LETTERS

Letters to the Editor

Warfarin and beetroot

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The recent Letter to the Editor about warfarin and beetroot by Louise Vanpraag and the response from Philip Tideman and colleagues[1] both miss the point about warfarin and beetroot. It is commonplace for those eating beetroot to have red urine (beeturia) or red faeces, or both, and such symptoms in those taking warfarin can be worrying. On many occasions, warfarin dosage has been adjusted unnecessarily and there have been many unnecessary urinary and bowel investigations. The beetroot-induced symptoms are of no importance and of course can occur in anyone eating beetroot.

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REFERENCES

1. Vanpraag L. Warfarin and beetroot [letter]. Aust Prescr 2015;38:150. http://dx.doi.org/10.18773/austprescr.2015.061

Philip A Tideman, Rosy Tirimacco, Andrew St John and Gregory W Roberts, the authors of the article, comment:

This is an excellent point, and any counselling regarding the signs of bleeding should include alerting the patient to the possibility of red or pink urine or faeces after eating beetroot. Likewise, clinicians should enquire about beetroot consumption for any patient presenting with pink or red urine or faeces.

Warfarin, St John's wort and INR

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In regards to the article on the management of warfarin therapy,[1] the statement on page 46 'drugs that may increase INR – macrolide antibiotics, imidazole antifungals, sulfamethoxazole/trimethoprim, amiodarone, statins, some non-steroidal anti-inflammatory drugs and some complementary medicines such as St John's wort' may not be correct.

In the literature, St John's wort *decreases* the INR through induction of cytochrome P450 (CYP)-mediated metabolism of warfarin and increases warfarin clearance.[2-9]

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REFERENCES

1. Tideman PA, Tirimacco R, St John A, Roberts GW. How to manage warfarin therapy. Aust Prescr 2015;38:44-8. http://dx.doi.org/10.18773/austprescr.2015.016
2. Jiang X, Williams KM, Liauw WS, Ammit AJ, Roufogalis BD, Duke CC, et al. Effect of St John's wort and ginseng on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects. Br J Clin Pharmacol 2004;57:592-9. http://dx.doi.org/10.1111/j.1365-2125.2003.02051.x
3. Jiang X, Blair EY, McLachlan AJ. Investigation of the effects of herbal medicines on warfarin response in healthy subjects: a population pharmacokinetic-pharmacodynamic modeling approach. J Clin Pharmacol 2006;46:1370-8. http://dx.doi.org/10.1177/0091270006292124
4. Yue QY, Bergquist C, Gerdén B. Safety of St John's wort (*Hypericum perforatum*). Lancet 2000;355:576-7. http://dx.doi.org/10.1016/S0140-6736(05)73227-X
5. Zhou S, Chan E, Pan SQ, Huang M, Lee EJ. Pharmacokinetic interactions of drugs with St John's wort. J Psychopharmacol 2004;18:262-76. http://dx.doi.org/10.1177/0269881104042632
6. Anticoagulants + Herbal medicines; St John's wort (*Hypericum perforatum*). In: Baxter K, editor. Stockley's Drug Interactions. London: RPS Publishing; 2015. www.medicinescomplete.com/mc [cited 2016 Mar 1]
7. Kaminsky LS, Zhang ZY. Human P450 metabolism of warfarin. Pharmacol Ther 1997;73:67-74. http://dx.doi.org/10.1016/S0163-7258(96)00140-4
8. Moore LB, Goodwin B, Jones SA, Wisely GB, Serabjit-Singh CJ, Willson TM, et al. St. John's wort induces hepatic drug metabolism through activation of the pregnane X receptor. Proc Natl Acad Sci USA 2000;97:7500-2. http://dx.doi.org/10.1073/pnas.130155097
9. Nebel A, Schneider BJ, Baker RK, Kroll DJ. Potential metabolic interaction between St. John's wort and theophylline. Ann Pharmacother 1999;33:502. http://dx.doi.org/10.1345/aph.18252

Gregory Roberts, one of the authors of the article, comments:

Thank you for pointing out the error in the article.[1] St John's wort induces CYP enzymes with a resultant increase in warfarin clearance and decrease in INR, not a possible increase in INR as described in the article. Decreases of 20% in AUC (area under the curve) have been noted in single warfarin dose studies,[2] so while prudent INR monitoring should be undertaken, the interaction is likely to be of clinically minor importance.

The Editorial Executive Committee welcomes letters, which should be less than 250 words. Before a decision to publish is made, letters which refer to a published article may be sent to the author for a response. Any letter may be sent to an expert for comment. When letters are published, they are usually accompanied in the same issue by any responses or comments. The Committee screens out discourteous, inaccurate or libellous statements. The letters are sub-edited before publication. Authors are required to declare any conflicts of interest. The Committee's decision on publication is final.

REFERENCES

1. Tideman PA, Tirimacco R, St John A, Roberts GW. How to manage warfarin therapy. Aust Prescr 2015;38:44-8. http://dx.doi.org/10.18773/austprescr.2015.016
2. Jiang X, Williams KM, Liauw WS, Ammit AJ, Roufogalis BD, Duke CC, et al. Effect of St John's wort and ginseng on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects. Br J Clin Pharmacol 2004;57:592-9. http://dx.doi.org/10.1111/j.1365-2125.2003.02051.x

Benzodiazepines

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I congratulate the authors of the recent article on benzodiazepines[1] for highlighting that, although not as bad as in the 1980s,[2] benzodiazepine abuse and misprescribing remain a problem, especially in the area of polysubstance abuse.

I would like to make a suggestion. Regarding the Table, I tend to classify flunitrazepam (also now a Schedule 8 drug) and nitrazepam as long-acting benzodiazepines. There are usually three groups of benzodiazepine cited for clinical action: short-, intermediate- and long-acting. The authors have grouped short and intermediate, but this can give a misleading impression to prescribers, especially regarding these two benzodiazepines notorious for their accumulation and morning-after effects. For example, the product information for nitrazepam states 'elderly debilitated patients may show a significant increase in elimination half-life.'

The other minor point I would make is that the approximate half-life of diazepam in the Table (20–80 hours) is misleading. Its active metabolite nordiazepam has a half-life of 96 hours according to the product information, and is marketed as an active compound in some countries.

Finally, a little mnemonic to help students, GP trainees and addiction trainees with outpatient benzodiazepine withdrawal is TTT i.e. Ten per cent reduction in dose per week over Ten weeks with an exponential/terminal Taper.

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REFERENCES

1. Brett J, Murnion B. Management of benzodiazepine misuse and dependence. Aust Prescr 2015;38:152-5. http://dx.doi.org/10.18773/austprescr.2015.055
2. McNamara K, Lewin T. General practitioners' recognition and management of psychiatric illness. Med J Aust 1989;151:250-1.

Bridin Murnion and Jonathan Brett, the authors of the article, comment:

Thank you for your observations regarding the half-lives of nitrazepam and flunitrazepam. Indeed we feel that any use of benzodiazepines in elderly debilitated people carries a significant risk regardless of half-life. The Table is perhaps an arbitrary division of benzodiazepines based on half-life as there is a degree of inter-individual variability and, as you say, active metabolites are also important. The pharmacodynamic effects of each drug may also differ to some degree and this may also impact on toxicity.

Prescribing for people in custody

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I read the article on prescribing for people in custody[1] with interest. It raised many valid points and covered several narcotics and other sedatives among high-risk medicines. I would like to draw attention to antihyperglycaemic drugs, especially insulin which requires expertise on site to monitor its use and potential misuse. This is more important for inmates with type 1 diabetes in high-security facilities who mostly do not have access to diabetic meals, and where food provided after hours is mostly not diabetes friendly. In my experience dealing with patients on insulin in custody is really challenging. Rigid schedules and limited availability of healthcare staff add to the complexity of this situation.

It is unfortunate that in spite of the high prevalence of diabetes in the community, especially in those who are disadvantaged, there is no specific policy on management of people with diabetes in custody.

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REFERENCE

1. Hampton S, Blomgren D, Roberts J, Mackinnon T, Nicholls G. Prescribing for people in custody. Aust Prescr 2015;38:160-3. http://dx.doi.org/10.18773/austprescr.2015.057