Safeguarding the process of drug administration with an emphasis on electronic support tools

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Similar to prescription errors also drug administration errors contribute to a large fraction of preventable medication errors and adverse drug events.
- Drug administration can be exceedingly complex with regard to dose form, route of administration, number of co-medications, and setting and accordingly, error rates may vary.

WHAT THIS STUDY ADDS

- The drug-specific drug administration process can be generically structured for distinct dosage forms to allow identification of particularly error prone steps and allocated prevention strategies.
- Potential research gaps in error epidemiology and prevention are highlighted.

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AIMS

The aim of this work is to understand the process of drug administration and identify points in the workflow that resulted in interventions by clinical information systems in order to improve patient safety.

METHODS

To identify a generic way to structure the drug administration process we performed peer-group discussions and supplemented these discussions with a literature search for studies reporting errors in drug administration and strategies for their prevention.

RESULTS

We concluded that the drug administration process might consist of up to 11 sub-steps, which can be grouped into the four sub-processes of preparation, personalization, application and follow-up. Errors in drug handling and administration are diverse and frequent and in many cases not caused by the patient him/herself, but by family members or nurses. Accordingly, different prevention strategies have been set in place with relatively few approaches involving e-health technology.

CONCLUSIONS

A generic structuring of the administration process and particular error-prone sub-steps may facilitate the allocation of prevention strategies and help to identify research gaps.

Introduction

Drug administration as a relevant part of the drug treatment process

In contrast to drug prescription, which mostly lies in the hands of health care personnel, drug administration is everyday practice for almost any human [1]. Hence, in ambulatory care, only a small fraction of drugs are administered by trained personnel such as mobile nursing services, while most drugs are actually administered by patients, family members, or even teachers and school secretaries, all of whom are untrained and have no medical background [2, 3].

Drug administration is an inherent part of everyday life for both adults and children and when asked, every second child (50.8% of 0–17 year olds) [4] and more than two-thirds of adults (71.5% of 18–79 year olds) in Germany stated that they administered drugs during the previous week (data from 2003–2006 [5]). More than 50% of adults administer drugs daily [6]. This fact, however, does not automatically make drug administration a safe and straightforward process and, indeed, drug administration errors are frequent and in the inpatient setting, roughly 30% of errors resulting in adverse drug events (ADE) happen during drug administration [7]. Comparably susceptible to errors is the prescription process [7]. Whereas for the prescribing process electronic prescription platforms with enhanced clinical decision support tools were implemented as promising error prevention strategy [8], similar and theory-driven approaches are only scarcely available for the administration process [9], even though introduction of electronic support in the drug administration process has shown to reduce error rates [10].

Drug treatment is a rather complex and demanding task (Figure 1) and depending on the setting and co-medication a great number of different errors may occur. The aim of this study was to structure the drug administration process (process 5 in Figure 1) in a way that allowed the allocation of current knowledge on frequent sources of errors as well as successful methods to prevent such errors with a particular emphasis on electronic tools. Concurrently, known unexplored sources of errors in the administration process are described to highlight critical, error prone steps and promising measures of error prevention. Therefore this paper should encourage research in the many areas of uncertainty, help generate knowledge of the administration process and ultimately stimulate system changes to eliminate the very numerous errors in this field.

Methods

Description of the drug administration process

To describe the drug administration process, we discussed in peer groups consisting of clinical pharmacists and a clinical pharmacologist drug administration processes for

Figure 1

Whenever a drug is prescribed, 10 processes must be carried out in a well-organized sequence to make treatment successful. Each of these processes makes special demands, may be diverse and complex and may be flawed by a range of errors thus requiring rigorous quality management. After selection of an appropriate drug and its prescription (1), the drug has to be dispensed (2) and the patient or health care provider has to be informed about its proper use (3). Then the patient has to be motivated to adhere to this treatment regimen (4) and to ultimately perform a more or less complex sequence of preparation and administration steps (5). In the subsequent pharmaceutical process (6) the drug has to be released from the formulation to get absorbed, distributed and ultimately eliminated (7). Only if the drug reaches the target compartment will it elicit its pharmacodynamic effect (8), which will ultimately produce the intended therapeutic response (or adverse events) (9). Finally, each drug therapy should be monitored appropriately (10) to differentiate between success, excessive exposure and nonresponse

relevant drug forms and routes of administration and described evident sub-steps in detail. Based on this specification we could identify similarities and differences. In order to check whether we missed important steps, we screened the literature on drug administration errors for sub-steps that reportedly trigger administration errors

(Medline search term: ('Drug Administration Routes/instrumentation'[Mesh] OR 'Drug Administration Routes/methods'[Mesh] OR 'medication administration') AND ('Medication Errors'[Mesh] OR 'drug administration error' [all fields])) (last search performed on 6 March 2013).

Within the process of drug administration, we determined that a correct drug administration process would not only require the appropriate preparation of the correct single drug dose, but also the consideration of time, route of administration, administration technique, context factors and appropriate monitoring (Table 1). Even if the distinct application step was performed correctly, drug administration could be erroneous in the context of the individual situation. A typical example is the simultaneous administration of infusions that are pharmaceutically not compatible and will therefore precipitate [11–13]. While we aimed to describe a drug-centred administration process, there are also setting-specific constraints (e.g. dispensing or picking errors in the pharmacy as well as selection of the wrong patient or faulty documentation of the administration process) that may be considered as administration errors and are therefore commonly reported in observational trials. Moreover, we put the main emphasis of this study on regular drug administration and we did not specifically consider particular drugs that require well-defined application techniques and have standardized or particular constraints, such as chemotherapeutics.

Epidemiology of drug administration errors and options for prevention

We employed the above mentioned literature search to identify the frequency and nature of drug administration errors. We aimed to describe the epidemiology of drug administration errors according to the above mentioned scheme of relevant sub-steps in drug administration (without focusing on specific indications but only on specific dosage forms) and allocated prevention strategies where appropriate. Hence, this approach would regroup different types of errors such as wrong dose errors, wrong time errors, omission and commission errors which served in many earlier studies as error categories [14].

To identify solutions based on electronic information and technology systems for prevention of administration errors we performed a specific search ('Drug Administration Routes'[Mesh] OR 'self administration'[Mesh] OR 'medication administration') AND 'Medication Errors'[Mesh] AND 'Decision Support Systems, Clinical'[Mesh]) (last search performed on 6 March 2013).

Results

Description of the drug administration process

We analyzed drug administration processes for frequent (according to [15]) or specific dosage forms, i.e. solid and

liquid oral drugs, inhalers, eye drops, nasal sprays, ointments, transdermal systems, suppositories, infusions and injections. As a result, we concluded that the drug administration process might consist of up to 11 drug-related sub-steps that can be grouped into the four sub-processes of preparation, personalization, application and follow-up and that are framed by three setting-related sub-steps (i.e. delivery of drug, identification of patient (before the drug-related administration process) and documentation (after drug-related administration process) (Figure 2, Table 1)). Hence, this description of the drug administration process complements the error- and process-related description of the administration process with the nine Rs [16].

Epidemiology of drug administration errors and options for prevention

Errors in drug handling and administration are diverse and frequent (Table 1) and in many cases not caused by the patient him/herself, but by family members [17] or the professional provider administering the drug [11–13, 17–19]. Accordingly, different prevention strategies have been set in place (Table 1). A substantial fraction of errors ultimately leading to flaws in the administration process is not linked to different steps of the administration process itself but rather to setting-related constraints such as the identification of the right patient [20, 21] or the documentation of drug administration (responsible for 13% of all errors classified as administration errors in one study [20]), or the administration at the right time. Most of the e-health technologies focus on these setting-related constraints, i.e. barcoding patients, automated dispensing systems and medication administration records.

Error frequency might vary along with the medication error detection method. In the inpatient setting, the most common technique is direct observation, where a third person, openly or disguised, observes the process of drug administration and documents important steps by using checklists [18, 22]. Direct observation can both reduce and increase error rates. On the one hand, observation can lead to increased attention of the person being observed ('Hawthorne' effect) and on the other, it can lead to increased nervousness and insecurity. However, while Hawthorne effects have been described [23], these effects seem to be reducible if the observation spans across a longer period of time [24]. Direct observation can also be employed with patients or family members to detect administration errors when using inhalers [25–28], insulin pens [29], eye drops [30, 31], parenteral drugs [17, 18, 32, 33] or per oral drugs [17], for instance. Such assessments form the basis to describe the epidemiology of administration errors as well as other influencing variables and are essential to describe the benefit of potential error prevention strategies.

Table 1

Process steps in drug administration, sources and frequencies of errors and options for error prevention

Number	Title	Description	Error sources and error frequencies	Prevention strategies	Electronic support
1	Identification and removal from the secondary packaging	Identification of the drug (prevention of sound-alike [62, 63] or look-alike [64] confusion) and opening of the secondary packaging to remove the drug are the first steps in drug administration.	• Ambulatory care: 2% of patients claimed to have difficulties in identifying the drug package and 10% in opening the secondary packaging [35]. • Hospital care: picking errors account for 23% of the strength errors and are mostly caused by confusions of the strength and more rarely of names [62]. About 2% of picking processes in the inpatient care setting are erroneous [55].	• Modification of the labelling (e.g. tall man lettering [65, 66]) or introduction of colour codes [67, 68]. (Contrastively discussed [69], especially because the introduction of new colour codes has been shown to be associated with higher error-rates during and right after the transition time [70]).	Hospital care: Automated dispensing cabinets or carousels [71] reduce identification errors with varying impact [72]; unit-based drug-dispensing cabinets reduce the overall medication error rate [73]. Scanning drug packages for identification reduced administration errors [20] and integration of RFID solutions might be future solutions [74].
2	Removal from the immediate packaging	Removal from the immediate packaging before application (e.g. blister, dropping device or ampoule). This is also important if capsules have to be removed from their blister to put them into an inhaler.	• 10–25% of elderly patients expressed difficulty removing drugs from blisters [75–78], 14% had difficulties in opening screw-tops [76], 40–62% in opening plaster packaging [77], 12–64% in opening childproofed closures [75, 77, 78] and two thirds of patients with rheumatic arthritis in opening suppository packaging [79] (54% could not remove suppository [80]).	• Before drug selection, the physical capabilities of the person in charge should be checked, e.g. by measuring hand grip strength [81, 82]. • If the person in charge is likely to fail and no alternative is available, medical aids can be added.	No support options with electronic tools have been reported.
3	Preparation of medical aids and devices	Medical aids can be part of the brand (e.g. insulin pen or inhaler), or may be added to the drug administration process to support the person in charge. They should be selected carefully to match the patient's needs.	• 17–29% of patients fail to open medication organizers (Dosett) [75, 78]. • Inappropriate devices to split tablets are frequently applied [83, 84] or proper use of the device is not appropriately trained [49]. • Parenteral administration systems must be prepared before administering the drug [85, 86].	• For these steps, education programmes and practical training courses for patients, family members and nurses have been developed and tested [13, 17, 48, 87, 88]. Besides verbal counselling, written information without [17, 89] and with pictograms [90, 91], video tapes [92] and practical training under supervision have been employed [17]. Also interactive teaching strategies [88] and implementation of medical aids such as calculators [25, 93] can reduce errors during this step, particularly if the teaching strategy is tailored to the target group [94].	Education and training can also be supported with e-learning modules [96, 97].
4	Preparation of drug	Drugs with differing dispensing and administration form need to be prepared in one step (e.g. solving effervescent tablets before use) or several sub-steps (e.g. preparing a powder for IV administration). Drug preparation may impact the stability of the drug and hence its storage conditions, shelf life (subsequent steps must be performed within a certain time frame) or even dosage.	• 30% of faulty intravenous administrations resulted from inappropriate solvents or wrong volumes [18, 32, 33, 98]. • In oral administrations, >50% of crushing or splitting processes and >80% of dissolving processes before administration via tube are erroneous [17], and in nursing homes, 10% of patients received oral drugs in an unauthorised modification [99] with crushing tablets and opening capsules being the most frequent administration errors [100]. • When administering inhalative drugs, 13–45% of the patients do not shake the inhaler before use [25–28]. • In 25% of administrations, dropping devices are incorrectly employed [48]. • With eye drops up to 80% higher doses are administered [30], and with nasal drops, up to 86% of patients administered wrong doses [101]. • Inconsistent labelling [102] or inappropriate measuring devices [103] result in wrong dosage of liquid formulations (67% vs. 15% when using an oral syringe vs. a cup). • 1% of tablets prohibited to split are split [104, 105] • Inhaled drugs are overdosed by 3–22% of patients [26, 28]. • Parenteral drug application is particularly error prone (calculation errors) [18, 32, 33, 98].	• For these steps, education programmes and practical training courses for patients, family members and nurses have been developed and tested [13, 17, 48, 87, 88]. Besides verbal counselling, written information without [17, 89] and with pictograms [90, 91], video tapes [92] and practical training under supervision have been employed [17]. Also interactive teaching strategies [88] and implementation of medical aids such as calculators [25, 93] can reduce errors during this step, particularly if the teaching strategy is tailored to the target group [94].	Education and training can also be supported with e-learning modules [96, 97].
5	Dose individualization	Before, during, after, or instead of drug preparation a dose preparation step might be necessary such as splitting a tablet (without preceding preparation), splitting a tablet before crushing it (before preparation) or measuring a syrup with a measuring container (after preparation).	• 10–25% of elderly patients expressed difficulty removing drugs from blisters [75–78], 14% had difficulties in opening screw-tops [76], 40–62% in opening plaster packaging [77], 12–64% in opening childproofed closures [75, 77, 78] and two thirds of patients with rheumatic arthritis in opening suppository packaging [79] (54% could not remove suppository [80]).	• Before drug selection, the physical capabilities of the person in charge should be checked, e.g. by measuring hand grip strength [81, 82]. • If the person in charge is likely to fail and no alternative is available, medical aids can be added.	No support options with electronic tools have been reported.

6	Disposition	Before the drug is applied, the medication is dispensed and eventually checked by a third party. Disposition can be bundled (for instance in long term care) and can also take place before step 4 and 5.	Context factors can facilitate the occurrence of disposition errors [42] and in a nursing home, 7% of drugs dispensed in pill organizers were wrong [105].	Disposition of drugs is often linked with handovers and information loss. Disposition errors can be reduced by introduction of unit dose systems [106] or single packaged drugs that allow identification of the single dose.	- Ward-based automated dispensing cabinets can reduce disposition errors [70]. - There are no electronic checks for pre-filled pill organizers.
7	Harmonization with the co-medication and context	Single doses have to be harmonized with the co-medication in order to prevent incompatibilities (e.g. precipitation) and maximize therapeutic efficacy.	- Intensive care: 6% of infusions were incompatible [11] and >50% of intensive care patients received at least one incompatible combination [13]. - Regular care: 3% of infusions were incompatible [98]. - Regular care: 2.3% [19] – 13.9% [107] of all administration errors were due to administration of oral drugs with food if fasting state would be recommended.	Prevention of incompatible drugs can be trained [11] and optimized by information leaflets [11, 13]. If process changes are induced, training effects are sustained [12].	Information on incompatible drugs can be provided in electronic CDS [108].
8	Application/intake	Depending on the route of application and the technique of intake, drug application consists of one to several more or less complicated sub-steps that determine the complexity of drug administration and, accordingly, potential training needs and odds for failure and success.	- Intensive care: 0.8 errors per administration for gastric tube applications (compared with 0.6 for parenterals and 0.2 for per orals [18]). - Nurses performed 40% of application processes faultily, patients up to 97% of processes [17, 18]. - Patients are prone to apply inhaled drugs wrongly (30–60% of patients with critical errors [25–28], followed by injection and oral liquids [109]. >70% of patients apply eye drops faultily [30, 31, 110]. 73.3% of i.v. errors refer to the rate of infusion and 33.3% to the volume [32, 111]. In another study, a too rapid bolus injection was the most frequent i.v. error (49.7%) [112].	- The distinct steps of drug application can be optimized by policies or educational training [11, 17, 26, 28, 30, 31]. - Medical aids can reduce error rates (e.g. eye drops dispenser with visual support [47], pre-filled insulin pens instead of using syringes and vials [29] or with specific techniques to reduce required strength [113]). - Unique devices (e.g. luer vs. non-luer) may prevent route errors, if tested [114].	The electronic device most frequently introduced and analyzed are smart pumps [115]. Benefit and potential risk must be closely monitored [116] and efficient error reduction requires linkage to EHR [117] and/or barcode-assisted administration [118].
9	End of application	Some drug applications require active termination (e.g. infusion pumps, transdermal systems).	Case reports describe excessive and potentially fatal doses if continuous application is not actively stopped [38, 39, 119].		Smart pumps usually support active termination by alarm signals.
10	Follow-up	Some medical aids need a follow-up (e.g. cleaning of inhalation devices).	Healthcare workers are exposed to unintended needlestick injuries (about 16.9 injuries /100.000 devices used [120,121].		
11	Monitoring	Specific monitoring for successful administration (e.g. that suppository remains in the rectum [123]).	A specific monitoring after inhaled drugs is neglected by up to 50% of patients [26].	Introduction of safety needle devices can reduce the error rates [120].	Video surveillance can identify [25] and monitor [122] patients with wrong inhalation technique.

CDS, clinical decision support; EHR, electronic health record; RFID, radio-frequency identification.

Figure 2

Depiction of different variants of process sequence in the drug administration process. Described are different drug dose forms and aligned medical aids. Dotted lines are sub-steps that are performed automatically or are not required

Discussion

When looking at the entire drug treatment process, early studies suggested that in inpatient care, one in three medication errors was related to the drug administration process [7]. At this time, there are few corresponding studies for the ambulatory sector. However in one paediatric study, 70% of preventable ADEs were related to drug administration by parents [34]. Given the frequency of drug administration, the complexity and multitude of required sub-steps, and the number of involved people some of whom are not trained in drug administration, it seems reasonable to assume that drug administration errors might even be far more prominent in the ambulatory setting than in the hospital setting. Moreover, in contrast to the prescription process, the administration process is the last step before the drug actually reaches the patient. Whereas drug prescription errors can be detected and corrected during the course of the treatment process (near-misses), drug administration errors are costly to detect, difficult to intercept, and may, therefore, have a high risk of reaching the patient and translating into an adverse patient outcome. Indeed, flaws and deficits in each sub-step of drug administration might entail adverse outcomes, while different outcomes are typically linked to distinct sub-steps. For instance, problems in correct identification of drug packages are likely to be associated with decreased adherence [35], as are difficulties in handling drugs during the personalization process (e.g. tablet splitting [36, 37]), whereas errors in drug dosage and drug application are related to non-response [38] or toxicity [39, 40]. Hence, the prevention of drug administration errors appears important, particularly in the ambulatory care setting, where the incidence rate might be higher and subsequent strategies to counteract adverse outcomes following administration errors might be less accessible. To minimize sources of error in drug administration, their identification and specification is crucial. Hence, various efforts were made to render the general classification of 'prescription and administration errors' more precise [14, 41] and develop the basis for a targeted implementation of error prevention strategies. Both explorative and qualitative assessments [42] as well as structured (semi-) theoretical approaches such as failure mode and effects analysis (FMEA) [43] with a specific emphasis on reliability [44] have been employed to describe drug administration processes. The more precisely the administration process is divided into its sub-steps, the easier observation techniques can be employed to assess drug administration [18] and the effect of intervention strategies. This will also form the basis for targeted interventions aimed at improving such deficits. Generally, administration errors can either result from treatment- or process-related faults (e.g. picking the wrong drug or treating the wrong patient) or from drug-specific challenges (e.g. crushing a sustained-release

tablet). Hence, approaches to reduce administration errors may focus on the drug itself, the entire process in a given setting as well as the individual patient or a specific patient population. In either case, the error source (e.g. slips or oversights, gaps in knowledge, violations of established rules, lack of skills or false beliefs) will determine the most appropriate set of prevention strategy.

To date, most interventions have aimed at reducing the overall rate of administration errors without focusing specifically on critical sub-steps. Such global measures were mainly intended to optimize or disentangle the entire process by improving the surrounding conditions (e.g. reducing disturbances) [45], introducing in-process controls [46], or selecting [29] or modifying [47] medical aids and appliances. These should, however, be chosen individually and integrated carefully to reduce errors successfully [26, 27, 48–51]. If the error is not linked to a particular step of the drug-specific administration but rather to the setting-specific treatment process (e.g. selection of the wrong patient), the implementation of barcoding has shown benefits both in reducing dispensing errors [52] as well as administration errors, particularly if the patient was also scanned before drug administration [20, 21]. This benefit is not seen in all studies [53] and is potentially more evident if barcoding is linked to electronic medication administration records [54]. Moreover, a simplification of the entire process by reducing or automating the necessary sub-steps can reduce error rates [55] or avoid errors altogether. For instance, pre-filled multidose inhalers [25] or pre-filled insulin pens [28], which can be more easily administered, show lower error rates than single dose inhalers or refill pens. Moreover, drug adherence is better with insulin pens than with syringes and ampoules [56].

Electronic information and technology systems have only been scarcely evaluated as approaches for error prevention within the distinct drug administration process and focus most often on the administration of intravenous drugs (smart pumps). However, there are a variety of electronic tools that have been assessed as reminder or alert systems before drug administration actually takes place with varying results. In one study, complete oblivion could be decreased by reminders via voice mail [57]. Text messages showed both higher persistence of adherence rates [58] as well as no impact in another patient population where text messages did not improve adherence [59]. Reminding systems might be particularly successful, if they consider context factors and issue dynamic alerts [60]. For ambulatory patients, complete medication management systems that are supposed to provide the patient with the right drug at the right time and remind him/her to take the medicine have been developed but not yet evaluated to measure their potential benefit [61].

Table 2 offers an overview of potentially risky sub-steps and currently available data on error frequencies and options for preventions. Hence, this table might guide both future research activities in order to close the gaps and

Table 2

Alignment of potentially error prone sub-steps of drug administration with reported errors and published evidence on error prevention

	Oral tablet (splitting)	Oral tablet (splitter)	Liquid oral dose form	Metered dose inhaler	Powder inhaler (multi-dose)	Powder inhaler (capsule)	Eye drops	Nasal spray	Ointments	Transdermal systems	Suppository	s.c. injections	s.c. injections (pen)	i.v. infusions
	E	P	E	P	E	P	E	P	E	P	E	P	E	P
Removal from secondary packaging	ER		ER		ER		ER		ER		ER		ER	
Opening and removal from immediate packaging	ER		ER		ER		ER		ER		ER		ER	
Preparation of medical aid of device	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Preparation of the drug	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Dose individualization	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Drug disposition	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Harmonization with co-medication	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Application/intake	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Termination of application	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Post-processing of device	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR
Monitoring	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR	ER	PR

empty cell = no information available; grey-shaded cell = sub-step is not necessary. ER, errors reported; PR, prevention reported.

serve as checklist to identify potentially error prone processes in an individual setting.

Competing Interests

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

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