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Adverse Drug Reactions
When the Risk Becomes a Reality for Patients

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Abstract

Communications about the safety of medicines are complex and generally poorly performed. Discussions may not be initiated by healthcare professionals and the lack of a 'common language' to express risk can cause confusion. In the event of a serious adverse drug reaction, prior failures in communication can cause difficulties, and patients may fail to receive adequate information about the nature of their experience. How to communicate openly with patients in order to minimize distrust and maximize future benefits from medicines requires exploration.

Everyday, thousands of patients experience harm from prescribed medication, sometimes resulting in life-changing consequences.[1,2] How prepared are they for this potential outcome, and do healthcare professionals know how to talk to them when it happens?

Communications about the risks of adverse drug reactions (ADRs) can be compromised by time constraints during consultations, and patient inhibitions, preventing them from asking questions about the potential harms from prescribed medicines.[3] In addition, prescribers may focus more on the benefits of the medication, rather than potential harms. Information provided to patients when a new drug is prescribed is patchy at best.[4] An analysis of 462 transcripts of doctor–patient interactions[5] found adverse outcomes were among the least discussed issues in these consultations, with only 8.2% discussing possible ADRs, 2% discussing the risk of occurrence, and 2.3% discussing precautions to avoid the ADR. Feng et al.[6] also found that in doctor consultations, the limitations of medicines were discussed less often than their effectiveness, with strategies for coping with potential ADRs discussed in only 10.3% of cases.

1. The Importance of Communicating Risk

Patients are becoming increasingly aware of the potential risks associated with medicines, and expect to be provided with information regarding their care, including the medicines they are prescribed.[7]

Individuals need information regarding the benefits and harms of a medicine before they decide whether or not to take it. Concerns about potential ADRs, and failure to receive adequate information about them may result in poor adherence to therapy,[8] but addressing these fears in consultations may help tackle this.[9] Failing to warn patients about the risk of a headache when prescribing isosorbide mononitrate (and how this adverse effect will ameliorate), for example, may lead to avoidable non-adherence. In addition,

informing patients of potential ADRs may help in their early detection and management should they occur.

Whilst the ADR profiles of established drugs are often well described, patients are not routinely told of the provisional nature of safety information concerning newly marketed medicines. Being prescribed a newly marketed drug is essentially a decision to participate in postmarketing surveillance (even if not explicitly stated). In the EU, article 23 of EU regulation 1235/2010[10] states that a public list of drugs requiring additional monitoring, such as newly authorized active substances and new biological medicinal products, will be marked by a black symbol in the summary of product characteristics and patient information leaflet, along with the statement ''This medicinal product is subject to additional monitoring''.

A similar symbol, the black triangle, has existed in the UK since 1983, when it was introduced in response to the withdrawal of benoxaprofen due to hepatoxicity.[11] Evidence from the UK suggests that black triangle drugs are associated with a higher rate of spontaneous ADR reporting rates than older established drugs.[12] A recent comparative study of potential safety signals found healthcare professionals' reports often arose from black triangle drugs, whereas patient reports were related to older established drugs.[13] With this in mind, introducing some kind of 'warning' in patient information leaflets for new drugs that not all ADRs are known may be useful. However, whether or not additional pharmacovigilance signals would be generated through such an intervention remains to be proven.

Communicating the potential risk for an, as yet, unknown risk of harm from a drug is a challenge. Historically we know that many serious ADRs are uncovered several years after marketing, making this an essential requirement. Without additional context from healthcare professionals, patients may not become aware of the limited safety data of new drugs.

2. How to Communicate Risk to Patients?

Even with access to established data for the risk of harm from medicines, delivering high quality and context relevant information to patients can be difficult in an increasingly pressurized work environment. Differences in risk perception between the public and healthcare professionals exist, and may be a barrier to clear communication. Verbal qualitative descriptors used by healthcare professionals to describe risk, such as 'rare' and 'common' are problematic, since both patients and healthcare professionals may have a different understanding of these terms.[14] When asked to give a probability estimate for the European Commission's descriptor 'very common', members of the UK general population provided a mean probability of 64%. When provided with 15% frequency instead of the verbal descriptor, they indicated the probability of an ADR would be 20%. Frequency terms such as 'very common' can be also be misread as meaning 'serious'.

The importance of correctly framing and communicating risks to patients has been well described by John Paling.[15] Using absolute numbers to describe risk instead of quoting relative risks in patient communication is often better as relative risk tends to overestimate the real risk posed to patients. For example, a 50% increase in relative risk could indicate an absolute rise in risk from 2 in 1000 to 3 in 1000.

The use of 'odds' to describe risk to patients (e.g. a 1 in 25 chance of developing a particular ADR) has also been popular, but may be confusing to patients as denominators may vary for the risk of different adverse effects; patients may thus find it difficult to accurately compare risks associated with different drugs.

Standardization of risks into frequencies with fixed denominators (e.g. 40 in 1000 patients replacing 1 in 25), however, makes it easier to compare the risks and benefits of treatment. Such standardization also lends itself well to pictorial depictions of harms and benefits, which may allow patients to gain a better understanding of risk. The National Prescribing Centre, part of the National Institute for Health and Clinical Excellence in the UK, has developed a number of patient decision aids (PDAs) which can be used within the consultation process.[16] For example, a matrix of 100 or 1000 images of 'smiley' or 'sad' faces may be used to depict the extent of benefit

or harm associated with a particular treatment, respectively (figure 1). Currently, around 25 PDAs have been developed, although more are to be developed shortly.

But do patients expect to be warned of all possible adverse effects associated with a particular drug? Ziegler et al.[17] examined the views of 2500 outpatients regarding the information they wanted to be given regarding the drugs they were prescribed. Overall, around 75% of all patients wanted to be informed about all adverse effects. However, those attaining a higher level of education expressed less interest in being informed of all risks associated with a drug, perhaps indicating a greater acceptance of dealing with uncertainty. In contrast, those who had previously experienced an ADR were more likely to want to know about all potential ADRs. Fraenkel and Peters[18] exposed patients attending an outpatient clinic to videos describing a rare (1 in 100 000), yet serious, ADR associated with an otherwise well tolerated drug. Female patients and those with poorer health status were more concerned about the potential of the ADR. Focus group work examining the perspectives of US pharmacists, physicians and patients also confirmed patients' desire for transparency regarding the risks of ADRs, although a minority found the 'litany' of potential side effects described to them as off-putting.[19]

3. How to Communicate When the Risk has Become a Reality for the Patient?

For a proportion of patients, the potential ADRs their medications are associated with become manifest. Much research has been undertaken focusing on the epidemiology of ADRs, and their associated morbidity and mortality. But what are the experiences of those who have experienced the effects of ADRs, and what is the long-term impact the ADRs have on the lives of patients?

Recent qualitative work on the impact of serious ADRs such as Stevens-Johnson Syndrome

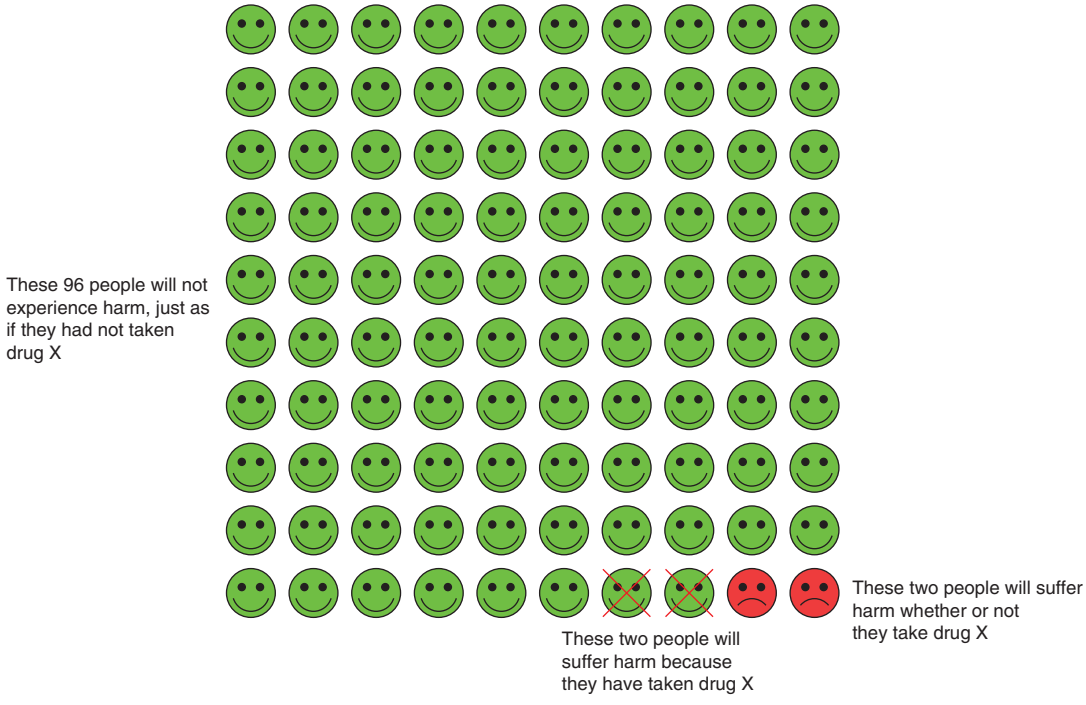

Fig. 1. A Cates plot in 100 people showing how drug X doubles the risk of an unspecified harm compared with no treatment (created using Visual Rx 3.0, which can be downloaded from Dr Chris Cates' EBM website [http://www.nntonline.net/]).

and toxic epidermal necrolysis on patients[20] found many of those who experienced a serious ADR felt that they lacked information at the time of the event, and this influenced their subsequent trust in healthcare professionals and in medicines in general. Such experiences affected their lives long term, and resulted in many avoiding medicines altogether, or avoiding seeking medical attention when ill, regardless of the impact on their health. Others also had unsubstantiated fears, for example, of food supplements or medicated lozenges, indicating that patient education and support after the event might be very useful.

Other research has shown that although patients felt angry and frustrated if they believed that their concerns about a potential ADR were not taken seriously by healthcare professionals, they were relieved that a drug was in fact responsible for their symptoms, rather than a potentially more sinister cause.[21]

Patients and families of those experiencing such serious ADRs also rely heavily on Internet sources for more information, with some contacting online patient support groups. An analysis of unsolicited patient narratives of serious ADRs on the Internet found that many posting on patient websites felt that they lacked information about the ADR they experienced; many had unanswered questions and concerns about the ADR after the event, and sought advice from others with similar experiences.[22] These findings might therefore be helpful in guiding healthcare professionals in communicating and managing those experiencing such ADRs more effectively in the future.

These findings also support work undertaken by Duclos et al.,[23] which examined medical injury claims made by patients; they found that many were frustrated by the lack of information provided to them by healthcare professionals following adverse medical events. Obtaining information was seen as a 'battle', and poor communication led to failure to maintain relationships with those caring for them, further worsening the patient experience.

Models for sharing information with patients already exist, and this is also true for ADRs resulting from medical error. Open disclosure of medical errors has been promoted for a number of years; patients have a right to know why the error occurred, how it will be dealt with, and the future implications of the error to their health.[24] Clear and honest communication during the acute phase of a serious ADR, along with patient education and support after the event also appears important.[20]

Although there is limited evidence that open disclosure discourages litigation, patients are often more upset as a result of poor communication regarding the medical error, rather than by the medical error itself.[25] Frank discussion of the cause of an ADR, future sequelae, and sensible avoidance strategies may therefore help patients make sense of their experience and avoid future distress.[23,26]

4. Conclusions

Communicating the risks of medicines to patients in a way that they can understand and use to make decisions regarding taking treatment may be complex. Many wish to be informed about all potential ADRs associated with medicines but, more importantly, those who do experience an ADR still struggle to find information at the time of the event, with many left with unanswered questions or concerns. Examining the effect of open communication strategies in patients experiencing serious ADRs and their subsequent views on medication safety may provide further insight into this complex area.

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