Automatic generic substitution: losing the right medication for the right patient

Traditionally, doctors have been encouraged to prescribe drugs using their generic names. Increasing cost constraints in both primary and secondary care have resulted in the Department of Health considering the introduction of 'automatic generic substitution' from 2010. Thus pharmacists receiving a prescription for a brand-named drug would automatically substitute it for a generic preparation where that was available. It is unlikely that the prescribing clinician would be notified of the substitution, and the patient would not be able to choose to receive his/her original medication.

The Department of Health recognizes that generic substitution is not always appropriate, as it has suggested but not clarified that certain medicines could be exempt from automatic substitution. They also indicate that prescribers could opt out of substitution on each prescription to ensure a branded medicine is given, possibly by use of a tick-box. These provisions indicate an awareness of clinical and safety reasons for some medicines not being prescribed generically. The requirement for exemptions suggests that dispensers might not always consider the safety and efficacy issues associated with generic substitution. The Department of Health announced in August 2009 that it plans to conduct a full, formal consultation on the arrangements for the implementation of automatic generic substitution this autumn, although there are not yet any details of how doctors can get involved with this.

Two key issues need addressing before automatic generic substitution is considered:

1. The impact of generic substitution on patients' medication concordance
2. The potential impact of varying bioavailability on efficacy and adverse events.

The impact on patients' medication concordance

Generic medicines often differ in size, shape, colour and packaging from each other, and from branded medicine. A patient could receive the same medication, with a different appearance and dosing schedule, on each visit to the pharmacy. In a German study by Himmel et al (2005), one in three patients who had generic substitution had to become accustomed to the different colour or shape of their medication.

Patients with chronic conditions often take multiple medications – in a study of patients prescribed antidepressants, over one-third of those aged 60 years or over received at least eight medications, and the most complex regimens included more than 20 medications (Silkey et al, 2005). Given this complexity, it is unsurprising that many patients develop routines based on the appearance of medications, and any change can be confusing.

Switching reduces adherence to treatment, and is associated with worse outcomes and increased costs (Bainbridge and Ruscin, 2009). These issues are particularly pertinent to older patients, who are more likely to be prescribed multiple medications (Silkey et al, 2005) and their poor adherence may be compounded by confusion, poor eye sight and decreased dexterity.

Further confusion is caused when switching results in changes in dosage schedules. For example, a patient switched from Adcal D3 to Natecal D3 would have to change from taking his/her medication twice daily, preferably in the morning and evening, to taking it 2 hours before or after meals, and must be informed about interactions with common foods, including tea and cocoa, which were not applicable to the original medication.

To avoid such problems, pharmacists would be required to explain the substitution and its implications in every case. However, in one study nearly half of pharmacy instructions were not patient friendly, and key information was missing in many cases (Wolf et al, 2009). In a study of generic substitution by GPs, nearly 50% of patients were dissatisfied with their substituted medicine, with a fifth being 'very unhappy' – the authors concluded that 'great care must be taken to inform patients appropriately' when substitutions are made (Himmel et al, 2005). Switching delivery devices is a particular problem – when switching an inhaled corticosteroid device without a doctor's consultation switched patients were nearly twice as likely to experience unsuccessful treatment (including one or more episodes of hospitalization) as matched control patients (Thomas et al, 2009).

These issues demonstrate that generic substitution without prior consultation between the patient and prescriber could cause confusion and be detrimental to patient care.

Varying bioavailability

Generic medicines have the same active ingredient as the branded medicine but the bioavailability can vary between branded and generic medicines, and between different generic medicines. Branded medicines undergo a rigorous process of clinical trials assessing safety and effectiveness. Generic medicines can be approved on the basis of pharmacokinetic studies demonstrating 'bioequivalence' to the branded medicine. For a generic medicine to be considered bioequivalent, the European Medicines Agency requires bioavailability to be within 0.8 and 1.25 of the original medicine's values. Thus patients being switched between different generic medicines could receive a medicine with 125% bioavailability on one occasion and 80% on the next.

Different patients respond differently to switches in medicines, and one simulation has suggested that as many as 10% of patients could be in potential danger from overdosing or under-treatment when switched between generic medicines (Yim, 2009). Furthermore, Hellstrom and Rudholm (2004) identified a significant increase in adverse events associated with the increase in market share for generic medicines. In a situation where patients could experience adverse effects, automatic substitution by the pharmacist without the prescriber's knowledge could put patients at unnecessary risk.

The Association of the British Pharmaceutical Industry has suggested that certain classes of medicines be exempted from automatic generic substitution. However, is it safe to assume that these are the only cases where generic substitution can be detrimental to the patient's health?

Theoretically, a pharmacist could switch a medication which alters the effects of an exempt medicine. This could be a particular issue for older patients, who often receive multiple medications. There are several clinical examples where generic substitution has resulted in efficacy and safety concerns – oral contraceptive failure (Keith et al, 2001), variable efficacy of proton pump inhibitors (Meredith, 2003), variable dissolution and dispersal of generic alendronate increasing further the risks of oesophageal ulceration (Solanki, 2008), and antiarrhythmics and breakthrough arrhythmias and possible deaths (Reiffel and Kowey, 2000). Generic steroid eye drops often result in precipitation of prednisolone reducing its efficacy while other generic ocular preparations have been associated with corneal toxicity (Fiscella et al, 2001).

In the UK generic prescribing is already high (83%). The General Practitioners Committee has suggested that saving more than 0.4% of primary care medicines costs through automatic generic substitution is unlikely, and inappropriate switching could put patients at risk. Implementing the scheme could also prove costly (Healthcare Republic, 2009). Prescribing clinicians also need to remember that medicolegally the prescriber and not the dispenser is responsible for any adverse event the patient may suffer – are we happy for this to happen or should the responsibility lie with the switching pharmacist?

Conclusions

There is increasing rhetoric from the Department of Health about patient safety, quality and choice. This proposal seems completely contrary to this rhetoric. BJHM

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KEY POINTS

- Under automatic generic substitution, medicine substitution could occur at the pharmacy without the knowledge or consent of the prescribing clinician.
- Automatic generic substitution could result in many switches between different generic preparations, with different preparations and dosing schedules, resulting in confusion and decreased adherence.
- Generic substitutions can result in under-treatment or increased adverse events depending on the bioavailability of the preparation dispensed.
- The prescribing clinician will remain responsible for any adverse events resulting from under- or over-treatment despite the fact that the switch may have occurred without his/her knowledge.

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