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# Prescribing errors in diabetes

ANTHONY R COX<sup>1,2</sup>, ROBIN E FERNER<sup>2</sup>

## Abstract

**P**rescribing errors in diabetes have the potential to cause serious adverse effects. Antidiabetic agents are a significant cause of admission to hospital. Prescribing errors can be caused by poor handwriting, failure to communicate clearly, and by the use of inappropriate abbreviations. Serious errors involving insulin have been reported in the UK media. While education and training may reduce the number of errors, experience shows that errors will continue to occur without changes to systems.

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**Key words:** adverse events, hyperglycaemia, hypoglycaemia, insulin, prescribing error, sulphonylurea

## Introduction

The publication of *To Err is Human*,<sup>1</sup> in the United States, and *An Organisation With A Memory*,<sup>2</sup> in the UK, highlighted the role of medication errors in iatrogenic illness. As well as the harm done to patients, there is also an increased risk of healthcare professionals being prosecuted for manslaughter following medication errors.<sup>3</sup> In 2001 the NPSA was created to improve patient safety in England and Wales by enabling healthcare professionals to identify and learn from errors.

A recent systematic review of the prevalence and incidence of prescribing errors, commissioned by the General Medical Council found median error rates of 7%, 52 errors per 100 admissions, and 24 errors per 1000 patient days.<sup>4</sup> The most common errors included dosage errors, failure to prescribe an indicated medication, incomplete prescriptions, illegibility, errors in dosing interval, incorrect formulations, drug–drug interactions, and transcription errors.

In diabetes, the key treatments to control blood glucose concentrations, the oral antidiabetic agents and insulin, have the potential to cause serious adverse effects. Profound and life-threatening hypoglycaemia induced by treatment is a

limiting factor in the management of diabetes. In addition, errors of omission can lead to hyperglycaemia and potentially ketoacidosis or hyperosmolar coma. Awareness of errors that contribute to or worsen such effects allows safeguards to put in place.

## Types of errors

A medication error has been defined as “a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient”.<sup>5</sup> Prescribing errors are a subset of errors that can have direct harmful effects, or can make the dispensing or administration of drugs unsafe by introducing ambiguities into the prescription.

A generic error-modelling system (GEMS) has been described by Reason,<sup>6</sup> which integrates the skill-based level (slips and lapses), the rule-based level (poorly chosen or inappropriate rules), and the knowledge-based level (application of knowledge to novel situation). Errors can be divided into two broad categories: errors in the planning of an intentional act, known as mistakes; and errors in execution of an act, known as slips (acts of commission) and lapses (acts of omission). Slips and lapses occur when a prescriber has the correct plan for treatment, but fails to carry it out accurately. They are unconscious acts or omissions. An example might be picking the wrong drug strength from a computer list when prescribing. Mistakes occur when error arises in an attempt to deal with a complex situation, through lack of knowledge, or the application of poor or inappropriate rules. An example would be an inadvertent overdose due to lack of knowledge of the use of a drug in renal failure.

An additional concern are violations, which are defined as deliberate – but not necessarily reprehensible – deviations from those practices deemed necessary to maintain the safe operation of a potentially hazardous system.<sup>6</sup> In the context of prescribing, an example might be the taking of deliberate short-cuts in a badly designed electronic prescribing system.

## Harm from antidiabetic medication

A national study of hospital admissions in the Netherlands found that insulin and other antidiabetic agents were the fourth most common group associated with hospital admission, and hypoglycaemia the third most frequent drug-associated diagnosis.<sup>7</sup> In a 2-month prospective review of hospitalised patients receiving any antidiabetic therapy, 9.5% of patients experienced one or more episodes of hypoglycaemia.<sup>8</sup> Of 484 hypoglycaemic events, 154 were associated with monotherapy (and 149 of those with insulin alone). Forty per cent of

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**Abbreviations and acronyms**

NPSA                      National Patient Safety Agency

hypoglycaemic episodes related to a failure to adjust the dosage of antidiabetic therapy following reduced enteral intake. These episodes were potentially preventable with adequate monitoring and dosage adjustments. Stepka *et al.*<sup>9</sup> examined 20,978 elderly diabetic patients hospitalised over a 15-year period. Two hundred and thirty-six patients (1.12%) were admitted with serious hypoglycaemia. Of 13 fatal cases, five were due to an error in the dosage of chlorpropamide (n=3) or insulin (n=2). Risk factors associated with hypoglycaemia include greater age, longer duration of diabetes, worse socioeconomic deprivation, and higher glycated haemoglobin.<sup>10</sup>

In ambulatory care, Gurwitz *et al.*<sup>11</sup> found antidiabetic agents responsible for 6.8% of adverse drug events; half of the cases were judged preventable.

Prescribing errors related to diabetes are not well reported in the literature, but do occur. Although no deaths caused by prescribing errors in relation to antidiabetic medication have been reported to the NPSA National Reporting and Learning System, 126 prescribing errors involving sulphonylureas and 1409 prescribing errors involving insulin preparations were reported between 1<sup>st</sup> January 2005 and 1<sup>st</sup> April 2008 (National Patient Safety Agency, Personal Communication June 2008).

Lesar *et al.*<sup>12</sup> in a paper examining nine years' worth of prescribing errors in a teaching hospital found that 1.7% of all prescribing errors were related to antidiabetic medication, with two errors per 1000 prescriptions. Another study of prescribing errors related to medication dosage forms found that antidiabetic agents were responsible for 9.7% of errors found.<sup>13</sup>

**Oral sulphonylureas**

Oral sulphonylureas are a common cause of hypoglycaemia.<sup>14</sup> An assessment of spontaneous reports of hypoglycaemia reported to French Regional Pharmacovigilance Centres found that 3% of all reports (n=98) were associated with prescribing errors.<sup>15</sup>

Literature relating to errors in the use of oral sulphonylureas commonly deals with erroneous delivery of a sulphonylurea to a non-diabetic patient.<sup>16,17</sup> However, poor prescription writing can also have the opposite effect. For example, a patient received chlorpromazine instead of chlorpropamide.<sup>18</sup>

Communication with patients, as well as other professionals, is essential when prescribing. Failure to explain to a patient that a repeat prescription of glipizide was not the addition of a new drug, but the continuation of current treatment, led to double dosing and repeated attacks of hypoglycaemia.<sup>19</sup> The new tablets were labelled generically, while his old tablets were labelled by brand name.

Failure to reduce the dosage of oral sulphonylureas in patients who have reduced food intake or renal failure can also

risk hypoglycaemia. Errors in the choice of drug can also occur; some sulphonylureas are more commonly associated with hypoglycaemia, such as chlorpropamide and glibenclamide.<sup>20,21</sup> A study of serious cases of hypoglycaemia in elderly patients found that glibenclamide was associated with a two-fold risk of serious hypoglycaemia compared with glipizide, comparable to the risk associated with chlorpropamide.<sup>22</sup>

**Insulin and other injectable antidiabetic agents**

Insulin treatment is an important cause of hospital admissions. Budnitz *et al.*<sup>23</sup> examined adverse events occurring in emergency department visits in patients over 65 years of age. Warfarin, insulin, and digoxin were responsible for 33.3% of emergency department visits for adverse drug events, despite representing only 2.6% of outpatient prescription visits. Insulin was responsible for 13% of the 4492 adverse events. Most adverse events for insulin were related to the dose of insulin given, 95.4% were related to hypoglycaemia, 24.1% involved loss of consciousness or seizure and 25.1% required hospitalisation.

It is debatable whether all preventable cases of hypoglycaemia have an element of error. Insulin has consistently appeared in the top five drugs associated with medication errors in the US Pharmacopeia (USP) medication error-reporting scheme *MEDMARX*.<sup>24</sup> From 1998 to 2003 insulin accounted for 3% of all errors. Insulin errors are also twice as likely to cause harm to patients as errors associated with other prescribed drugs.<sup>25</sup> Reasons for errors cited by the USP include omission errors, incorrect doses, prescribing errors, and inaccurate transcriptions.<sup>26</sup> We searched *Nexis UK* – a database of UK newspapers – from 2000 onwards for serious errors related to insulin and found a number of cases reported in the UK newspapers (table 1).

The US Institute for Safe Medication Practices has also determined insulin to be a high-alert medication, defined as a drug in the group that has the highest risk of causing patient injury when misused.<sup>27</sup> The most common forms are errors of omission (leading to hyperglycaemia) and inaccurate doses (leading to both hyperglycaemia and hypoglycaemia).

In a study that examined prescribing errors involving medication dosage forms, 9.2% of errors related to dosage form prescribing errors were attributed to insulin, with insulin errors disproportionately making up 57% of the total number of fatal severe or serious error types in the same study.<sup>28</sup>

Concern has been expressed about the number of commercially available insulin mixtures that may contribute towards errors,<sup>29</sup> and confusion between preparations with similar names, such as Humalog and Humulin, has been reported. Potential confusion may arise due to the similarity between single component insulins (e.g. Humalog) and mixed insulins (Humalog Mix30).

A number of specific prescribing errors relating to the use of insulin have been described. Table 2 sets out common errors that have been reported by a variety of sources.<sup>30-34</sup>

The introduction of new recombinant human insulin analogues, such as insulin detemir and insulin glargine, has led to new potential errors. Prior to their introduction intermediate to

**Table 1.** Recent cases of error related to insulin use in the UK published in UK newspapers since 2000

Year	Nature and outcome of error
2001	Blood glucose reading misinterpreted, and failure to monitor insulin pump Fatal
2001	Junior doctor ignorant of insulin syringe use; ten times overdose; attributed to lack of training Fatal
2002	70 units to be administered to child by nurse, instead of 7 units; error spotted before administration by parent No harm.
2002	Misheard advice over phone; led to 50 units being prescribed instead of 15 units Patient died, but coroner did not attribute death to error
2003	Junior doctor administered 50 units instead of 5 units Fatal
2003	Overdose of insulin; no details available Coroner recorded verdict of death by natural causes, but patient did not recover consciousness following error
2004	Poor handwriting in prescribing records led to 40 units being given instead of 4 units Fatal
2005	Junior doctor used wrong syringe, believing 1 unit of insulin in 1ml; 100 times overdose; attributed to lack of training Fatal

long-acting insulin preparations had been cloudy solutions. However insulin detemir and insulin glargine are clear. This has already led to documented cases of confusion and consequent hypoglycaemia.<sup>35,36</sup> Prescribers should be aware of the potential for error and counsel patients appropriately.

Failure to change insulin prescriptions in the face of severe dietary restrictions, such as 'nil by mouth' orders, has also led to preventable harm.<sup>37</sup> Lack of co-ordination between hospital catering and patient visits to other departments, leading to

missed meals after administration of insulin, has been cited as a major cause of hypoglycaemia in hospital care.<sup>38</sup>

Sliding scale insulin protocols are commonly used in the seriously ill, but are subject to error as well as erratic glycaemic control.<sup>39</sup> Attempts to rationalise sliding scale protocols within institutions appear to have reduced the incidence of hypoglycaemia<sup>40</sup> and hyperglycaemia<sup>41</sup> significantly. However, some have argued that sliding scale insulin regimes should be avoided because of the risk of hypoglycaemia.<sup>42</sup> Staff using insulin algorithms should be appropriately trained on practical aspects of their use.<sup>38</sup>

Knowledge of insulin and the characteristics of insulin preparations is limited among non-specialist staff as has been demonstrated in hospital staff<sup>43</sup>, and primary care.<sup>44</sup> This can lead to dangerous medication errors by prescribers, and associated staff, particularly for newer insulin preparations with which they may be less familiar.

An injectable incretin mimetic, exenatide, is available in pre-filled pens in two strengths (5 µg/dose and 10 µg/dose). A nurse attempting to administer 5 µg of exenatide was unable to activate the pen.<sup>45</sup> She disassembled the pen, drew up the entire contents into a syringe, and administered a 300 µg dose (a 60-fold error). The outcome was not recorded. Concern has also been expressed about the potential for error due to similar product codes for these two strengths.<sup>46</sup>

## Discussion

A key component of reducing errors in prescribing in diabetes is education.<sup>47</sup> There is some limited information about the effect of education on doctor prescribing of insulin,<sup>48</sup> with some success in improving insulin prescribing: reducing the proportion of prescriptions not using the specific word 'unit' from 65 to 40%. Specific advice on the type of errors that occur in prescribing, such as the use of dangerous abbreviations, is warranted and this should occur at the undergraduate level. There have been attempts to improve the teaching of prescribing at undergraduate level,<sup>49</sup> and lobbying for curricula that address this key skill within medical schools.<sup>50</sup>

However, while education and training may reduce the number of errors, experience shows that errors will continue to

**Table 2.** Common errors made in the prescribing of insulin

Error	Potential consequence
U100 insulin concentration on prescription	Read as 100 unit dose
U as abbreviation for units	U mistaken as 0 leading to 10 times overdose. (e.g. 80 units given when 8 units prescribed) U has also been interpreted as a 4, 6, and CC
Use of '/' to separate doses	10/5 units (meaning 10 units a.m., 5 units p.m.) can be interpreted as 15 units or even 105 units.
IU as abbreviation for units	I mistaken as 1. e.g. 61 units given instead of 6 units, when 6IU prescribed
SS for sliding scale insulin	Mistaken as 55 units
SSRI for sliding scale regular insulin	Mistaken as selective-serotonin reuptake inhibitor
SSI for sliding scale insulin	Mistaken as strong solution of iodine



### Key messages

- Insulin and other antidiabetic agents are a significant cause of hospital admission
- Medication errors involving insulin are responsible for a disproportionate number of serious adverse events
- Several common errors are known to occur in the prescribing of insulin
- Education and training may prevent some errors

occur if changes are not made to systems. Skill-based errors, such as slips and lapses, cannot be eliminated by training. The American College of Endocrinology and American Diabetes Association have issued a consensus statement with a strong focus on safety issues. They advocate the use of electronic records, computerised prescribing, checklists, written protocols, and improved communication.<sup>51</sup>

All prescribed insulin should be easily viewable to healthcare professionals and should be grouped together. Fragmented prescribing may cause items to be overlooked, leading to erroneous changes in dose.<sup>42</sup> Appropriate monitoring of blood glucose concentration is also crucial for safe prescribing and dose adjustment. Dietary changes and disruptions to meal times in hospitals should be either avoided or accounted for in prescribing.

It has been proposed that insulins should be reclassified according to the timing and purpose of administration, rather than on the basis of appearance. As well as the advantages brought by clarification in the minds of users about the use of insulin, such a classification system also has the potential to reduce prescribing errors, especially if consideration were given to potential name changes to other products in order to eliminate risk.<sup>52</sup>

Risks often occur at the difficult boundaries in healthcare, when moving patients between secondary to primary care. The NPSA recently published safety guidance in order to improve the standard of drug history taking when patients are admitted to hospital, to ensure that the medicine prescribed on admission corresponds to those that the patient was taking before admission.<sup>53</sup> Similar care should be taken when transferring information to primary care.

### Conclusion

Hypoglycaemia from insulin and sulphonylureas remains common and some cases are potentially avoidable. Education and training may reduce prescribing errors related to diabetes, but systems approaches are also required.

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