

fluoroquinolone antibiotics in patients dependent on and withdrawing from benzodiazepines. Participants of an online benzodiazepine withdrawal support group (www.thetrap.org.uk) who reported fluoroquinolone use were asked to fill out a structured questionnaire. Eleven participants reported severe or very severe adverse reactions, one participant reported a moderate adverse reaction, and a further participant reported no reaction to fluoroquinolone treatment. In most cases adverse symptoms resolved within 1 month of cessation of fluoroquinolone dosing. However, in some cases the symptoms persisted with gradual improvement for a period of several months. All participants reported adverse effects similar to those of acute benzodiazepine withdrawal which included depression, anxiety, psychosis, paranoia, severe insomnia, paraesthesia, tinnitus, hypersensitivity to light and sound, and tremors. Four patients became acutely suicidal.

One participant, a female aged 44 years, who had detoxed off high prescribed doses of benzodiazepines 3 months previously, experienced an acute psychotic reaction within 1 hour of commencing norfloxacin and attempted suicide. Her condition quickly deteriorated and she developed repeated seizures; this progressed to status epilepticus, which

failed to respond to treatment in ICU. Worryingly, her medical attendants continued to prescribe norfloxacin while in ICU. Her seizures were only controlled after finishing her norfloxacin course.

Chronic use of benzodiazepines causes compensatory adaptations which cause GABA receptors to become less sensitive to GABA. On discontinuation of benzodiazepines, withdrawal symptoms typically develop which may persist for weeks or months.¹ Antagonism of the GABA_A receptor is believed to be responsible for the CNS toxicity of fluoroquinolones affecting 1–4% of patients treated.² Fluoroquinolones have also been found to inhibit benzodiazepine receptor binding.³ The results of this small study seem to confirm that adverse reactions to fluoroquinolones occur more frequently in the benzodiazepine-dependent population than the 1–4% seen in the general public and may be severe.

Possible explanations for the adverse fluoroquinolone-induced reactions in the current reported patient group include:

- Fluoroquinolones compete directly with benzodiazepines for the benzodiazepine receptor site displacing benzodiazepines and precipitating an acute withdrawal effect.
- Alterations in the GABA_A-benzodiazepine receptor complex

(during benzodiazepine tolerance/dependency status) may increase fluoroquinolone-induced stimulation of the receptor complex.

- Benzodiazepine dose-tapering and/or cessation might be associated with GABAergic underactivity but rebound neuro-excitation following fluoroquinolone exposure.

Participants were asked in the questionnaire about medication and alcohol or drug usage at time of adverse reaction. None of the participants reported anything which could explain their adverse reaction apart from the introduction of a fluoroquinolone. Physicians should, wherever possible, avoid fluoroquinolones in patients who are dependent on or withdrawing from chronic benzodiazepines.

John Girvan McConnell

*Ulster Hospital, Care of the Elderly,
Dundonald, Belfast.*

E-mail: girvin.mcconnell@setrust.hscni.net

REFERENCES

1. Ashton H. Protracted withdrawal syndromes from benzodiazepines. *J Subst Abuse Treat* 1991; **8**: 19–28.
2. Halliwell RF, Davey PG, Lambert JJ. Antagonism of GABA_A receptors by 4-quinolones. *J Antimicrob Chemother* 1993; **31**: 457–462.
3. Unseld E, Ziegler G, Gemeinhardt A, *et al*. Possible interaction of fluoroquinolones with the benzodiazepine-GABA_A-receptor complex. *Br J Clin Pharmacol* 1990; **30**: 63–70.

DOI: 10.3399/bjgp08X280317

Correction

In the April 2008 issue of the *BJGP* we incorrectly published the key of Figure 1 in the following letter:

Thurlow VR, Bailey IR, Payne NM. Centralised pathology services. *Br J Gen Pract* 2008; **58(549)**: 278–279.

In Figure 1 (Effect of temperature and phlebotomy on the incidence of hyperkalaemia) the labels for the key were transposed. We apologise for this error. The corrected version is available online.

DOI: 10.3399/bjgp08X280326