NORTHERN IRELAND
MEDICINES MANAGEMENT

HSC Health and Social Care Board

Learning from SAIs involving Tacrolimus

May 2021

Background

A number of incidents have been reported recently where clarithromycin was prescribed to patients who are taking tacrolimus. In the example cases below, the interactions were picked up before the patient came to any long term harm, but they could have been fatal.

Immunosuppressants like tacrolimus can increase susceptibility to infection such as lower respiratory tract infections (LRTIs). However, clarithromycin is predicted to increase the concentration of tacrolimus (BNF potential severe interaction) and therefore the Shared Care Guideline (SCG) notes that clarithromycin **should not be initiated by a GP unless discussed with specialist.**

Example Case One

A transplant patient attended the emergency department complaining of facial swelling, vomiting, diarrhoea, severe tremor and headache. Bloods were taken that revealed a high tacrolimus level and reduced kidney function. The patient had been prescribed clarithromycin to treat an upper RTI.

Why did it happen?

The GP issued clarithromycin as the warning on the GP clinical system was missed and the GP did not know about the interaction. The prescription was then dispensed in a pharmacy that did not have the patient's medication records, i.e. not the patient's regular pharmacy. After becoming unwell, the patient phoned the out of hours GP who advised continuing with the antibiotic and prescribed an anti-emetic. The patient was later admitted to the emergency department. The doctor in the emergency department advised the patient to continue with the antibiotic and discharged the patient. As symptoms hadn't improved, the patient contacted the GP to request further clarithromycin, and was prescribed a second course. This time the patient attended her regular pharmacy — the pharmacist questioned the interaction but continued to supply as the patient said that she had already completed one week of the course and relayed the assurance given by the prescriber that this was the correct antibiotic. The patient was admitted to the emergency department a second time, when bloods were eventually taken.

Example Case two

A renal transplant patient attended for a routine clinic appointment, feeling unwell, tired and lethargic. The patient had received 3 courses of antibiotics over recent weeks to treat a LRTI, the most recent of which was clarithromycin. Routine bloods revealed a high tacrolimus level and the patient developed an acute kidney injury with a creatinine level of 151 mmol/l.

Why did it happen?

The GP issued clarithromycin, which the patient had taken previously, but not since starting tacrolimus. Although the clinical system warned of an interaction between tacrolimus and clarithromycin, the prescriber incorrectly presumed the patient had taken the *combination* before without ill-effect so ignored the warning. The BNF and SCG were not checked during the consultation.

When the prescription was dispensed at the pharmacy, an interaction warning again appeared on the computer system, noting this major interaction could lead to renal toxicity and required renal function monitoring and possible adjustment of the tacrolimus dose. The warning label was printed off and attached to the bagged prescription but the interaction was not discussed with the prescriber or the patient when the medication was collected.

See over page for what this GP practice and community pharmacy have done to prevent recurrence.

What has been done to prevent recurrence?

In the GP practice:

- The issue and processes were discussed with all clinical staff
- Prescribers assess clinical system alerts before bypassing. Where required, alerts are acted on and appropriate records made
- Patients on tacrolimus have their notes flagged with a warning **"******on tacrolimus caution with clarithromycin and erythromycin – speak to specialist*****"**
- Note: the practice originally wanted to record the interaction as causing an allergy in all patients taking tacrolimus. This was ruled out as these antibiotics could be prescribed in certain circumstances under *specialist* supervision (i.e. if no other antibiotics were suitable to treat an infection)
- Prescribers refer to SCG when making changes to treatment plans
- Contact details for secondary care shared care providers are documented in the record of patients taking immunosuppressant drugs and a process put in place to ask for specialist advice when needed
- Prescribers now have a lower threshold for considering referral for x-ray or other investigations before prescribing repeated antibiotic courses
- Patients are reminded of the need for blood tests if exhibiting ongoing symptoms.

In the Community Pharmacy:

- The pharmacy updated their SOPs for:
  - ◊ Interactions: all interactions flagged by the pharmacy computer system must be brought to the attention of the pharmacist for assessment. The pharmacist should use their professional judgement to assess if the interaction should be brought to the attention of the prescriber and/ or if the patient needs counselled. Guidance is available in the BNF on levels of severity and evidence behind each interaction to help the pharmacist make this decision. Interactions must not be left for patients / carers to follow-up
  - ◊ Handing out medication: guidance on when pharmacists need to speak to patients/ representatives and how this is highlighted to other staff
  - ◊ High risk drugs: when pharmacists need to provide guidance and information to patients, e.g. when presented with repeated prescriptions for antibiotics for immunosuppressed patients, checking with the patient if they are having their bloods checked, contact prescriber as needed etc.
  - ◊ Authorising appropriate levels of staff members to carry out specific tasks
- All staff including pharmacists were trained on the new processes.

Actions

- GP practices and community pharmacies are asked to review their processes relating to management of interactions and high risk drugs and amend as appropriate to reduce the risk of similar incidents.

This newsletter has been produced for GPs and pharmacists by the Regional Pharmacy and Medicines Management Team.

If you have any queries or require further information on the contents of this newsletter, please contact one of the Pharmacy Advisors in your local HSCB office:

Belfast Office: 028 9536 3926 South Eastern Office: 028 9536 1461 Southern Office: 028 9536 2104

Northern Office: 028 9536 2812 Western Office: 028 9536 1010