**TRANSLATING DATA FROM AN ELECTRONIC PRESCRIBING AND MEDICINES
ADMINISTRATION SYSTEM INTO KNOWLEDGE: APPLICATION TO DOCTOR-NURSE TIME
DISCREPANCY IN ANTIBIOTICS ORDERING AND ADMINISTRATION**

BRIEF TITLE: TRANSLATING EPMA SYSTEMS INTO KNOWLEDGE

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ABSTRACT

Background: Electronic Prescribing and Medicines Administration (EPMA) systems are being widely implemented to facilitate medication safety improvement. However, translating the resulting big data into actionable knowledge has received relatively little attention.

Objective: To use routinely collected EPMA data in the study of exact time discrepancy between physicians' order and nurses' administration of systemic antibiotics. We evaluated first and follow-up dose administration and dose intervals and examined multi-factorial determinants in ordering and administration explaining potential discrepancy.

Methods: We conducted an observational study of electronic health records for all medical patient stays with antibiotic treatment from January to June 2018 (n=4392) in a large Belgian tertiary care hospital. Using an EPMA system with Barcode Medication Administration, we calculated time discrepancy between order and administration of first doses (n=6233), follow-up doses (n=87 960) and dose intervals. Multiple logistic regression analysis estimated the association between time discrepancy and various determinants in ordering and administration.

Results: Time discrepancy between physician order and nurse administration was less than 30 minutes for 48.7% of first doses and 61.7% of follow-up doses with large variation across primary diagnoses. Greater dose intervals, oral versus intravenous administration, and order diversion from regular nurse administration rounds showed strongest association with less timely administration.

Conclusion: Electronic Prescribing and Medicines Administration systems show huge potential to generate actionable knowledge. Concerning antibiotics treatment, having physicians' orders coincide with regular nurse administration rounds whenever clinically appropriate,

further taking contextual factors into account, could potentially improve antibiotics administration timeliness.

Keywords: “Electronic Prescribing”, “Medication Systems, Hospital”, “Medication Errors/classification/*statistics & numerical data”, “Anti-Bacterial Agents/*administration & dosage/adverse effects”

INTRODUCTION

Medication errors account for almost 40% of detected adverse events.¹ Electronic Health Records (EHRs), and Electronic Prescribing and Medicines Administration (EPMA) specifically, are often cited as important means to reduce such adverse events in inpatients.^{2–8} In the US, adoption of EHRs is government-imposed by the HITECH Act, which aims to achieve improvements in care delivery by EHR implementation.⁹ When (medicine) entries into a patient's EHR come with a time stamp, this offers previously unimagined opportunities for research and safety programs into the IOM's six domains of health care quality¹⁰, not in the least to better comprehend timely delivery of care. Prior research established the importance of timely first dose antibiotic administration after admission, showing reduced mortality and hospital length-of-stay.^{11–15} Some authors considered a 30-minute window before or after medication order time to determine timeliness. Even though this '30-minute rule' has generated much controversy^{16,17}, administration outside this window might affect bioavailability of time-critical medication¹⁸. No studies have previously looked in an integrative way to the time discrepancy between scheduled physician order and actual nurse administrations. We provide a glance at the quality improvement and research utilization of the high-quality data that are generated by EPMA systems. Our aim was twofold. We first quantified time discrepancy between physician order and nurse administration in medical patients for first and follow-up dose antibiotics and their dose intervals. We then assessed for multi-factorial determinants in ordering and administration explaining this discrepancy.

METHODS

Study design

A single-center retrospective observational study.

Setting

University Hospitals Leuven is a 1995-bed tertiary care teaching hospital in Belgium. An in-house closed-looped EPMA system recording to EHRs was set in place for all inpatients in 2009. Nurses carry a computer-on-wheels-trolley containing planned medicines and IV-solutions during medication administration. Barcode Medication Administration (BCMA) provides additional safety by scanning a patient's wristband and medication before administration and provides an exact timestamp of when and by whom medication was administered. EPMA data were available for all wards, but BCMA is yet to be implemented on the emergency unit, intensive care units, operation theatre and recovery room.

Study measures

We studied all adult non-psychiatric medical inpatient stays between January and June 2018 with at least one antibiotic administered. To describe our sample, we collected data on patient age, gender, date of admission, nationality, type of admission (elective/non-elective), severity of illness (minor, moderate, major, extreme) and verified primary diagnosis (coded in ICD-10). All antibiotics for systemic use were extracted using the World Health Organization Anatomical Therapeutic Chemical (WHO ATC) Classification System. Various potential predictors of time discrepancy were considered. Firstly, we distinguished between time-dependent (beta-lactams) and non-time-dependent antibiotics (other). Secondly, we established the match between physician order and nursing administration round. Although ward variations occur, all even hours are generally regular drug rounds, except 18:00 (evening meal) and 22:00 (night-staff handover). Several orders were not on the hour (e.g. 21:15). We therefore categorized 'Order at nursing administration round' into 'Yes' (all even hours without 18:00 and 22:00) and 'No' (all others). Thirdly, we considered the effect of dose intervals on order-administration discrepancy. Fourthly, we studied if weekend administrations are timelier, based on a recent study showing higher proportions of patients

receiving antibiotics within one hour after admission during weekends.¹⁹ Fifthly, severity of illness was considered as an explanatory variable of timely administration.²⁰ Sixthly, we explored variation across clusters of medical disciplines (oncology, abdomen, locomotor, internal medicine, reproduction and growth, thoracic, sensory), each with their own physician and nursing management structure. Lastly, we evaluated effects of prescriber type, i.e. attending physician or resident.

Statistical analysis

We first described our sample characteristics. Next, we described and visually displayed the method for calculating discrepancy between order and administration, and between order interval and administration interval. We then present findings on order-administration discrepancy for the overall sample and for primary diagnoses, for first and follow-up doses separately. Subsequently, we present findings for order and administration interval discrepancy for follow-up doses for the overall sample and for primary diagnoses. Last, we studied the effect of potential predictors of order-administration discrepancy. We first cross-tabulated discrepancy and each explanatory variable's category. We conducted a multiple logistic regression analyses to estimate statistical significance of these associations. Random intercepts accounted for the repeated measures on patients, with separate analyses for first-dose and follow-up doses. The analyses for this paper were generated using SAS software, Version 9.4 of the SAS System for Windows.

Ethical considerations

The study protocol was approved by the Medical Ethics Committee of University Hospitals Leuven.

RESULTS

Sample

Our final sample included 94 193 antibiotics administrations, of which 6233 first and 87 960 follow-up doses administered using BCMA. These data were for 4392 medical patient stays (3680 unique patients), of which 51.3% (n=2254) and 94.1% (n=4133) concerned male and Belgian patients, respectively. Median age was 64.5 (IQR: 54-79). Slightly more than 7 in 10 stays (71.2%, n=3172) resulted from non-elective admissions. Severity of illness was as follows: unknown (4.7%, n=209), minor (6.5%, n=284), moderate (26.9%, n=1180), major (48.0%, n=2110), extreme (13.9%, n=609). Staff nurses administered 98.5% and 99.1% of first and follow-up doses, respectively, next to trial nurses and residents. Time-dependent beta-lactam antibiotics represented 70.9% of all administrations.

Calculation of order-administration discrepancy

Figure 1 graphically depicts order-administration discrepancy as calculated for an individual patient's 10 consecutive antibiotic orders and administrations from the Electronic Prescribing and Medicines Administration system. The connected grey dots are physician orders. The squares are nurse administrations. Order-administration discrepancies under and above 30 minutes are shown by green and red squares, respectively. For example, the first dose of intravenous amoxicillin + enzyme inhibitor is ordered at 21:00 on March 23th and administered at 20:54 on March 23th, which is a discrepancy of 6 minutes. Similarly, the interval with the ordered follow-up dose at 03:00 on March 24th is 360 minutes, and the administration interval is 356 minutes, resulting in a discrepancy of 4 minutes. Each row of the data set prepared for analysis corresponds to one order (interval) and its associated administration (interval), the order-administration (interval) discrepancy, and values for the explanatory variables at the

patient-level (e.g. severity of illness) or at the time of order (e.g. weekend vs week, order at nursing administration round or not).

Discrepancy between order and administration

Order-administration discrepancy was below 30 minutes for 48.7% (19.4% within 30 minutes before order and 28.4% within 30 minutes after order) of all first-dose administrations (Figure 2). Follow-up doses were administered timely in 61.7% (28.7% before versus 32.9% after) of follow-up administrations. 26.4% of first doses were delayed at least one hour, with 13.3% administered more than two hours late, compared to 3.0% in follow-up administrations. Order-administration discrepancies for the 10 primary diagnoses with most frequent antibiotics administration (Figure 3) confirm these overall patterns. In all but one case, time discrepancy exceeded 30 minutes more often in first administrations compared to follow-up administrations.

Discrepancy between order interval and administration interval

For our analysis of discrepancy between order and administration intervals, we included five order intervals reflecting 92.8% (n=75 520) of all intervals: 4-hour (n=8071, 9.9% of all intervals), 6-hour (n=26 863, 33.0%), 8-hour (n=21 769, 26.8%), 12-hour (n=12 173, 15.0%), and 24-hour (n=6644, 8.2%). The sixth most frequent interval was 48-hour, reflecting only 826 observations or 1.0% of all intervals. 12-hour and 24-hour order intervals show greater discrepancy between order and administration intervals, as seen from the wider density curves and larger standard deviations (Figure 4).

Determinants of discrepancy between order and administration

Findings from the descriptive and regression analyses are shown in Table 1. Some rare observations were disregarded, i.e. orders prescribed by medical students, first-dose amphenicols and route of administration different from intravenous or oral. This did not

significantly affect our previous findings. Order coinciding with nursing administration rounds was the strongest predictor of timely administration in first (56.6% versus 36.0%, $\beta=-0.8437$, $P<0.0001$), as well as follow-up doses (67.3% versus 34.4%, $\beta=-1.3145$, $P<0.0001$). Compared to first-dose administrations ordered by attending physicians, administrations that were ordered by residents were more timely (51.7% versus 47.3%, $\beta=0.2111$, $P=0.0060$). Compared to weekday administrations, weekend administrations were timelier, especially in first doses (54.1% versus 50.0%, $\beta=0.2245$, $P=0.0076$). Intravenous follow-up dose administrations outperformed oral follow-up dose administrations (67.5% versus 59.8%, $\beta=-0.2918$, $P<0.0001$). With the exception of 8-hour intervals, larger intervals scored significantly poorer compared to 4-hour intervals. First and follow-up dose time-dependent beta-lactams were more timely administered. Abdominal services scored worst for both first and follow-up dose administrations (44.8%, $\beta=-0.2134$, $P=0.0008$ and 55.0%, $\beta=-0.2439$, $P<0.0001$). Last, higher severity of illness showed a statistically significant decrease in timely administration of follow-up doses.

DISCUSSION

To our knowledge, this is the largest hospital-wide assessment documenting exact order and administration timeliness. Other studies have focused on other parts of the administration process and often in selective samples using a limited number of patients only.^{14,15,21}

Timeliness of antibiotics administration appears to have much room for improvement as administration within the assigned 30 minutes occurs in only about 50% of first dose and 60% of follow-up dose administrations. The large sample size allowed us to show consistency of our findings across primary diagnoses and examine a large number of prescriber and administrator effects on timeliness. For various effects the magnitude of difference is small, perhaps clinically of little importance, and statistically significant differences are partly due to

the large sample size. However, greater dose intervals, oral versus intravenous administration, and particularly order diversion from regular nurse administration rounds, showed strong statistically significant and clinically relevant associations with less timely administration. Although future studies in other sites are needed to ensure the generalizability of these findings, our illustration highlights that adding organizational, patient-level, or order-level data to EPMA systems may boost hospital quality managers to identify modifiable contributors to timely medication administration. Based on our findings, physicians could for example aim to have order administrations coincide with regular nurse administration rounds. Intravenous follow-up doses being more timely administered compared to oral follow-up doses, and less frequent orders being less timely administered may imply that nurses perceive these as less critical to the patient's health, showing the need for an intervention focusing on nurses' knowledge, perceptions and attitudes towards the appropriate use of antibiotics. The case presented in Figure 1 gives a good idea of how EPMA systems can be used as catalysts in designing such improvement interventions. Each individual order and administration can be linked to individual care providers. As these patient cases can be randomly generated at any given moment, possibilities arise in organizing tailored individual or group feedback. Moreover, the application is immediately generalizable to any medication type and other electronical care documents can be associated. Several study limitations merit attention. Firstly, we only partly examined the medication administration process. Studying EPMA systems could allow further innovative insights into timely medication delivery concerning e.g. pharmacy dispensing, operational failures and time difference between nurses' drug preparation and administration. Secondly, by not including ER and ICU data in our analysis, we potentially excluded truly urgent orders and missed insight into the full administration process. Nevertheless, our analysis still covered about 79% of all first administrations in 2018.

Thirdly, the feasibility of nurses administering within 30 minutes should be considered. It was shown internationally that Belgium scores poorly on hospital nurse staffing, with on average 10.8 patients per nurse²⁴. 10.4% of Belgian nurses reported having insufficient time for medication administration. Lack of resources (e.g. time and staffing) has been cited²² as a barrier in practice guideline implementation and should be further studied. Fourthly, generalizability is limited as only one tertiary care hospital was studied. Lastly, the observational design does not allow for causality to be established.

CONCLUSION

Studying routinely collected datasets like EPMA systems can be valuable in developing tailored healthcare quality improvement strategies. Looking specifically at antibiotics administration timeliness, we observed high rates of time discrepancy between physician order and nurse administrations, potentially harming patient safety. Future research will have to ensure the generalizability of these findings.

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FIGURE LEGENDS

Figure 1. Example of using Electronic Prescribing and Medicines Administrations for calculating time discrepancies in individual patients

The connected grey dots are CPOEs. The squares are eMARs. Order-administration discrepancies under and above 30 minutes are shown by green and red squares, respectively.

Figure 2. Overall time discrepancy between physician antibiotic order and nurse administration

Bars present the minutes deviation between order and administration for first (top) and follow-up (bottom) doses. Green bars present a deviation below 30min. Red bars present a deviation larger than 30min. The green horizontal line that spans the green vertical bars illustrates a discrepancy from 30 minutes before to 30 minutes after the order.

Figure 3. Overall time discrepancy between physician antibiotic order and nurse administration by 10 most frequent primary diagnoses

Bars present the minutes deviation between first dose order and administration. Green bars present a deviation below 30min. Red bars present a deviation larger than 30min. The green horizontal line that spans the green vertical bars illustrates a first dose discrepancy from 30 minutes before to 30 minutes after the order. The black series plot shows the distribution for follow-up administrations. The black horizontal line illustrates a first dose discrepancy from 30 minutes before to 30 minutes after the order.

Figure 4. Overall time discrepancy between physician antibiotic order interval and nurse administration interval