Developing consensus on hospital prescribing indicators of potential harm for infants and children.

Abstract

Aims

To develop a list of hospital based paediatric prescribing indicators that can be used to assess the impact of electronic prescribing or clinical decision support tools on paediatric prescribing errors.

Methods

Two rounds of an electronic consensus method (eDelphi) were carried out with 21 expert panellists from the UK. Panellists were asked to score each prescribing indicator for its likelihood of occurrence and severity of outcome should the error occur. The scores were combined to produce a risk score and a median score for each indicator calculated. The degree of consensus between panellists was defined as the proportion that gave a risk score in the same category as the median. Indicators were included if a consensus of 80% or higher was achieved and were in the high risk categories.

Results

Each of the 21 panellists completed an exploratory round and two rounds of scoring. This identified 41 paediatric prescribing indicators with a high risk rating and greater than 80% consensus. The most common error type within the indicators was wrong dose (n= 19) and the most common drug classes were antimicrobials (n=10) and cardiovascular (n = 7).

Conclusions

A set of 41 paediatric prescribing indicators describing potential harm for the hospital setting have been identified by an expert panel. The indicators provide a standardised method of evaluation of prescribing data on both paper and electronic systems. They can also be used to assess implementation of clinical decision support systems or other quality improvement initiatives.

What is already known about this subject

- Prescribing errors are common in the paediatric setting
- Prescribing indicators can be used to measure or monitor the accuracy of prescribing
- There are no validated paediatric prescribing indicators for the hospital setting

What this study adds

- A set of 41 prescribing indicators specific for the UK hospital paediatric setting
- A standardised method for assessing the impact of electronic prescribing on high risk medicines

Introduction

The use of medication to treat disease, alleviate symptoms and prevent illness is the most common intervention used in healthcare. The vast majority of medication does not cause harm. However, all medicines carry some level of risk. Medication errors are common in hospital practice[1] and evidence suggests possibly more common in children.[2] Determining the harm caused by these errors is vital to be able to understand how interventions might be targeted to reduce the risk of harm. Methods for determining harm vary considerably. Some studies use a severity scale for determining harm, scored by the researcher or by obtaining consensus between a number of healthcare professionals.[3, 4]

The same methodologies for identifying prescribing errors and harm in adult patients have been used in the paediatric setting. Prescription review often by hospital pharmacists yields large numbers of potential prescribing errors often with low or no harm.[4, 5] This make is difficult to determine the impact of any change or improvement.

Trigger tools look for indicators of harm rather than specific errors, for example a high International Normalised Ratio (INR) indicates that a potential error with warfarin may have occurred and requires checking to confirm this. Triggers for the paediatric setting have been described in the literature. Stockwell *et al* recently published a paediatric harm measurement tool contained 51 triggers, including 21 medication related triggers.[6] Trigger tools such as this provide a standard method of identifying errors but they require extensive retrospective case note review in order to identify firstly the trigger and then any subsequent medication related harm.

Prescribing indicators are a valid standardised way of measuring or monitoring an area of prescribing where changes in prescribing or putative improvement require evaluation either prospectively or retrospectively. Adult prescribing indicators have been developed in several settings in the UK.[7-10] Thomas *et al*[11] published a set of adult prescribing indicators for the hospital setting. Using an eDelphi methodology, consensus on a set of 81 indicators was achieved. They describe prescribing errors which have the risk of causing significant harm.

The aim of this research was to create a set of paediatric prescribing indicators for the hospital setting that can be used to assess the impact of electronic prescribing.

Method

While evidence-based medicine is the gold standard approach to care, there, remain vast swathes of medicine where evidence is lacking or incomplete. This is often due to the rare nature of a condition and the subsequent difficulty in running a randomised controlled trial. The Delphi method is based on the idea that an accurate and reliable consensus can be gained by consulting a panel of experts and accepting the group consensus. Its use in health services research includes guideline development,[12] outcome measures for primary health care research[13], drug related mortality,[14] high acuity paediatric conditions[15] and the design of a paediatric pharmaceutical care model.[16] Importantly the method has been used extensively to develop prescribing indicators for general practice,[8, 9, 17-20] and hospital adult in-patients.[11] Based on the validated use thus far, the Delphi technique was selected to gain consensus opinion on paediatric prescribing indicators, from a range of both paediatric physicians and pharmacists.

Expert Panel Selection

A list of potential panellists was generated by the research team from networks via the Royal College of Paediatrics and Child Health (RCPCH) and the Neonatal and Paediatric Pharmacists Group (NPPG). Additional contacts were made through research links with a National Institute of Healthcare Research (NIHR) programme grant investigating the impact of electronic prescribing. An email invitation was sent to 39 potential panellists requesting their participation, along with a summary of the proposed research. Panellists were general paediatricians, paediatric pharmacists and paediatric clinical pharmacologists from across the UK. Panellist information was collected on the total number of years of paediatric experience, and experience with electronic prescribing systems. Out of the 39 people invited, 24 agreed to participate. This achieved the target number of at least 20 panel members, comparable to the number used in a similar Delphi study.[11]

Identifying Potential Indicators

Information was gathered from a variety of sources (Table 1) on paediatric prescribing errors by the lead researcher and assessed for their suitability according to the inclusion and exclusion criteria, by the research team.

Inclusion

- The indicator describes a prescribing error relating to a specific drug
- The indicator is specific to the hospital paediatric setting

Exclusion

- The indicator describes a prescribing practice not routinely undertaken in paediatric hospital settings
- The indicator describes an error that would not be amenable to clinical decision support or electronic prescribing
- Extraction of data for the indicator from hospital records is not likely to be feasible
- The indicator describes a failure to monitor
- The indicator describes errors relating to the administration or dispensing of a drug

The eDelphi Process

Exploratory Round

The 24 panellists were sent the initial list of indicators for the exploratory round. They were instructed to review each indicator for relevance and possible modification to ensure clarity. They also had the opportunity at this stage to suggest additional indicators that had not been identified by the research team. The additional indicators were collated and reviewed and, if appropriate, included in the final indicator list used for round one of the eDelphi process. Panellists were also made aware of the reasons for exclusion of any suggested indicators.

Round One

In round one panellists were asked to rate each indicator for its likelihood of occurrence and severity of harm should it occur. The scoring system used was based on the National Patient Safety Agency scale in common use in UK hospitals REF (Table 1) and allowed identification of indicators with the greatest clinical risk. The panellist scores were converted into a risk score using the matrix. The median risk scores for each indicator were then calculated, allowing the indicators to be divided into groups based on their risk scores.

Round Two

In round two, each panellist was sent the indicators, the median likelihood and severity scores from the panel and the individual panellist's original scores from round 1. Panellists were then asked to review their scores in light of the median scores and were given the opportunity to either maintain their original judgement or modify their scores in line with the majority of the group. The median scores were then re-calculated for each indicator and the

level of consensus determined. Indicators with a median risk score greater than 8 (high or extreme) and at least 80% consensus were then considered to have achieved an adequate level of consensus and therefore inclusion into the final list.

Results

Prior to the exploratory round, a total of 179 potential indicators were identified from the resources listed above (Table 1). The research team reviewed each indicator against the inclusion and exclusion criteria resulting in a final list of 100 indicators; 77 indicators were identified from a single source, 23 from two or more sources.

The exploratory stage and rounds one and two were completed by 21 of the 24 panellists who had originally agreed to take part. Table 3 summarises the panellists' levels of experience, profession and location type. The panel comprised of 8 pharmacists with a total of 181 years of paediatric experience, and 13 paediatricians with a total of 256 years experience. Panellists had a total of 91 years of experience with electronic prescribing.

During the exploratory round, 75 new indicators were proposed by the panel and reviewed by the research team, 34 of which were included in round one. In addition, nine of the original indicators were removed and one reworded following the comments and suggestions of the panel. Typical reasons for exclusion were that the indicator described a cause of an error rather than an error itself, that the indicator was non-specific and would relate to numerous drugs or that the issue would be captured by another indicator. This resulted in a final list of 125 indicators for round one.

Following two rounds of scoring, 41 of the indicators were considered high risk by consensus; these are summarised in table 4. None of the indicators were assessed as extreme risk by the panellists.

The 41 indicators include 34 different drugs or classes from the following therapeutic groups; gastrointestinal (n=1), cardiovascular (n=7), respiratory (n=1), central nervous system (n=3), antimicrobials (n=10), endocrine (n=2), immunosuppression (n=6), fluids and electrolytes (n=1), musculoskeletal (n=2) and anaesthesia (n=1).

The most frequent error type identified as high risk was dosing (n= 19) with drug-drug interactions (n=7) and clinical contraindications (n=6) the next two most frequent error types.

Discussion

The eDelphi process has identified 41 high risk prescribing indicators for the paediatric hospital setting. They can potentially be used to monitor the impact of electronic prescribing

or clinical decision support tools. To the authors' knowledge, this is the first set of prescribing indicators for paediatric patients in the hospital setting. However, other work has attempted to identify high risk medicines in this setting.

The consensus process used to derive the indicators involved a panel consisting of 21 paediatricians and paediatric pharmacists all of whom complete two rounds of scoring, limiting any bias introduced by missing responses.

Nearly half (n = 19) of the final 41 indicators related to dosing errors. This is not surprising since dose errors account for the majority of the indicators identified for rounds 1 and 2. This is likely influenced by the fact that dosing errors are the most common error type reported in paediatrics.[21-23] Drugs with known risks such as gentamicin, phenytoin and methotrexate were included in the dosage indicators; however, "lower risk" drugs such as meropenem, ceftriaxone and domperidone are also present. This may reflect, in the case of the antimicrobials, the relatively serious clinical indications in which these drugs are used and the need to prescribe the correct dose to avoid treatment failure as well as heightened awareness as a result of antimicrobial stewardship. Or; in the case of domperidone the relatively recent publicity relating to adverse reactions.[24]

Previously published work has identified high-alert medicines within paediatrics. Maaskant *et al*[25] published a list containing fourteen specific drugs and 4 medication classes of high-alert medications. Comparing this with our prescribing indicators shows that 10 of the individual drugs and three of the drug classes are duplicated. The four high-alert drugs not identified in our prescribing indicators are all infusions commonly used in intensive care areas, such as dopamine and noradrenaline. Reference to errors involving infusions was excluded from our research because the reported incidents all related to errors occurring as a result of incorrect administration or infusion preparation rather prescribing.

The high-alert drug class from Masskant *et al*'s[25] report that is not included in our prescribing indicators relates to parenteral nutrition. Errors reported relating to parenteral nutrition concern administration or preparation errors rather than prescribing. This possibly reflects UK practice in terms of these medications where standard prescriptions and electronic systems for parenteral nutrition have been developed to prevent errors at the prescribing stage.

Stockwell *et al*[6] published a list of paediatric triggers developed using an eDelphi technique and an international panel. From their list of 21 triggers relating to medicines, 11 also appear in our paediatric prescribing indicator list. The triggers describe adverse events that could result from any incorrect use of a medicine. For example the administration of

Digibind® could be triggered by an error in the prescribing, dispensing, administration or monitoring of digoxin. This is an appropriate way of identifying an adverse event *after* it has occurred. Our indicators, however, are specific for the prescribing process and can be used to identify errors at the prescribing stage, which may be in advance of the medicine being administered. This can tell us whether quality improvement interventions such as ePrescribing can prevent the 'potential' for harm occurring.

Many of the paediatric indicators for the exploratory round were derived from the adult indicators previously published.[11] The final list of 41 paediatric indicators contain 28 indicators modified from the research conducted in adult medicine. Many of the remaining indicators were related to specific paediatric settings or medicines not usually classed as high risk in adults as such as meropenem, as discussed above.

Reports of the incidence of prescribing errors in the paediatric setting vary between 7 and 13%.[22, 26] This is partly because there is no standard definition of what and how to collect information about errors. Studies use different data collection methods and different definitions of medication error.[27] This lack of standardisation makes comparison between reports difficult to assess.

Prescribing indicators can be used to assess the impact of a safety improvement intervention by standardising both pre- and post-implementation data collection. The objective nature of these data would allow comparisons and conclusions to be drawn and provide more robust evidence across healthcare settings. The standardisation means that for the first time, comparisons can be made between hospitals and different initiatives.

The indicators can also be used to optimise the capability of electronic prescribing systems, such as with the provision of complex clinical decision support to highlight and avert such errors at the point of prescribing. This also has the potential to focus alerts on high risk areas, with the advantage of reducing alert fatigue.[28]

While the paediatric indicators described here are focused on the secondary care setting, many could be applicable to general practice. There are currently no primary care related exclusive paediatric trigger tools published in the literature

Limitations

The initial list of indicators was derived from an extensive literature search and therefore, unpublished cases of medication errors would not have been included. However, we aimed to minimise this effect by including the exploratory round so panellists had the opportunity to propose indicators they see in practice.

The work is entirely UK based and as such may not have applicability in other global settings. Lastly, as new evidence emerges and new drugs begin to be used, other potential indicators may become relevant. The adult indicators previously cited are currently under review and if the paediatric indicators described here become extensively utilised a program of periodic review will be necessary.

Conclusions

Paediatric prescribing errors with the potential to cause harm have been identified by an expert panel. The indicators provide an objective tool that can be used to collect routine prescribing data in both electronic or paper-based environments. Standardisation of what is collected will allow a better understanding of what errors are occurring in paediatrics. Without this knowledge, it is difficult to target quality improvement projects, and also inform under- and postgraduate education of paediatric prescribing.

They could also be used to refine alerting systems used in electronic prescribing to target warnings and alleviate alert fatigue.

The use of these paediatric indicators in combination with previously described adult indicators for the hospital setting provides a comprehensive tool that can be used to evaluate changes across a wider age range.

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328 Table 1

Table 1 - Sources used to identify indicators
Adult indicators previously published[11]
Literature Search
National Reporting and Learning (NRLS) data[29]
Local pharmacy intervention data
Trust incident forms
National Patient Safety Alerts

329 Table 2

330 Table 2: Scoring likelihood and severity of the errors occurring (from the UK National Patient Safety
331 Agency Risk Matrix) [30]

	Likelihood				
Consequence	**1 Rare** *This will probably never occur*	**2 Unlikely** *Do not expect it to occur but it is possible it may do*	**3 Possible** *This might occasionally occur*	**4 Likely** *This will probably occur*	**5 Almost certain** *This will undoubtedly occur, possibly frequently*
5 Catastrophic *Leads to death, multiple permanent injuries, or irreversible health effects*	5	10	15	20	25
4 Major *Major injury leading to long-term incapacity/ disability*	4	8	12	16	20
3 Moderate *Moderate injury requiring intervention*	3	6	9	12	15
2 Minor *Minor injury or illness requiring minor intervention*	2	4	6	8	10
1 Insignificant *No risk of patient injury or harm and no intervention required*	1	2	3	4	5

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1-3 Low risk	4-6 Moderate risk	8-12 High risk	15-25 Extreme risk

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336 Table 3 – Experience and type of hospital for expert panel members.

Position	Years of Experience	Years of Electronic Prescribing experience	Type of Hospital
Senior Paediatric Pharmacist	35	2	General Teaching
Clinical Pharmacy Manager	25	3	Specialist Children's
Neonatal Pharmacist	32	0	General
Consultant Pharmacist	26	21	General Teaching
Medication Safety Pharmacist	20	11	General Teaching
Clinical Pharmacist	12	5	Specialist Children's
Associate Professor of Child Health	18	1	Specialist Children's
Consultant Paediatrician	19	1	Specialist Children's
Consultant Paediatrician	24	1	Specialist Children's
Consultant Neonatologist	19	0	Specialist Children's
Specialist Registrar	10	0	Specialist Children's
Consultant Paediatrician	30	0	General Teaching
Senior Lecturer Paediatric Pharmacology	20	0	Specialist Children's
Consultant Paediatrician	20	14	General Teaching
Lead Informatics Pharmacist	22	15	General Teaching
Paediatric Pharmacist	9	3	Specialist Children's
Consultant Neonatologist	20	0	General
Consultant Paediatrician	19	10	General
Consultant Paediatrician	17	4	General
Consultant Paediatrician	19	0	General
Consultant Paediatrician	14	0	General

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339 Table 4 – Final list of indicators high risk with >80% consensus.

Indicator	Possible Outcome	Therapeutic Class	Error Type	Level of Consensus
Domperidone prescribed at > 1.2mg/kg/day max 20mg (prolongation of QT interval, sudden cardiac death)	Increased risk of arrhythmias and sudden cardiac death	Gastrointestinal	Dosing	86%
Digoxin dose not reviewed in light of reduced renal function	Risk of supratherapeutic doses increasing risk of adverse effects	Cardiovascular	Dosing	95%
Potassium-sparing diuretic (excluding aldosterone antagonists) prescribed to a patient also receiving an ACE inhibitor or angiotensin-II receptor antagonist *(Increased risk of severe hyperkalaemia)*	Increased risk of severe hyperkalaemia	Cardiovascular	Drug-Drug Interaction	90%
Amiodarone prescribed to a patient on digoxin without review of the digoxin dose	Risk of digoxin toxicity	Cardiovascular	Drug-Drug interaction	81%

Beta-adrenoceptor blocking drug prescribed to a patient with asthma (Increased risk of bronchospasm and acute deterioration)	Beta-adrenoceptor blocking drugs are known to cause bronchoconstriction in asthmatics, and can cause acute deterioration	Cardiovascular	Clinical Contraindication	81%
Low molecular weight heparin prescribed to a patient with renal impairment without dose adjustment *(Increased risk of bleeding)*	Increased risk of bleeding with the dose of low molecular weight heparin is not adjusted for renal function	Cardiovascular	Dosing	86%
Antiplatelet prescribed to a patient with a concurrent bleeding disorder (Increased risk of bleeding)	High risk of bleeding when antiplatelets prescribed to patients with a past medical history of bleeding disorders	Cardiovascular	Clinical Contraindication	81%
Prescribing of intravenous heparin infusion for treatment of thromboembolic event using the wrong dose or infusion rate based on local protocol (risk of toxicity or therapeutic failure)	Risk of supratherapeutic or subtherapeutic dose of heparin	Cardiovascular	Dosing	86%
Two concomitant opiate analgesics that are not in line with the WHO pain ladder *(Injudicious use of two opiates risk of toxicity)*	Increased risk of opioid toxicity	Central Nervous System	Therapeutic Duplication	86%
Prescribing of incorrect or inequivalent morphine (opiate) dose via multiple routes. (Risk of toxicity)	Oral and intramuscular doses are not equivalent, risk of therapeutic failure or toxicity	Central Nervous System	Therapeutic Duplication	81%
Phenytoin dose not reviewed in light of low albumin (potential for toxicity)	Increased risk of phenytoin toxicity	Central Nervous System	Dosing	86%
Penicillin containing compound prescribed to a penicillin allergic patient without reasoning (e.g. a non-allergy such as diarrhoea or vomiting entered as an allergy where the indication for penicillin is compelling) (Risk of hypersensitivity reactions)	Contraindicated in pts with history of penicillin allergy. Risk of hypersensitivity reaction	Anti-Microbial	Allergy	81%
Nitrofurantoin prescribed to a patient with renal impairment, avoid if eGFR <60ml/minute/1.73m^2 *(Risk of peripheral neuropathy and inadequate concentration in urine)*	Risk of peripheral neuropathy and reduced therapeutic effect	Anti-Microbial	Dosing	80%
Gentamicin prescribed to a patient with at least mild renal impairment without dose frequency adjustment (Increased risk of toxicity)	Increased risk of toxicity	Anti-Microbial	Dosing	81%
Gentamicin dose calculated based on actual body weight rather than ideal body weight in an obese patient *(Risk of excessive dosing and toxicity)*	Risk of excessive dosing and toxicity	Anti-Microbial	Dosing	100%
Macrolide antibacterial prescribed concomitantly with warfarin without appropriate dose adjustment or increased INR monitoring *(Increased risk of bleeding)*	Macrolide antibacterials can reduce the metabolism of warfarin, causing an increase in the INR and an increased risk of bleeding	Anti-Microbial	Drug-Drug Interaction	90%

Co-prescribing of macrolides with interacting drug (QT prolongation)	Risk of prolongation of QT interval and ventricular arrhythmia	Anti-Microbial	Drug-Drug Interaction	86%
Co-prescribing of a macrolide with ciclosporin or tacrolimus (increases plasma levels of anti-rejection agent)	Increased plasma concentration of ciclosporin	Anti-Microbial	Drug-Drug Interaction	86%
Vancomycin prescribed intravenously over less than 60 minutes (Rapid infusion of vancomycin can cause severe reactions)	Increased risk of infusion reactions	Anti-Microbial	Intravenous Rate	81%
Amphotericin B prescribed without additionally stating both brand name and the dose in mg/kg (Risk of fatal overdose due to confusion between lipid based and non-lipid	Specification of brand name to reduce risk of wrong formulation being administered and resulting toxicity	Anti-Microbial	Drug Name	90%
Soluble insulin prescribed to a patient on a when required basis (Increased risk of serious episodes of hypoglycaemia and nocturnal hypoglycaemia post dose)	Increased risk of serious episodes of hypoglycaemia and nocturnal hypoglycaemia especially if given more than 1 stat dose. Not managing the long-term condition	Endocrine	Clinical Contraindication	85%
Methotrexate prescribed to a patient with a clinically significant drop in white cell count or platelet count (Risk of bone marrow suppression)	Risk of bone marrow suppression	Immunosuppressant	Clinical Contraindication	90%
Oral methotrexate prescribed to a patient with an inappropriate frequency (Increased risk of toxicity)	Oral methotrexate should be dosed ONCE WEEKLY, and the prescription clear as to which day of the week this should be	Immunosuppressant	Dosing	100%
Methotrexate prescribed to a patient with abnormal liver function tests *(Risk of liver toxicity)*	Risk of liver toxicity	Immunosuppressant	Clinical Contraindication	85%
Methotrexate prescribed concomitantly with trimethoprim *(Increased risk of haematological toxicity)*	Trimethoprim suppresses activity of dihydrofolate reductase - potential for additive effect to produce folate deficiency. Increased risk of haematological toxicity when methotrexate given with trimethoprim (including trimethoprim containing compound - co-trimoxazole)	Immunosuppressant	Drug-drug interaction	85%
Allopurinol prescribed concomitantly with mercaptopurine *(Allopurinol enhances effect of mercaptopurine and increases risk of toxicity)*	Increased risk of toxicity and enhanced effects of mercaptopurine when given concomitantly. The dose of mercaptopurine should be one quarter of usual dose	Immunosuppressant	Drug-drug interaction	80%
Potassium chloride supplements continued for longer than is required (based on age appropriate local reference ranges approx 3.5–5.3 mmol/litre) (Increased risk of hyperkalaemia)	Failure to act on potassium chloride monitoring and continuing treatment for longer than required risks hyperkalaemia	Nutrition	Duration	81%
Potassium chloride infusions exceeding 40 mmol/litre prescribed to administered via the	Intravenous administration of potassium chloride solutions exceeding 40mmol/litre should	Nutrition	Route	86%

peripheral route *(Peripheral administration risks venous pooling, which can lead to sudden high concentrations of potassium chloride being delivered to the heart provoking an arrhythmia)*	be prescribed via the central route to avoid arrhythmias			

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