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Medication Errors Caused by Confusion of Drug Names

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Abstract

Many drug names can look or sound like other drug names, which leads to confusion and potentially harmful medication errors. While various types of drug names exist, brand (proprietary) names are most commonly confused. Examples of the numerous drug names that have been confused because they look and/or sound similar include Celebrex® (celecoxib), Cerebyx® (fosphenytoin), and Celexa® (citalopram). Factors such as poor handwriting and clinical similarity may exacerbate the problem. This problem can be alleviated through actions by regulatory agencies, pharmaceutical manufacturers, healthcare professionals, and patients. To address the problem, significant changes in the pharmaceutical regulatory process have occurred in the US and Europe.

1. The Problem of Drug Name Confusion

While it is often easy to simply blame healthcare providers involved in a medication error, errors are often the result of unsafe systems.[1-3] Detailed analysis of a medication error often identifies multiple system failures that contributed to the error. Effective error reduction strategies seek to correct the underlying system causes.

Confusion of drug names is a common system failure that results in potentially harmful medication errors. Many drug names can look or sound like other drug names. At least one quarter of the error reports received by the US Pharmacopeia/Institute for Safe Medication Practices (USP/ISMP) Medication Error Reporting Program involve look-alike and sound-alike drug names.[4-6] In a study that evaluated factors contributing to medication prescribing errors, a significant number of errors were related to drug nomenclature.[7] Kenagy and Stein estimate that confusion of drug names is responsible for 10 000 patient injuries each year in the US.[8] In 2001, the Joint Commission on Accreditation of Healthcare Organisations (JCAHO), a body that accredits and sets standards for most US hospitals, published a sentinel event alert on look-alike and sound-alike drug names.[9] Clearly, this is a major issue for clinicians since the JCAHO publicises sentinel events on a periodic basis, and they state that these events require organisations to investigate and respond to the issue.[10]

Two comprehensive reviews[11,12] and numerous anecdotal reports on the problem of look-alike and sound-alike drug names have been published.[13-25]

Extensive tables of similar looking or sounding drugs have been compiled.[5,11,26-28] In computer-based memory tests, Lambert and others found that pharmacists and college students confused drug names at a similar rate.[29] In the study, similarity in both spelling and sound of drug names contributed to name confusion.

An evaluation of the literature suggests that the problem is not new. In 1969, Teplitsky published a list of ten look-alike or sound-alike drug names in the *Journal of the American Medical Association (JAMA)*.[13] Furthermore, as the number of drugs on the market increases, the problem will likely grow. Healthcare practitioners need to be aware of the role drug names play in causing medication errors and the system changes that can be made to prevent them.

2. Derivation and Selection of Drug Names

To fully understand how drug names can lead to medication errors, one first must understand the various types of drug names.[30] More detailed discussions of drug naming processes have been published,[8,31,32] but a brief introduction is presented below.

All drugs have a chemical name that chemists use, but these names have limited utility for practising healthcare professionals. Many drugs have code designations that are used during research and development. Each drug is also assigned a generic (non-proprietary) name, which is essential for communication on that product regardless of other names used for the drug. Some drugs also may have trivial names, which are informal names usually derived during the research process. These names may cause additional confusion once the drug has established generic and brand names. Pharmacopeias have also proposed pharmacy equivalent names for complicated products, such as combination products. These names, while not official, often are useful to simplify drug names and thereby reduce confusion. Finally, brand names, also called proprietary or trade names, are trademarked names developed when the drug is marketed.

The drug name selection process also is important to understand. Through global cooperation, many drugs have the same generic (or non-proprietary) name throughout the world. The WHO International Nonproprietary Names (INN) committee works to develop generic drug names that will be accepted worldwide.[33] In the US, the US Adopted Names (USAN) Council, a group with representatives from medical, pharmaceutical, and regulatory organisations, assigns generic drug names.[34] The USAN will only designate drug names after the WHO INN committee approves the name. During this process, measures are taken to ensure that proposed names do not conflict with existing brand or generic names. In the UK, the British Pharmacopoeia Commission also adopts INN names as British Approved Names (BAN).[35] If an INN name does not exist, a BAN will be developed based on a set of guiding principles.[36] Despite these efforts, INN USAN and BAN names for the same generic drug can differ (e.g. paracetamol – INN and BAN, acetaminophen – USAN; glibenclamide – INN and BAN, glyburide – USAN).[37]

Much thought and market research goes into the selection of a drug's brand name. Brand names may be developed using various techniques, including connection with the drug's use, dosage, company, or generic name.[38] Drug brand names may differ significantly between countries, and drugs marketed by more than one pharmaceutical company may have more than one brand name. The brand names must have US FDA approval in the US or European Agency for the Evaluation of Medicinal Products (EMEA) approval in Europe. Approval is based on specific criteria such as not implying promise beyond data, and not containing an unapproved indica-

tion or dosage schedule, and other factors. Some brand names may be contrived and designed for ease in spelling, pronunciation, and remembrance. Typically, most drug brand names introduced today are contrived. Historically, potential for confusion with other drugs has not been considered during the naming process, but regulatory changes have occurred to address this issue.

3. Examples of Easily Confused Drug Names

Drug brand names that look or sound alike are often a source of confusion and medication error. Examples of common, confusing US drug brand names that have resulted in patient harm include Celebrex®[1] (generic name: celecoxib), Cerebyx® (fosphenytoin), and Celexa® (citalopram).[39] Celebrex® is a cyclo-oxygenase-2 inhibitor (COX-2 inhibitor) used to treat arthritis and acute pain. Cerebyx® is an intravenous antiepileptic, and Celexa® is a selective serotonin reuptake inhibitor (SSRI) used to treat depression. Although these drugs have vastly different uses, numerous errors have been reported to the USP/ISMP Medication Error Reporting Program because their brand names look and sound very similar. Other recent examples of confusing US drug brand names include the antiepileptic Lamictal® (lamotrigine) and the antifungal Lamisil® (terbinafine),[40] the antihistamine Zyrtec® (cetirizine) and the antipsychotic Zyprexa® (olanzapine),[41] as well as the oral antineoplastic Xeloda® (capecitabine) and the antiobesity agent Xenical® (orlistat).[42] The above examples are just a few of the hundreds of confusing proprietary drug names that currently are on the market (table I).

Although it seems most errors with look-alike and sound-alike drug names involve brand names, generic drug names also can be confusing. For example, confusion between the antiarrhythmic amiodarone and the inotropic agent amrinone has resulted in multiple errors and even one death.[43] In this case, the USP and the USAN acted in 2000 to change amrinone's generic name to inamrinone in an effort to avoid future errors and fatalities.[44]

Medication errors from confusing drug names are not limited to names that look or sound alike. Drug name acronyms or abbreviations are commonly used, especially for antiretroviral and anticancer drugs, and can result in error and confusion. Drug name abbreviations should be avoided.[45,46] Since one drug can have more than one brand name, patients can take twice the proper dose if they take two different brand names of the same drug. Such an error occurred when a patient took two different brands of verapamil (Verasal™ and Veramex™) that was prescribed by different physicians.[47] The patient's total daily dose of verapamil was 720mg, and she was admitted to the hospital for treatment. Fortunately, the patient quickly recovered and was discharged without lasting sequela.

4. Factors That Exacerbate the Problem

Several factors may increase the potential for a drug to be involved in an error of name confusion.

First, poor handwriting may cause drug names that do not look similar when printed to be confused. An excellent example of this phenomenon occurred when the anticoagulant Coumadin® (warfarin) was dispensed in place of the antidiabetic Avandia® (rosiglitazone) [figure 1].[4,41] This error between Avandia® and Coumadin® has been reported to have occurred not once, but three times.

Similarity of clinical factors also may contribute to errors of confusion. Similar dosage strengths, dosage schedules, indications for use and route of administration may increase the risk of confusion between two names that already may have some similarity when handwritten or spoken. In the above

1 Use of brand names is for identification purposes only and does not imply endorsement.

Table I. Examples of US drug names that may be confused because they look or sound like other drug names[a,b][4,5,11,23,26-28]

Confusing name pair		Confusing name pair	
Accupril®	Accutane®	folinic acid	folic acid
acetohexamide	acetazolamide	fosinopril	lisinopril
Alfenta®	Sufenta®	furosemide	torsemide
Altace®	alteplase	glipizide	glyburide
amitriptyline	nortriptyline	Imdur®	K-Dur®
Anzemet®	Aldomet®	Inderal®	Isordil®
Ativan®	Atarax®	Inderal®	Toradol®
Aventyl®	Bentyl®	lactulose	lactose
azidothymidine	azathioprine	Lorabid®	Lortab®
Bactroban®	bacitracin	Lorazepam	Alprazolam
Bactroban®	baclofen	Mebaral®	Mellaril®
bepridil	Prepidil®	metaproterenol	metoprolol
Betagan®	Betoptic®	methotrexate	metolazone
Bupivacaine	mepivacaine	metronidazole	mivacurium
bupropion	buspirone	metoprolol	metolazone
Carafate®	Cafergot®	Narcan®	Norcuron®
carboplatin	cisplatin	nifedipine	nicardipine
calciferol	calcitriol	Norvasc®	Navane®
Cardene®	Cardura®	Paraplatin®	Platinol®
Cefotan®	Ceftin®	Paxil®	Taxol®
cephalexin	cephalothin	pentobarbital	phenobarbital
Citracal®	Citrucel®	Plendil®	Prinivil®
chlorpropamide	chlorpromazine	Platinol®	Patanol®
clofazimine	clozapine	Premarin®	Primaxin®
clonidine	quinidine	Prevacid®	Pravachol®
clonidine	Klonopin®	Prilosec®	Prozac®
codeine	Cardene®	quinidine	quinine
Coumadin®	Cardura®	ranitidine	rimantadine
cycloserine	cyclosporine	reserpine	Risperdal®
cyclosporine	cyclophosphamide	Ribavirin	riboflavin
Cytoxan®	Cytosar®	Sublimaze	Sufenta
Demerol®	Demulen®	sulfasalazine	sulfadiazine
Diaβeta®	Zebeta®	sumatriptan	somatropin
diclofenac	Diflucan®	terbutaline	tolbutamide
dopamine	dobutamine	TobraDex®	Tobrex®
doxorubicin	idarubicin	Toradol®	Tramadol
dronabinol	droperidol	Vantin®	Ventolin®
DynaCirc®	Dynacin®	Verelan®	Ferralyn®
Elavil®	Mellaril®	vinblastine	vincristine
Eldepryl®	enalapril	Virilon®	Verelan®
Estraderm®	Testoderm®	Xanax®	Zantac®
ethambutol	Ethmozine®	Zostrix™	Zofran®
fentanyl	alfentanil	Zosyn®	Zofran®
Flomax®	Fosamax®	Zyprexa®	Zyrtec®
fluoxetine	fluvastatin		

a This is not an exhaustive list. A more complete list can be found in Davis.[28]

b Generic names are in lower case.

Fig. 1. Poor handwriting can contribute to the problem of confusion of drug names. In this example, the anticoagulant Coumadin® (warfarin) was dispensed rather than the antidiabetic Avandia® (rosiglitazone). Reproduced with permission from Institute for Safe Medication Practices (ISMP).

example, both Coumadin® and Avandia® are available in 4mg dosage strengths and are administered once daily.

Verbal or telephone orders may increase the possibility that sound-alike drugs will be confused. Finally, if drugs with similar names are stored near one another the potential for confusion and error expands.

5. Solutions to the Problem

Various strategies can be employed to reduce the problem of medication errors caused by confusion of drug names. While the process of naming drugs is beyond the control of individual healthcare providers, action can be taken by regulatory agencies and pharmaceutical manufacturers to identify and use brand names that have been tested prior to drug marketing and have been shown to have less likelihood of confusion. In addition, the systems used by prescribers and pharmacists can be improved to help reduce confusion of drug names. Patients too, need to be educated about their drug therapy to help prevent errors with look-alike and sound-alike drug names.

5.1 Regulatory Authority Intervention

Action by regulatory authorities with regards to drug naming was one of the recommendations in the recent Institute of Medicine report on medical error,[2] and it has already begun to take place. Both the US FDA and the EMEA have developed initiatives to evaluate drug brand names for their error potential before they are introduced into use.

Until recently, the evaluation of proprietary drug names at the US FDA was under the purview of the Office of Post-Marketing Drug Risk Assessment (OPDRA), a division of the Center for Drug Evaluation and Research (CDER).[48] In January 2002, another organisational revision occurred within CDER, which gave way to a new set of names and reporting relationships. This resulted in the Office of Drug Safety, with the Division of Medication Errors and Technical Support (DMETS) being one of the units under the Office of Drug Safety. The Office of Drug Safety has taken over many of the responsibilities that were those of OPDRA, including the review of trademarks proposed by pharmaceutical companies.

The US FDA process includes review by an expert panel, handwriting and voice analyses, computer analysis, review of labelling and packaging, and an overall evaluation of the drug brand name.[49] An example, the name review for the Unithroid™ brand of levothyroxine, has been published on the FDA website and gives further details.[50]

The EMEA also has taken regulatory measures to establish safer names for drug products.[51] The EMEA's Committee for Proprietary Medicinal Products (CPMP) created a subcommittee in October 1999 called the Name Review Group (NRG) to review proposed drug brand names. The NRG reviews the potential name for verbal or written confusion. The agency also has issued guidelines that drug brand names must meet. The final guideline was released in January 2002.

Under the EMEA process, pharmaceutical manufacturers may submit up to three potential brand names in order of preference 4–12 months before the marketing application is submitted. The EMEA then contacts the National Competent Authorities to consider the trademarks. The National Competent Authorities are requested to inform EMEA within 30 days of any objections on the grounds of safety concerns. At their next meeting, NRG reviews the

potential name(s) for the product and presents its findings, including any concerns, to the full CPMP meeting. After presentation to the full CPMP, the decision is conveyed to the manufacturer.

Because of recent regulatory changes described above and the recent publicity surrounding medication errors, many pharmaceutical manufacturers have taken an active role in ensuring that their proposed drug brand names have less risk of confusion. Lambert has developed computer software that is helpful in identifying similar drug names.[52,53] Potential drug names may be evaluated internally or reviewed by an outside consultant. Several companies provide this service for drugs that will be marketed worldwide.

5.2 Improving Prescribing and Dispensing Systems

The processes used to prescribe medications can be improved to reduce the risk of harmful medication errors due to confusion of drug names. Writing both the generic and brand name on the prescriptions can help eliminate confusion. Another simple measure to improve prescription writing is to note the indication for use next to each drug that is prescribed. Including a space for the diagnosis or condition on prescription pads can encourage this function. The indication then acts as a double check when the drug name is confusing or indecipherable, since most confusing name pairs have different indications. If the prescriber that wrote the prescription for Avandia® in the example in figure 1 had written 'for diabetes' somewhere on the prescription blank, the error might have been prevented. Since Coumadin® is not a therapy for diabetes, the pharmacist would have likely investigated the prescription further.

Another possible action is to standardise prescription order writing through preprinted forms. When used properly, preprinted order forms help eliminate problems associated with illegible orders, including confusion of drug names.[54] Care must be taken that preprinted order forms are clear and correct since poorly written forms actually may introduce error into the system.

Another form of prescription order standardisation that may reduce legibility problems associated with confusion of drug names is computerised prescriber order entry (CPOE). When programmed correctly, CPOE can also provide the prescriber with clinical warnings to improve patient care that are pertinent to the individual situation. (e.g. overdose, allergy, drug interaction, etc.). Since look-alike errors may occur even with drug names on a screen, CPOE systems should highlight drug names that look similar. Several studies have demonstrated that CPOE can significantly reduce medication errors.[55,56]

To this point, CPOE systems have been used primarily in the inpatient setting, but numerous systems are being developed for ambulatory use. In April 2000, ISMP issued a white paper that advocated the elimination of all hand written prescriptions by 2003.[57] While this is an ambitious goal, progress is being made in this area, especially in the institutional setting. For an excellent review of CPOE, including barriers for its implementation, see the article by Schiff and Rucker.[58]

In many settings, CPOE systems may not be available for several years. Even when fully implemented these systems will not prevent all medication errors caused by the confusion of drug names. Pharmacists should be aware of common drug names that tend to cause confusion and lead to medication errors. Pharmacists should then establish systems within the entire medication use process to prevent medication errors caused by the confusion of drug names. For example, pharmacists can identify drug names that are most likely to be confused in their setting and program alerts into their computer system.

5.3 Patient Education

Finally, proper patient education can act to help reduce errors from confusion of drug names. If patients understand their drug therapy and disease states, they can help identify and prevent medication errors, including those caused by confusion of drug names.

Unfortunately, evidence from robust empirical studies is not available for many of the solutions proposed above, but this does not mean these approaches are not worthwhile. Leape and others have proposed that patient safety practices (including medication safety practices) be based on a several different types of evidences, not just research.[59] Practices can be based on human factors principles, process inferences, accepted practices from other industries, and even common sense.

6. Conclusion

Look-alike and sound-alike drug names are a common source of medication errors. The literature is replete with examples of confusing drug name pairs. Feasible solutions exist to help reduce the potential for errors from confusion of drug names and include actions by regulatory agencies, pharmaceutical manufacturers, healthcare practitioners, and patients. Working together, these groups may help reduce this common problem in the future.

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