LEARNING LIGHT

Patients are less likely to be infected by HIV if they are given antiretrovirals shortly after exposure. Adherence to therapy and avoiding drug interactions are vital for success of post-exposure prophylaxis

Use of antiretrovirals for post-exposure prophylaxis against HIV

By **Sharon Byrne**, MRPharmS, and **David Annadale**

Grisho / Dreamstime.com

Timely initiation of antiretrovirals can help prevent HIV in people exposed to an infected source

Post-exposure prophylaxis (PEP), sometimes called post-exposure prophylaxis following sexual exposure (PEPSE), is the treatment given to people after suspected exposure to HIV. Research indicates that there is a period after exposure to HIV when antiretrovirals could be used to inhibit viral replication and prevent integration of the virus into host DNA, thereby aborting HIV infection.

After HIV crosses the mucosal barrier it can take 48–72 hours to detect the virus in regional lymph nodes and up to five days before it can be detected in blood.[1] Therefore, early initiation of antiretrovirals is crucial, ideally within one hour and definitely within 72 hours of exposure. Studies suggest that PEP may be protective in certain circumstances and that delays in starting PEP may adversely affect its efficacy.[1] PEP should be started promptly after any high-risk exposure (see below) and stopped later if the source is found to be HIV negative.[2]

Risk assessment

The likelihood of acquiring HIV varies according to the type and source of exposure, and PEP is not always recommended.

Whether PEP is recommended depends on the viral load of the source (if known to be HIV positive), or whether the source is from a high prevalence group or area (if HIV status is unknown). Clear guidance on when PEP is recommended can be found on the British Association for Sexual Health and HIV website.

The estimated risk of transmission per exposure from a known infected source is:

- >90% for a blood transfusion
- 0.3% for a needlestick injury
- 0.03–3.0% for sexual exposures, with a greater risk associated with receptive anal intercourse
- 0.67% for sharing injecting equipment
- 0.09% for exposure to mucous membranes

Starting treatment

Patients requiring PEP are most likely to present to occupational health, accident and emergency departments and genitourinary medicine clinics; to facilitate rapid access to treatment, many of these locations keep starter packs of PEP that contain five- or seven-day supplies of the required antiretrovirals.

The current PEP regimen is Truvada (tenofovir disoproxil plus emtricitabine) one tablet daily and Kaletra (lopinavir boosted by ritonavir) two tablets twice a day for one month.

A blood test should be taken at baseline to measure a patient's full blood count, urea and electrolytes, liver function tests, and lipid and glucose levels. The patient is also screened for hepatitis B and C, and other sexually transmitted infections if necessary. Women should be screened for pregnancy and asked about contraception use.

Patients are seen for follow-up after five to seven days (to receive further supply of PEP and a hepatitis B vaccine if required), after two weeks (to measure liver function tests and urea and electrolytes) and again at one month when the PEP regimen has been completed.

A final test to check for HIV infection is performed at 12 weeks. A positive result warrants the referral of the patient to an HIV clinic for counselling and further care.

Adherence issues

Plasma drug levels need to be maintained above therapeutic values throughout treatment; therefore, appropriate counselling on the importance of strict adherence to the timing of doses is crucial

FOR DISCUSSION

- Is there a post-exposure prophylaxis (PEP) policy at your organisation?
- Should non-HIV specialists be involved with the provision of PEP?
- What factors need to be considered when a patient who requires PEP is taking an interacting drug?

OBJECTIVES

Studying this article will help you gain a better understanding of:

- The concept of using post-exposure prophylaxis (PEP) to prevent HIV infection
- The antiretrovirals used in PEP and the main counselling points for ensuring adherence to therapy
- Potential drug interactions and their management

TEST YOURSELF

1 How long after HIV crosses a mucosal barrier can it take for the virus to be detected in blood?

a) Up to an hour
b) Up to one day
c) Up to five days
d) Up to three weeks
e) Up to two months

2 Which of the following types of exposure from an infective source is the most likely to lead to the transmission of HIV?

a) Blood transfusion
b) Sexual intercourse
c) Exposure to a mucous membrane
d) Needlestick injury
e) Sharing injecting equipment

3 The current first-line post-exposure prophylaxis treatment regimen is:

a) Truvada one tablet twice a day
b) Truvada one tablet daily
c) Kaletra two tablets twice a day
d) Answers a and c
e) Answers b and c

4 Which of the following blood tests taken at baseline is checked after two weeks?

a) Full blood count
b) Liver function tests
c) Lipid levels
d) Glucose levels
e) Hepatitis B screen

5 Which of the following medicines is appropriate to use with Kaletra?

a) Pravastatin
b) Simvastatin
c) St John's wort
d) Budesonide plus formoterol (Symbicort)
e) Ethinylestradiol plus levonorgestrel (Microgynon 30)

to optimise the success of PEP in preventing HIV infection. The first dose should be taken immediately and subsequent doses can be taken at convenient times. This may mean that the next dose is closer to the first than normal. Patients should also be advised:

- That each dose should be taken within an hour of the scheduled time
- That if they miss a dose they should take it as soon as they remember unless it is a few hours before the next dose, in which case they should omit it and take the next dose as normal
- To see their prescriber if a dose is more than 72 hours late
- That if they vomit within one hour of taking the dose they need to take another dose

Box 1: Notable drug interactions with Kaletra

DRUG	PROBLEM	MANAGEMENT
Simvastatin	Large increases in simvastatin levels. Much higher risk of myopathy, including rhabdomyolysis	Contraindicated with Kaletra. Stop immediately and switch to pravastatin or low-dose atorvastatin
St John's wort	Enzyme induction lowers Kaletra levels. Effect remains for approximately two weeks after cessation	Kaletra not recommended. Use alternative regimen
Corticosteroids	High systemic absorption of inhaled or intranasal fluticasone or budesonide	Avoid during therapy and change to beclometasone
Hormonal contraception	Reduced effectiveness of oral, implant and patch contraceptives	Use barrier method of contraception for duration of therapy and four weeks after

Short-term toxicity can have a major impact on adherence. The most common side effects associated with Kaletra are diarrhoea, nausea and vomiting; for Truvada the most common are headache, dizziness and nausea. Taking tablets with food can help reduce nausea, but they can be taken without food.

Symptoms tend to be worse in the first few days of treatment but usually improve within two weeks — yet some patients continue to experience side effects, particularly diarrhoea and nausea, for the duration of treatment.

It is important to counsel patients on how to recognise and manage side effects effectively using antiemetics and antidiarrhoeals. Because prevention of nausea is more effective than treatment, patients should be advised to take an antiemetic, such as domperidone, 20–30 minutes before each dose of PEP for the first few days. Domperidone and loperamide are included in PEP starter packs and can be continued for the duration of treatment if necessary. Paracetamol can be used to manage headaches.

In some cases it may be necessary to change the PEP regimen if side effects are impacting on a patient's daily life and affecting adherence.

Drug interactions

Ritonavir (in Kaletra) is a potent inhibitor of the cytochrome p450 isoenzyme CYP3A4. This inhibitory effect is used to increase lopinavir concentrations so that lower doses can be administered; however, for other medicines metabolised by CYP3A4, this effect can be problematic. There are many drug interactions possible with Kaletra and so it is essential to take an accurate drug history — including herbal preparations, inhalers and nasal sprays, recreational drugs and recently stopped medicines. Examples of some of the most common drug interactions are described in Box 1 and more information can be found in the BASHH guidelines and at www.hiv-druginteractions.org.

Management of the interaction may involve changing the dose of the existing medicine or switching treatment. When stopping a medicine, enzyme induction effects can take time to dissipate; furthermore, if the medicine has a long half-life then high levels of the drug could remain in the blood for some time after the medicine is stopped. In such cases, an interaction could still occur and a different PEP regimen, which does not include Kaletra, might need to be prescribed, eg, Truvada one tablet daily and raltegravir 400mg twice a day.

References

1 British Association for Sexual Health and HIV. National guideline for the use of post-exposure prophylaxis for HIV following sexual exposure. December 2011. www.bashh.org/documents/4076.pdf (accessed 3 July 2013).
2 Department of Health. HIV post-exposure prophylaxis: guidance from the UK Chief Medical Officers' expert advisory group on AIDS. London: The Department; 2008.

Sharon Byrne is co-chair of the HIV Pharmacy Association and UK Foundation for AIDS Research trustee. David Annandale is specialist pharmacist at Brighton and Sussex University Hospitals NHS Trust.
E: sharonjay2011@gmail.com

Answers

1 c; 2 a; 3 e; 4 b; 5 a