Ps not infrequently ask me to see patients for a home medicines review (HMR) where there appears to be a subtherapeutic response to treatment. Perhaps not surprisingly, there is often a suspicion of poor adherence and persistence with medication.

Neville was one such patient. With a history of a stroke, controlling Neville’s hypertension had been a priority and not only had this proved challenging, but recent readings both in the clinic and with Neville’s home blood pressure monitoring showed greater fluctuation than normal. Neville, a 78-year-old widower, had been prescribed perindopril and indapamide, atorvastatin and aspirin for several years, and with previous problems of lercanidipine-induced oedema, atenolol had been added around six months ago to try to optimise blood pressure control. It was following this most recent change that the fluctuations in Neville’s blood pressure had become most apparent.

Looking beyond compliance

Given this background, I obtained a copy of Neville’s pharmacy dispensing history and was somewhat surprised to see regular monthly supplies of all his antihypertensive medications. While never a guarantee of compliance, the fact that even pensioners in Australia pay something for most of their medication does tend to result in more judicious requests for repeats; but as usual, I approached the review with an open mind.

It emerged that Neville had clear routines for his medication: packing his own Dosette box once a week, taking all his medications together each morning, and he denied any swallowing problems. When I created the opportunity for ‘non-compliance confession time’ by asking what he did when he forgot his tablets, I thought I was about to be given my marching orders. Poor compliance was looking increasingly unlikely to be the problem, so we moved on to discuss intake of salt, liquorice and energy drinks; but all to no avail.

Then, just as I was thinking his blood pressure control issues were going to remain a mystery, I asked Neville about what he took his tablets with and suddenly a plausible explanation became apparent.

Fruit juice interactions

Grapefruit juice was identified as being a culprit in numerous drug interactions well before the millennium. However, since then, other fruit juices have also been found to alter the effect of certain medications. While grapefruit juice interactions occur by increasing the bioavailability of drugs metabolised by CYP3A4, some of the more recently discovered fruit juice interactions work via a different pathway, namely the organic anion-transporting polypeptides (OATPs).

Naturally-occurring compounds in apple, orange and grapefruit juice have been found to inhibit the OATPs found in the gut, and OATPs facilitate the absorption of several medications – including atenolol. Neville mentioned that he sometimes had a glass of apple juice with his breakfast.

The amount of information on these OATP-mediated interactions varies, as does the extent to which absorption is compromised and consequently the likely significance. The drugs for which the effect appears to be particularly clinically significant are aliskiren, atenolol, ciliprolol, ciprofloxacin and fexofenadine. In the case of the beta-blockers, fruit juice may reduce exposure to these medications by around 80%.

Table 1 lists medications that are either known to be affected by OATP-mediated fruit juice interactions, or where there is the potential for an interaction based on an awareness that OATP plays a role in their absorption. With CYP3A4-mediated juice interactions, the effect is long-lasting and total avoidance of grapefruit juice is usually recommended; however, OATP-mediated interactions can be avoided by separating the intake of relevant fruit juice from those medications.
More to learn

So what happened with Neville? I explained the potential issue with fruit juice and Neville was happy to take his tablets with water every morning – and if he fancied a glass of juice, he would drink it separately at lunchtime. Neville’s blood pressure stabilised on subsequent monitoring, but unfortunately it still remains higher than ideal, so other causes for this and possible management options are now being explored.

Atenolol remains the second most widely prescribed beta-blocker in the UK, with over 600,000 prescriptions typically being dispensed each month in England.\(^5\) Given this, it is timely to raise awareness among both health professionals and patients that apple, orange and grapefruit juice can significantly reduce the effect of atenolol if given within four hours.

With further research underway, it is likely that our understanding of fruit juice interactions will continue to evolve.

References


Declaration of interests

None to declare.

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