NSAIDs expose patients to cardiovascular risk. There is no pharmacological fix other than a decision not to prescribe, or to choose an NSAID with the lowest known risk. The risk is incurred in patients without existing cardiovascular risk factors, even after short-term use.

The recent history of NSAIDs serves as an example of just how hard it can be to influence prescribing attitudes in the face of evidence that clearly indicates harm.

**Cardiovascular safety**

It was following the voluntary withdrawal of the COX-2 inhibitor rofecoxib in 2004 that the cardiovascular safety of NSAIDs as a whole came under scrutiny. Aggressively marketed as a safety breakthrough in terms of gastrointestinal events as a result of its lack of inhibition of COX-1, rofecoxib was later found in clinical trials to cause cardiovascular events. The NSAIDs were already spread along a continuum of harm with respect to their gastrointestinal toxicity, but similar differences in the cardiovascular risk associated with individual NSAIDs began to emerge as systematic reviews and meta-analyses were performed.

By 2005 the Medicines and Healthcare products Regulatory Agency was advising on the increased thrombotic risk associated with nonselective NSAIDs, noting that diclofenac’s risk was possibly similar to that of the coxibs. A 2006 European review again highlighted diclofenac’s coxib-like risk. Both naproxen and ibuprofen carry a lower cardiovascular risk, with evidence suggesting naproxen’s effect on cardiovascular events is neutral.

**Evidence into practice**

How much careful consideration of this evidence is apparent in prescribing data? Not enough seems to be the answer. A recent paper usefully examines how this evidence translated into action within 15 countries. Taking sales and prescription data of NSAIDs in 2011, as a percentage of total sales the high-risk diclofenac accounted for 28 per cent while the relatively low-risk naproxen accounted for less than 10 per cent. Off-evidence prescribing is very common.

While the increased cardiovascular risk to an individual patient may be low, this risk accumulates within the population causing a significant public health issue. Patients may accept the risk of NSAIDs for the symptomatic relief they can provide, but they should be aware of the differing risks they accept with individual drugs.

From 2007 to 2009 the then National Prescribing Centre undertook a large educational intervention including therapeutic bulletins, e-learning materials and therapeutic workshops to influence NSAID prescribing. A time-series analysis of primary-care prescribing data showed a small decrease in total NSAID use, but more importantly a significant fall in diclofenac prescribing and a proportionate increase in the use of naproxen and ibuprofen. However, there was considerable variation between PCTs, and diclofenac continued to account for 39 per cent of prescribed NSAIDs (naproxen 14 per cent).

Continued resistance to the evidence on NSAIDs was ascribed to the ingrained intuitive decision-making processes prescribers employ. Synthesis of new evidence into practice is not easy, requiring more long-term efforts to instil new evidence into normal practice.

Despite these praiseworthy efforts, there is continued therapeutic inertia on diclofenac. A regulatory solution could be the outcome in Europe. A new NSAID would be unlikely to overcome regulatory hurdles with a cardiovascular risk similar to rofecoxib, especially given the lower-risk alternatives on the market already. Why should an older drug be any different purely because of its history?

**Conclusion**

Drug withdrawals are not without cost for patients. After the withdrawal of the NSAID benoxaprofen in the 1980s, following cases of hepatotoxicity, the playwright Dennis Potter complained he had been left ‘high and dry’. A proportion of patients taking diclofenac might react similarly if shifted to an alternative.

More recent prescribing data may show diclofenac losing pole position to naproxen, but given its continued
high proportion of total NSAID prescribing, relying on influencing prescribers may be too optimistic a policy. Evidence of compliance with regulator warnings is mixed, and some form of restriction on availability may be the future.

References

Declaration of interests
None to declare.

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