The rebound effect

Dear Editor

Thank you for the article on adverse drug reactions[1] (*AFP* January/February 2013). A drug effect that could be classified as an adverse reaction is a not uncommon phenomenon that I have observed. I call it the 'rebound effect'.

It manifests as a recurrence (often an amplification) of the actual symptom that the drug is being used to treat, as the effect of the drug wanes between doses or if the drug is ceased. This occurs particularly with long term use.

Symptoms often persist for days or weeks if the drug is not re-introduced, usually subsiding of their own accord. I have particularly noticed this effect with:

- analgesics, particularly opiates and tramadol, but also chronic use of paracetamol +/– codeine
- benzodiazepines, including temazepam
- antidepressants of any type
- proton pump inhibitors
- non-steroidal anti-inflammatory drugs
- nasal decongestants.

I find it helpful to discuss this with patients, as they tend to assume that it is the original problem recurring and that they need to stay on the medication. Sometimes this may be the case, but often it is a drug effect. In the case of long term analgesics, people seem to become sensitised to lower levels of pain. People who have previously been on opiates will often say that the wear-off pain was excruciating and that it took quite a period of abstinence for it to settle.

I wonder if this is perhaps because the drug binds to the endorphin receptors that are useful for natural pain modulation.

It appears that in some cases, the continued use of a symptom modulating medication is primarily treating its own rebound effect. In essence, it has created a need for itself.

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Reference

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Adverse drug reactions

Dear Editor

I enjoyed reading the article 'Adverse drug reactions: Allergy? Side-effect? Intolerance?'[1] (*AFP* January/February 2013), especially the new categorisation of type 4 allergic reactions.

There is, however, a more refined classification of adverse drug events, pioneered by the late Jan Venulet from the World Health Organization Adverse Drug Reactions Monitoring Unit.

The system exonerates or implicates the drug in the putative reaction, at different levels of certainty. The reaction may be 'definitely related', 'probably related', 'possibly related', 'unlikely to be related' or there is 'insufficient information' available about the case to make a decision about drug involvement and causality in the reported side effect.

There are algorithms that can be used to assess causal relationships between drug and side effect.[2] In addition, information about comorbidity, drug-to-drug conjugate, and the age, weight and ethnic origin of the patient are also useful in assessing the cause of adverse drug reactions.[3]

Sometimes long latency drug reactions are also important to be aware of (eg. vaginal carcinoma in users of diethylstilboestrol).

There is under reporting of drug reactions in the community and in the hospital setting. The drug reaction may not be recognised by the patient. If recognised by the patient, the doctor may not report it to the company manufacturing the drug. When the report is received by the drug monitor in the pharmaceutical company, the report may not contain enough detailed information to assess the relationship between drug intake and side effect. Thus, product information produced by the manufacturer may not be accurate. The degree of market penetration of the drug may affect the incidence of reported side effects, as may the 'me too effect' of reporting distort the adverse drug reaction profile of the drug.

A very interesting and enjoyable article, thank you.

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2. Venulet J, Berneker GC, Ciucci AG. Assessing causes of adverse drug reactions. London: Academic Press, 1982.
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Letters to the Editor

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