CME) on prevention of VTE in hospitalized patients and on the eAlert system was provided to the staff physicians of the medical ward. The rate of appropriate prophylaxis during this pilot study averaged 76%, as compared to a much lower rate of 44% observed in a cross-sectional 1-day survey prior to the implementation of computerized physician order entry (CPOE) (16, 18). The prospective pilot study focused on physicians’ compliance. It did not consider data on the prophylaxis rate in patients treated in the same medical ward immediately before or after the study period, and no data were available on patients treated in other wards during the identical period, in the absence of eAlerts.

The purpose of the present analysis was to comparatively assess the sustainability of the eAlert system over time.

**Materials and methods**

Two wards of the University Hospital of Zurich, Switzerland, introduced CPOE in 2006, i.e. a medical ward (intervention group) and a surgical ward (control group). Then, CPOE was limited to these wards, including 22 beds in medicine and 23 beds in surgery, respectively. The remaining wards in medicine (164 beds) and surgery (239 beds) were not considered since they introduced CPOE not before 2009.

In the medical intervention ward, but not in the surgical ward, an eAlert was displayed in the electronic chart of each patient who did not receive a pharmacological or mechanical thromboprophylaxis order within six hours after admission (16). Prophylaxis
guidelines including a VTE risk score are displayed by default when the physician acknowledges the eAlert button.

All patients admitted to the study wards from April 2006 to December 2009 were enrolled if they stayed for at least 24 hours in these wards and (i) either entered these wards directly or (ii) entered these wards via the emergency department; i.e. in-patients transferred from other wards were excluded. The electronic charts of the included patients were searched for orders of pharmacological and mechanical prophylaxis. All orders of prophylaxis were considered for the time period from admission to discharge or transfer of the patient to another ward.

We analyzed 5317 hospital cases during 2006-2009: 1854 cases from the medical intervention ward with eAlerts and 3463 cases from the surgical ward without eAlerts. The overall study period included 45 months: (a) pre-implementation phase 1, 4/2006-8/2007, (b) eAlerts implementation phase 2, 9/2007-12/2008, and (c) post-implementation phase 3, 1/2009-12/2009. The eAlert module was implemented in the intervention ward at the beginning of phase 2 and included monitoring of the appropriateness of the ordered VTE prophylaxes (16). The eAlerts remained in operation in the intervention group also during phase 3. Only during phase 2 was specific CME on indications for prophylaxis provided to the physicians of the intervention group. No specific CME was offered to the physicians of the control group. This quality improvement initiative study was approved by the local ethics committee and patient consent was waived.

The rate of prophylaxis was defined as the percentage of patients with at least one order for VTE prophylaxis during their stay in the admitting ward. Combined prophylaxis was defined as orders of both pharmacologic and mechanical prophylaxes.

Clinical outcome at discharge was assessed for all three phases by searching the patient charts for diagnoses of PE and DVT (I26.0, I26.9, I82.8, I82.9; International Classification of Diseases [ICD-10], World Health Organization, Geneva, Switzerland). All VTE diagnoses were independently adjudicated by two physicians, classifying them into pre-existing events and hospital-acquired complications. Hospital-acquired VTE events were considered if they were symptomatic and objectively confirmed by an imaging test.
No imaging confirmation was required for in-hospital deaths where PE was considered as likely cause.

Chi-square tests of independence were used for statistical analysis of frequencies in 3x2 contingency tables and Fisher’s exact tests were used for 2x2 contingency tables, using the software EpiData V2.2.1.171 (EpiData Association, Odense, Denmark). The p-levels of ≤0.05 were considered significant.

Results

Cases studied

A total of 5,317 cases with a minimal stay of 24 hours in the wards of admission were analyzed, including 4,156 patients. The length of stay in the admitting wards averaged 5.0 days, the median was 3.0 days (medical ward: average 7.4 days, median 5.0 days, surgical ward: average 3.7 days, median 3.0 days). Thromboprophylaxis was prescribed in 4,232 cases during hospitalization in the two wards (79.6%). These patients received either pharmacological thromboprophylaxis alone (2,464 of 4,232 cases; 58.2%), a combination of pharmacological and mechanical measures (39.1%), or mechanical prophylaxis alone (2.7%).

eAlert intervention

The rate of thromboprophylaxis increased significantly after implementing the eAlert function in the clinical information system of the intervention group, from 43.4% during phase 1 to 66.7% during phase 2 (p<0.001; Tab. 1). The percentage further increased during phase 3 to 73.6% (p=0.011). No significant changes in the rate of prophylaxis were noted over the three phases in the surgical control group (p=0.16).

During the three study phases, the number of patients with a hospital-acquired VTE event in the medical ward was 2 (pre-implementation), 0 (eAlerts implementation) and 3 (post-implementation); in the surgical ward 3, 2, 1, respectively. Analysis of the data of each group revealed no statistically significant changes between the study phases.
Timing of order entry

Orders of VTE prophylaxis were frequently placed before planned admissions to the surgical ward, i.e. in patients hospitalized for elective procedures (1,898 of 3,113 orders, 61.0%). In contrast, very few pre-admission orders were issued by physicians of the medical ward (19 of 1,119 orders, 1.7%). Of the 2,315 orders placed after admission, 51.8% were entered within the first 6 h, 23.7% within 6-12 h, and 24.5% at a later stage (average time of ordering after admission 15.4 h, median 5.7 h).

After eAlert implementation, the physicians of the intervention group entered orders for thromboprophylaxis sooner than they did in the pre-implementation phase. The percentage of orders placed within 12h after admission of the patients increased from 52.1% (146 of 280) to 67.1% (550 of 820; p<0.001) (Fig. 1). In particular, a higher percentage of orders were placed in the time frame 6-12 h after admission of the patients, i.e. during the period immediately following the eAlert activation (27.1% vs. 35.9%; p=0.008). In contrast, no increase of orders placed 6-12 h after admission was observed in the control group.

Discussion

CDSS are successful in supporting preventive care (20) and offer great potential to assist physicians in improving the quality of treatment (21, 22). In most evaluations, the impact of interventions for quality assurance is assessed by comparing data observed during a study period with data of historic or simultaneous controls. Some studies documented a beneficial effect of eAlerts on thromboprophylaxis over a limited period (14-16). One study considered whether the impact of these eAlerts on the rate of prophylaxis could be maintained beyond the initial study period, by comparing the long-term data with historic controls (23). The present study confirms a sustained effect of the eAlert system observed during the eAlert implementation phase by comparing the data to both the pre-implementation phase and the post-implementation phase.
The VTE prophylaxis rate in the medical intervention ward remained high during the post-implementation phase despite cessation of specific CME and withdrawal of accompanying study staff. The stability in the rates of thromboprophylaxis orders, particularly in the rate of early orders, confirm that the physician compliance with the eAlert system was sufficient over time. Only in the intervention group, but not in the control group, did the percentage of orders within 6-12 h increase, i.e. immediately after activating eAlerts.

Although eAlerts for hospitalized medical patients can not and should not produce thromboprophylaxis rates found in surgical patients, they improve adherence to guidelines and may provide sustained efficacy without evidence of alert fatigue (17) or the Hawthorne effect (24, 25), sometimes affecting the generalizability of clinical research. The rates of thromboprophylaxis obtained for the identical time periods from the surgical control ward were stable over time, with an average of 90%, confirming that thromboprophylaxis rates are higher in surgical than in medical patients (13, 26). The appropriateness of thromboprophylaxis was not assessed in the surgical patients, but it is unlikely that the introduction of eAlerts on this surgical ward would further improve the use of appropriate prophylaxis.

The present study focused on the rates of thromboprophylaxis over time, considering neither the appropriateness of ordered prophylaxis nor the appropriateness of omitted prophylaxis. In fact, both underuse and overuse of VTE prophylaxis occur (18). The aim of CDSS is to improve adherence to guidelines for prescribing VTE prophylaxis and the use of institution-tailored tools has been advocated (26, 27). The adequacy of prophylaxis has been assessed in the intervention group during phase 2 only, resulting in a rate of appropriate VTE prophylaxis in 76% as compared to 44% prior to the introduction of CPOE (16). These numbers are in line with the impact of the eAlerts on the rate of prophylaxis assessed in the present analysis, showing an increase from 43% to 67% due to the introduction of eAlerts, up to 74% thereafter.

Limitations of our study include that the appropriateness of prophylaxis orders and the VTE events following discharge were not monitored. Although the rate of appropriate
prophylaxis orders among medical patients was high (76%) during the eAlert implementation phase, we cannot rule out with certainty that this rate decreased over time in the post-implementation phase. However, eAlerts significantly reduced the rate of inappropriate VTE prophylaxis orders in a recent management study in which our institution participated (28). In addition, the in-hospital VTE rate was very low in both the medical ward (5 events in 1854 cases) and the surgical ward (6 events in 3463 cases). Therefore, our study was likely underpowered to detect significant differences in VTE rates between the three phases.

The major increase of the thromboprophylaxis rate due to the implementation of eAlerts illustrates the well-known gap between clinical practice and evidence-based guidelines (29). Reasons for insufficient adherence to guidelines include complexity of guidelines, lack of physician awareness, concerns over the risk-to-benefit ratio of prophylaxis and lack of hospital resources (8). In particular, inexperienced interns starting their career in a teaching hospital may feel uncertain about ordering VTE prophylaxis. Thus, eAlerts may be considered as trainers for better adherence to guidelines in order to improve patient safety. The ACCP explicitly recommends the use of CDSS to increase guideline adherence (10). Linking CDSS with evidence-based risk scores and up-to-date guidelines may help to enhance the quality of treatment (27).

However, lack of physician compliance with electronically generated suggestions is a well-known problem. Design and quality of the user interface of a clinical information system may contribute to its acceptance. Various strategies were proposed to limit alert fatigue, e.g. providing concise context-sensitive online information, reducing the number of alerts with low relevance, enforcing user response by interruptive alerts or by implementing multi-screen alerts (30). Furthermore, the specificity of an alert may be increased, e.g. by displaying alerts only to selected health care professionals (17, 31). Indeed, different strategies may be required to overcome alert fatigue, also depending on national or regional cultures and incentives.

The present eAlert module was designed to reduce the number of unnecessary prompts. It gives the physician an adequate amount of time to place orders, and an alert is
issued only if no prophylaxis order has been placed within a predefined time frame after admission. The eAlert module does not identify high-risk patients based on calculation of a VTE risk score since the identification of individual risk factors by computers may be unreliable, particularly during the initial hospital stay, owing to incomplete or missing information in the patient database. However, the guidelines for prophylaxis indications are displayed by default when the physician acknowledges the eAlert button.

In conclusion, advanced eAlerts for hospitalized medical patients may provide sustained efficacy with stable rates of thromboprophylaxis over time.

Acknowledgments

N. Kucher is co-inventor of the WIPO patent application (WO/2006/052952) for a system and method for determining whether to issue an alert to consider prophylaxis for a risk reduction (Applicant: Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA).
References

Legends to figures and tables

Table 1: Rate of prophylaxis during three phases in an intervention ward with eAlerts compared to a control ward without eAlerts.

Figure 1: Timing of orders for thromboprophylaxis in the medical intervention ward.
### Table 1

<table>
<thead>
<tr>
<th>Intervention with eAlerts</th>
<th>Pre-implementation</th>
<th>eAlert Implementation</th>
<th>Post-implementation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>286 / 659</td>
<td># 43.4 %</td>
<td>449 / 673</td>
<td>66.7 %</td>
</tr>
<tr>
<td>Surgical</td>
<td>1129 / 1274</td>
<td>88.6 %</td>
<td>1128 / 1244</td>
<td>90.7 %</td>
</tr>
</tbody>
</table>

* # cases with thromboprophylaxis / total number of cases
What is known about this topic?
- Appropriate use of prophylaxis to prevent VTE is an important strategy for improving safety among hospitalized patients.
- Many patients at risk do not receive prophylaxis despite evidence-based guidelines.
- Computer decision support systems can improve adherence to guidelines on thromboprophylaxis. However, alert fatigue may compromise the long-term impact of such systems.

What does this paper add?
- An advanced eAlert system did provide sustained efficacy over time, resulting in enhanced rates of thromboprophylaxis orders among hospitalized medical patients.
- Cessation of specific continuing medical education and withdrawal of accompanying study staff did not reduce the prophylaxis rate.
- Orders were entered sooner as a result of good physician compliance with the eAlert system.
Figures

Figure 1

Phase 1
Prophylaxis ordered before admission
6
Phase 2
Prophylaxis ordered 0-6h after admission
70
Phase 3
Prophylaxis ordered 6-12h after admission
76
Prophylaxis ordered >12h after admission
134
No prophylaxis
373