Journal of Pharmacovigilance

OPEN ACCESS Freely available online

Research Article

Can Electronic Medical Record be used for Reducing DOAC Prescription Errors in Inpatients?

Friederike Steffen, Constantin von zur Mühlen, Armin Nemani, Timo Heidt, Johannes Schulte, Christoph Bode, Marvin Krohn-Grimberghe*

Department of Cardiology and Angiology I, University Heart Center Freiburg - Bad Krozingen, Faculty of Medicine, University of Freiburg, Germany

ABSTRACT

Background: Direct oral anticoagulants (DOACs) are commonly used for treating or preventing thromboembolic events. At the same time anticoagulants are a notorious cause of medication errors. Such medication errors can jeopardize patients' health and challenge the economy of healthcare systems. With the potential of e-health systems for reducing medication errors, our study investigates the effects of medication highlighting.

Methods: To highlight medications with anticoagulatory properties in the electronic health records of cardiologic inpatients, a color scheme was introduced at our university hospital. We performed chart reviews of DOAC-related medication errors due to co-prescription of more than one anticoagulatory drug or omitted pausing of DOACs before interventions with increased bleeding risks. Chart reviews were performed before and after the introduction of medication highlighting. Patients having received a DOAC prescription at any point in time during their hospital stay were included.

Results: 305 (out of 1.045) patients had received DOAC before and 277 (out of 1.062) received DOAC within a three-month period after the color scheme introduction. DOAC-related medication errors occurred in 25 of the 305 (8.2%) inpatients in total before medication highlighting, while 6 errors occurred in 277 inpatients (2.2%; p= 0.0013) afterwards.

Conclusion: Highlighting anticoagulatory medications in the electronic medical record led to a reduction of DOAC-related prescription errors.

Keywords: Oral anticoagulation; DOAC; Medication error; E-health; Patient safety

INTRODUCTION

The approval of the five direct oral anticoagulants (DOACs) dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban (not approved in every country) has expanded the options of oral thromboprophylaxis [1-3]. DOACs are used for the treatment and prophylaxis of deep vein thrombosis and pulmonary embolism as well as for stroke prevention in patients with non-valvular atrial fibrillation and other indications [3,4]. Current guidelines state that DOACs should not be combined with other drugs having anticoagulatory properties and should be paused before scheduled procedures that carry an increased bleeding risk [3]. Medication errors (MEs) can jeopardize patient safety and create enormous economic challenges for healthcare systems. Of all medication classes, cardiovascular drugs are most frequently involved in MEs, and anticoagulants represent the largest portion within this class [5]. Furthermore, about half of anticoagulation-associated adverse drug events are caused by MEs [6]. The WHO reports that MEs lead to 1.3 million injuries per year and cause on average one fatality per day in the USA [7]. The global annual costs are estimated at $42 billion or rather at about 1% of the total global health expenditure each year [7]. Several studies demonstrated a reduced number of MEs by using e-health systems [8–10]. Our study investigated whether adding color-highlighting of direct oral anticoagulants and antiplatelet drugs in an electronic medication chart can further reduce the number of MEs.

METHODS

Chart reviews for DOACs and MEs prescription were performed three months before and three months after the introduction of a color scheme for highlighting medications with anticoagulatory or anti-platelet properties on the cardiological wards of our university hospital in January 2018. Before the intervention,

***Corresponding to:** Marvin Krohn-Grimberghe, Department of Cardiology and Angiology I, University Heart Center Freiburg - Bad Krozingen, Faculty of Medicine, University of Freiburg, Germany; Tel: 004976127034010; E-mail: marvin.krohn-grimberghe@uniklinik-freiburg.de

Received: July 27, 2021, **Accepted:** August 14, 2021, **Published:** August 21, 2021

Citation: Steffen F, von zur Mühlen C , Nemani A, Heidt T, Schulte J, Bode C, et al. (2021) Can Electronic Medical Record be used for Reducing DOAC Prescription Errors in Inpatients? J Pharamacovigil 9:329. doi-10.35248/2329-6887.21.9.329.

medications were grouped by route of administration in an alphabetical order without the use of color coding for specific drug classes. To reduce bias, no further intervention was performed and the treating physicians were not aware of the study. Current guidelines for antithrombotic management and DOAC prescription as well as standard operating procedures at our hospital were used as a reference to verify whether a correct management was followed. Treatments were independently classified by F. S. and M. K.-G. In case of disagreement, concerning cases were jointly discussed to reach agreement (about 5% of all cases). In the case of failed agreement, C. v. z. M. would have made the final decision. Since agreement was reached in all cases, the latter did not occur. The study was performed following national and international law as well as ethical standards and was approved by the ethics committee of the University of Freiburg (number 95/20).

Study population

A total of 2.107 consecutive inpatients treated on three cardiological wards were screened three months before and three months after medication highlighting was introduced (before n= 1.045; after n= 1.062). Patients were included when they were under long-term DOAC treatment or had received a DOAC at any point of time during their hospital stay. Patients to whom a DOAC was not prescribed were excluded.

Classification

Patients were classified as having received either correct or incorrect co-prescriptions of anticoagulatory medications (e.g. incorrect simultaneous treatment with DOAC + low-molecular-weight or unfractionated heparin (LMWH / UFH); DOAC + vitamin K antagonist (VKA); DOAC + 2nd DOAC) or periinterventional handling (e.g. no DOAC therapy pausing while planned intervention or operation carrying high bleeding risk). Co-prescription of antiplatelet medications was deemed acceptable. Other possible forms of medication errors, such as incorrect dose adjustment in case of (chronic) renal failure, were not evaluated. Standard operating procedures of our institution do not recommend bridging of DOAC with LMWH before procedures with increased bleeding risk. Still, such bridging was deemed acceptable as long as no simultaneous treatment with both was found.

Data analysis

P-values were calculated by using fisher's exact test for categorical and unpaired t-test for numerical variables. All tests were two-sided. Results were considered statistically significant at $p<0.05$. All calculations were performed by using Graph Pad Prism version 8.4.3.

RESULTS

Patient Characteristics

Table 1 shows the demographic and clinical characteristics of the patients as well as the number of prescribed DOACs.

Medication errors

Of the 2.107 screened patients, 582 received a DOAC prescription at any point of time during their hospital stay (Table 1). 305 patients had received DOAC before the color scheme was introduced; 277 receivers were counted within three months afterwards. These total numbers correspond to a DOAC prescription rate of 29.2% (305 out of 1.045 inpatients) before the color scheme introduction and 26.1% afterwards (277 out of 1.062 inpatients).

Pre-highlighting, we observed medication errors in 25 of the 305 (8.2%) inpatients having received DOAC (Table 2). 15 out of the 25 errors were due to wrong co- prescription with other anticoagulatory medications; in the remaining 10 patients an incorrect perioperative handling was detected. After the introduction of highlighting, 6 errors occurred in 277 inpatients receiving DOAC (2.2%) (Table 2). Thus, the color scheme led to a significant reduction of DOAC prescription errors from 8.2% to 2.2% ($p = 0.0013$). During the three months directly following the intervention, all errors were caused by the incorrect combination of DOAC with other anticoagulatory medications, while before the intervention incorrect combination made up 60% of the errors with the remaining 40% being caused by incorrect perioperative handling (Figure 1).

Table 3 further sub-groups the prescription errors by the specific DOAC and incorrect co-prescription found. In 77 of 100 DOAC prescriptions rivaroxaban was used.

Table 4 shows the distribution of errors among the treating physicians including their respective number of errors. Only physicians with at least one mistake are listed. The total number of physicians on the wards did not change during the study.

Table 1: Patient characteristics before and after the intervention.

Characteristics (all patients N= 2.107)	Before (n= 1.045)	After (n= 1.062)	P–value (before vs. after)
Age in years, mean (SD)	69.18 (14.35)	68.45 (14.34)	0.2452
Female (%)	375 (35.9%)	353 (33.2%)	0.2161
DOAC prescription (n = 582)	305 (29.2%)	277 (26.1%)	0.1189

P-values were calculated using fisher's exact test for categorial and t-test for numerical variables. Abbreviations: DOAC: direct oral anticoagulants; SD: standard deviation; vs: versus.

Table 2: DOAC prescription errors before and after the intervention.

Prescription errors (DOAC prescriptions)	Before (n= 305)	After (n= 277)	P–value (before vs. after)
Total (n= 31)	25 (8.2%)	6 (2.2%)	0.0013
Incorrect combination (n= 21)	15	6	0.1174
Incorrect perioperative handling (n= 10)	10	0	0.002
Other reasons	0	0	–

P-values were calculated using the fisher's exact test. Abbreviations: DOAC: direct oral anticoagulants; vs: versus.

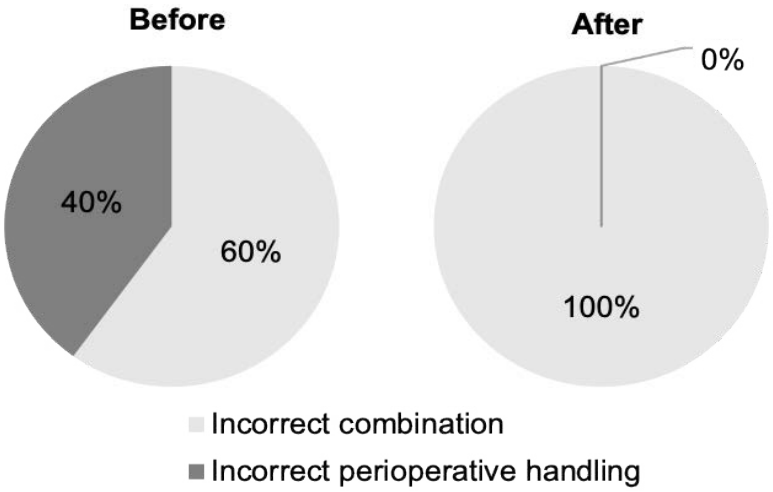

Figure 1: Distribution of error types before and after the intervention.

Table 3: Prescription errors sub-grouped by type.

Prescription errors (all errors n= 31)	Before (n= 25)	After (n= 6)
Incorrect combination	15	6
· DOAC + LMWH / UFH	15	6
o rivaroxaban + LMWH / UFH	10	5
o apixaban + LMWH / UFH	3	1
o dabigatran + LMWH / UFH	1	0
o edoxaban + LMWH / UFH	1	0
· DOAC + VKA	0	0
· DOAC + 2nd DOAC	0	0
Incorrect perioperative handling	10	0
· Left / right heart catheterization	9	0
o rivaroxaban	6	0
o apixaban	3	0
· MitraClip	1	0
o apixaban	1	0

Abbreviations: DOAC: Direct oral anticoagulants; **LMWH:** Low-molecular-weight heparin; **UFH:** Unfractionated heparin; **VKA:** Vitamin-k-antagonist.

Table 4: Prescriber and number of errors before the color scheme introduction and afterwards.

Before		After	
Prescriber	**No. of errors (n= 25)**	**Prescriber**	**No. of errors (n= 6)**
MD1	1	MD2	2
MD2	1	MD7	1
MD3	1	MD14	2
MD4	2	MD15	1
MD5	1		
MD6	5		
MD7	4		
MD8	1		
MD9	2		
MD10	1		
MD11	1		
MD12	4		
MD13	1		

Abbreviations: MD: Medical doctor; **No:** number.

DISCUSSION

Recent studies show an increasing rate of atrial fibrillation as well as other indication for oral anticoagulation [11-13]. Furthermore, the number of DOAC prescriptions expands, while the use of VKAs decreases [2,4,14,15]. These observations illustrate a great need for the development of strategies to prevent MEs during DOAC prescription. In our patient population nearly 28% of all patients received DOAC, with rivaroxaban making up 77% of all cases. As a result, the majority of medication errors occurred with rivaroxaban. Herein the finding of our study is in line with other studies, as rivaroxaban was the most frequently prescribed DOAC in the ambulatory setting in the USA (48.2% of all DOACs prescriptions for patients with atrial fibrillation) and the most often registered DOAC in medication error reports [14,15]. Many MEs are associated with anticoagulants, and the majority of MEs happens during prescription writing [16,17]. We focused on cardiology wards where anticoagulants are among the most commonly prescribed and most error prone medications. Color highlighting could easily be tailored to the most commonly prescribed or potentially most harmful drug-class in each department or ward (e.g. chemotherapeutics on the haemato-oncology wards and immunosuppressants on the transplant wards). The color scheme led to a reduction of prescription errors from 8.2% to 2.2% in patients receiving DOAC (p= 0.0013). By using pre-post comparisons, Pontefract et al. [9] showed that computerized decision support is able to reduce MEs. Other studies have demonstrated a decreased number of MEs by using e-health systems [8,10]. Moreover, these studies revealed that the reduction of anticoagulation related MEs result in lower probability for clinically relevant complications, such as bleedings and thromboembolic events, as well as a significantly reduced hospitalization and mortality rate [10]. Since our study would be underpowered for detecting changes in clinical outcomes, we did not analyze the clinical consequences of MEs.

The results of our study show that on one hand errors were caused or unnoticed by many physicians at least once and that on the other hand some doctors made a particularly large number of errors. The latter information could be used for targeted education programs for these prescribers.

The most common reason for MEs was incorrect combination of two drugs with anticoagulatory properties. Most frequently rivaroxaban was incorrectly co-prescribed with LMWH. This kind of prescription error occurred mainly during the first days of an inpatient's stay. Quite likely, doctors did not recognize that a patient's medication plan already included a DOAC and accidentally co-prescribed subcutaneous LMWH for thromboembolism prophylaxis. This finding is in line with the results from the study by Rahmanzade et al. [18], which found that most erroneous duplication of anticoagulants happen during the first or last days of an inpatient's stay. Similar to our findings, DOACs were frequently combined with LMWH in their patient population. The remaining prescription errors in our study occurred when DOAC were not paused before interventions carrying increased bleeding risk. Henriksen et al. [17] report that most MEs in orally anticoagulated patients occur when patients were admitted to or discharged from the hospital or when they were moved within the hospital (e.g. to a different ward to receive surgery or other interventions).

The intervention led to a greater reduction of errors related to perioperative and periinterventional pausing of DOACs than with double prescriptions. Thus, further interventions should be studied to further reduce the latter kind of medication error. For example, automated pop-up prompts could be integrated into the electronic health record to warn physicians when they are about to co-prescribe LMWH to patients already treated with a DOAC.

STRENGTHS AND LIMITATIONS

One limitation of our study is its monocentric, retrospective nature. Thus, the results need to be repeated in other patient settings and with other electronic health records. Furthermore, our study focused on the prescription of DOACs and did not investigate whether prescribing errors lead to patient harm. This correlation, however, has already been established in several other studies [15,17,18].

Other forms of medication errors, such as incorrect dose adjustment in the case of reduced glomerular filtration rate, were not evaluated. It seemed unlikely that they would be affected by the color scheme and the electronic health record used in our hospital already included a tool that alerted doctors about incorrect or missing dose adjustments of medications during the medication prescription phase.

Strengths of the study are that data were independently analyzed by two persons and treating physicians were unaware of the study. Furthermore, our study impressively shows how a simple and cost-effective method is able to significantly improve patient safety.

CONCLUSION

In summary, the rate of prescription errors could be reduced in patients receiving DOACs by highlighting medications with anticoagulatory properties in an electronic health record. Future research is needed to confirm these results and develop further tools to reduce prescription errors. The increasing availability of electronic health records lends itself to the incorporation of different tools for improving prescription. Not least the intervention studied here could be incorporated in electronic health records at very low costs and without further complicating the prescription process for treating physicians.

END-MATTER

Contributorship

The study was planned and organized by M. K.-G. F. S. and M. K.-G collected and analyzed data and wrote the manuscript. A. N. and J. S. assisted in data collection. C. v. z. M., T. H. and C. B. assisted in writing the manuscript.

Declaration of conflicting interests

The authors declared no conflicts of interest concerning the research, authorship, and/or publication of this article.

Sources of funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

The raw data underlying this article cannot be shared publicly due to limitations set by the ethics committee of the University of Freiburg to protect the privacy of the participants of this study. Anonymzed versions of the data will be shared on reasonable request to the corresponding author.

REFERENCES

1. Van der Hulle T, Kooiman J, Den Exter PL, Dekkers OM, Klok FA, Huisman MV. Effectiveness and safety of novel oral anticoagulants as compared with vitamin K antagonists in the treatment of acute symptomatic venous thromboembolism: a systematic review and meta-analysis. J Thromb Haemost 2014; 12(3):320-328.
2. Olesen JB, Sørensen R, Hansen ML, Lamberts M, Weeke P, Mikkelsen AP, et al. Non-vitamin K antagonist oral anticoagulation agents in anticoagulant naive atrial fibrillation patients: Danish nationwide descriptive data 2011–2013. Ep Europace. 2014; 17(2):187-93.
3. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al. The 2018 European Heart Rhythm Association Practical Guide on the use ofnon-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation.Eur Heart J. 2018; 39:1330–93.
4. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016; 37:2893–962.
5. Muroi M, Shen JJ, Angosta A. Association of medication errors with drug classifications, clinical units, and consequence of errors: Are they related? Appl Nurs Res. 2017; 33:180-5.
6. Piazza G, Nguyen TN, Cios D, Labreche M, Hohlfelder B, Fanikos J, Fiumara K, Goldhaber SZ. Anticoagulation-associated adverse drug events. Am J Med. 2011; 124(12):1136-42.
7. WHO Launches Global Effort to Halve Medication-Related Errors in 5 Years [Internet]. [cited 2020 Mar 2];Available from: https://www.who.int/news-room/detail/29-03-2017-who-launches-global-effort-to-halve-medication-related-errors-in-5-years
8. Ambwani S, Misra AK, Kumar R. Medication errors: Is it the hidden part of the submerged iceberg in our health-care system? Int. J Appl Basic Med Res. 2019; 9(3):135.
9. Pontefract SK, Hodson J, Slee A, Shah S, Girling AJ, Williams R, et al. Impact of a commercial order entry system on prescribing errors amenable to computerised decision support in the hospital setting: a prospective pre-post study. BMJ Qual Saf 2018; 27:725–36.
10. Prochaska JH, Göbel S, Keller K, Coldewey M, Ullmann A, Lamparter H, et al. e- Health-based management of patients receiving oral anticoagulation therapy: results from the observational thrombEVAL study. J Thromb Haemost. 2017; 15:1375–85.
11. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014; 129:837–47.
12. Heeringa J, van der Kuip DAM, Hofman A, Kors JA, van Herpen G, StrickerBHC, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006; 27:949–53.
13. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation. 2004; 110(9):1042-6.
14. Barnes GD, Lucas E, Alexander GC, Goldberger ZD. National trends in ambulatory oral anticoagulant use. Am J Med. 2015; 128(12):1300-5.
15. Valentine D, Gaunt MJ, Grissinger M. Identifying Patient Harm from Direct OralAnticoagulants p: 17.
16. Dreijer AR, Diepstraten J, Bukkems VE, Mol PG, Leebeek FW, Kruip MJ, et al. Anticoagulant medication errors in hospitals and primary care: a cross-sectional study. Int J Qual Health Care. 2019; 31(5):346-52.
17. Henriksen JN, Nielsen LP, Hellebek A, Poulsen BK. Medication errors involving anticoagulants: data from the Danish patient safety database. Pharma Res Persp. 2017; 5(3):e00307.
18. Rahmanzade R, Cabrera Diaz F, Zaugg C, Schuetz P, Salili AR. Therapeutic duplication of anticoagulants: a retrospective study of frequency and consequences in a tertiary referral hospital. Thromb J 2020; 18(1):1-9.