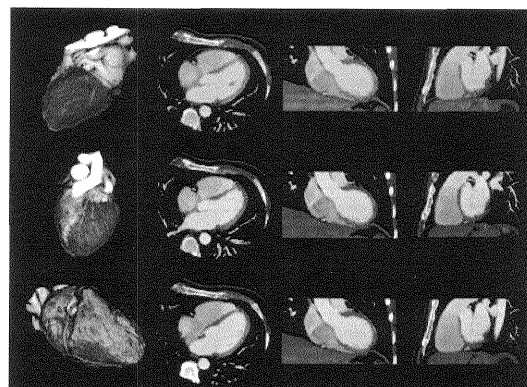


Using glyceryl trinitrate spray

By Josie Hughes and Ella van Tienen



Case study

Simon, a 55-year-old, slightly overweight gentleman comes into the pharmacy with a prescription for Nitrolingual Pumpspray to be used when required, metoprolol 25 mg twice daily, aspirin 100 mg daily and atorvastatin 40 mg daily. He is a little shaken up as he had to call an ambulance over the weekend because he was experiencing severe chest pain. Fortunately he only had to stay in hospital overnight and the doctors told him he had had an attack of angina. He has now been to his GP who prescribed him these new medications and he is a little overwhelmed. You notice a packet of cigarettes in his top pocket.

Learning objectives

After reading this article you should be able to:

- Provide a customer with useful information on angina.
- Counsel a customer on how to use a GTN spray.
- Describe symptoms that warrant referral to a doctor.

Competencies addressed:

2.1.1, 2.1.2, 3.1.1, 3.1.2, 3.1.3, 3.1.5, 3.2.2, 4.2.2, 7.3.2

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Can you tell me more about angina?

Angina, also called angina pectoris, is a clinical syndrome characterised by discomfort in the chest, jaw, shoulder, back or arm.¹ Symptoms may also include shortness of breath, nausea and sweating.² It occurs when the oxygen demands of the heart exceed the supply, resulting in myocardial ischaemia. Angina fits broadly into two classifications:

- **Chronic stable angina** is most commonly brought on by exertion or emotional stress,² and is relieved by rest or the use of a short-acting nitrate.³ It is most commonly caused by atherosclerotic coronary heart disease, in which a fixed obstruction in one or more coronary arteries restricts the blood flow to the heart. This type of angina results in ischaemia only when the myocardial oxygen demand is increased.²
- **Unstable angina** is an acute coronary syndrome which is intermediate between chronic stable angina and acute myocardial infarction (AMI). It usually occurs due to disruption of an atherosclerotic plaque, resulting in platelet aggregation, thrombus formation and vasoconstriction. Unstable angina, like chronic stable angina, is usually a result of coronary atherosclerosis. However, in unstable angina the blood flow to the heart is restricted to the extent that ischaemia can occur even when the heart does not have an increased oxygen demand.² The presentation is not as predictable as with chronic stable angina, and it often presents as severe and frequent attacks. It can cause recurring or prolonged

angina attacks at rest and often has diminished responsiveness to sublingual nitrates.²

Angina, therefore, indicates the presence of coronary heart disease (CHD) which is responsible for 17% of all deaths in Australia.⁴ Patients who suffer from angina have 2.5–3.2 times the risk of dying from CHD compared to patients who do not suffer from angina.⁵

The risk factors for angina include increasing age, male sex, family history, elevated serum LDL cholesterol levels, diabetes, smoking, high blood pressure, obesity and physical inactivity.³

How does GTN spray work?

Glyceryl trinitrate (GTN) is a short-acting nitrate used to help restore the balance between supply and demand of oxygen to the heart. Nitrates provide the body with an additional source of nitric oxide which is responsible for vasodilation. Through dilating coronary vessels, nitrates improve myocardial perfusion, reducing myocardial ischaemia and associated ischaemic pain.

Due to its rapid onset of action and established efficacy, sublingual GTN is considered the drug of choice for the acute relief of an attack of chronic stable or unstable angina.⁶

How do I use GTN spray?

Sublingual GTN spray is suitable for immediate relief of angina.¹ If the patient experiences chest pain, they should rest, and stop immediately if they are engaging in physical activity. They should be advised to spray one dose (400 mcg) of GTN under the

tongue.⁷ They should be instructed to sit or lie down as they may experience light-headedness and dizziness. If the pain or discomfort does not go away with the first dose, the patient can repeat the dose after five minutes up to a maximum of two metered doses.⁸ After 10 minutes, if complete relief of symptoms has not occurred, the patient should be instructed to dial 000 for an ambulance.⁹

GTN can also be used to prevent the onset of exercise-induced angina.^{1,7} The patient can spray one dose of GTN under the tongue approximately 5–10 minutes prior to physical activity which is expected to trigger angina.⁷

Will it produce any side effects?

Most adverse effects of sublingual GTN are due to the vasodilator effects of the GTN, and include headache and hypotension which are generally dose-related.⁸ Rare cases of a drop in blood pressure and/or orthostatic hypotension have been reported when GTN was used for the first time or the dose was increased, which may be accompanied by a reflex increase in heart rate, somnolence, dizziness and weakness, especially on standing.⁸

Could I take anything else?

Alternatives to GTN spray include GTN sublingual tablets (containing GTN 600 mcg) or isosorbide dinitrate 5 mg sublingual tablets. With both of these alternatives, one tablet should be dissolved under the tongue, and then repeated every five minutes if pain persists up to a maximum of three tablets.¹⁰ The patient should be instructed not to swallow the tablet, but place it under the tongue or in the cheek. Either of these alternatives may be used during episodes of angina or before an activity expected to bring on angina, as with the GTN spray.^{7,11}

A benefit of the sublingual tablets is that, once the pain is relieved, the tablet can be removed from the mouth or swallowed to avoid adverse effects, such as headaches.⁷ However, the GTN tablets are not as stable as the spray and must be kept away from moisture, heat and light. They must be stored in the manufacturer's bottle, should not be carried close to the

body or other heat source, and should be discarded three months after opening.⁷ The spray, therefore, is often a more appropriate option for those with infrequent angina.

What other medications are used to prevent angina?

There are a number of medications available to assist in the prevention of angina. Before starting treatment with anti-anginal drugs, the management of risk factors should be considered. Low dose aspirin should be used in all patients with ischaemic heart disease¹² and the management of dyslipidaemia and hypertension will reduce the risk of AMI. Statins should be prescribed to all patients with ischaemic heart disease regardless of their cholesterol level to prevent serious vascular events and death from any cause.¹² The patient should be informed early in the course of treatment of the benefits of taking multiple medications for preventing angina and minimising their risk of other cardiac events.¹²

The role of anti-anginal drugs is to improve the balance of oxygen supply and to reduce demand on the myocardium to relieve angina symptoms. Drug choice is affected by the severity of angina and any coexisting diseases, and may be used alone or in combination.¹³

Beta-blockers are recommended as first-line therapy to reduce the frequency of angina, prolong exercise capacity and decrease the risk of adverse cardiac events and mortality.¹³ They have also been shown to reduce the risk of re-infarction, sudden death and mortality post-AMI.¹⁴ Carvedilol, bisoprolol and controlled-release metoprolol are useful in patients with co-existing heart failure.¹³ Side effects include cold extremities, bradycardia, fatigue and nightmares.¹⁵ Beta-blockers should be used with caution in diabetic patients as they can mask important signs of hypoglycaemia, and they are contraindicated in asthma.¹⁵

Calcium channel blockers may be used in combination with beta-blockers, or as an alternative if beta-blockers are contraindicated, and exhibit similar symptomatic efficacy in angina to beta-blockers.¹³ Peripheral oedema, headache, flushing and palpitations are common side effects of

the dihydropyridines, and constipation is a common side effect of verapamil.¹⁶ Caution should be used if diltiazem is combined with a beta-blocker, and verapamil should not be combined with a beta-blocker due to the risk of bradycardia and heart block.¹³

Long-acting nitrates are used for the prevention of angina in patients who suffer from frequent ischaemic symptoms. They act by causing a reduction in venous return and preload to the heart, reducing the oxygen requirements of the heart.¹⁷ Common side effects include headache, flushing, palpitations, orthostatic hypotension, fainting and peripheral oedema.¹⁷ Nitrate tolerance can occur with continuous use of nitrates. To avoid this, a nitrate-free interval of 10–12 hours should be observed each day at a time when symptoms are least likely (e.g. overnight).¹³

Is there anything else I can do to help?

Risk factor modification is essential in controlling angina and preventing coronary events. Reversible risk factors such as smoking and obesity should be addressed as much as possible. For smokers, after 12 months of not smoking, their increased risk of dying from heart disease is halved, and after 15 years, their risk of AMI is reduced to the same level as for people who have never smoked.¹⁸ Weight loss can often have the additional benefit of reducing the severity of angina.³

The National Heart Foundation of Australia has developed guidelines for preventing cardiovascular events in people with coronary heart disease which include the lifestyle/behavioural risk factors and management described in Table 1.¹⁹

Are there any warning signs that I need to look out for?

The National Heart Foundation of Australia has a 'Will you recognise your heart attack?' leaflet which can be accessed at: www.heartattackfacts.org.au/Warning-signs.aspx (Figure 1). This is a valuable counselling tool to use with all consumers presenting with prescriptions suggesting a history of coronary heart disease.

Table 1. Guidelines for preventing cardiovascular events
(adapted from the National Heart Foundation of Australia)

Risk factor	Counselling guide
Smoking	
Goal: <ul style="list-style-type: none"> Complete cessation Avoidance of second-hand smoke 	<ul style="list-style-type: none"> Strongly encourage patient and family to stop smoking and provide smokers and those exposed to second-hand smoke with appropriate facts Refer to Quitline (13 QUIT) Consider pharmacotherapy for patients smoking >10 cigarettes daily
Nutrition	
Goal: <ul style="list-style-type: none"> Establish/maintain healthy eating including saturated and trans fatty acid intake no more than 8% of total energy intake Consumption of approximately 1 g Eicosapentaenoic acid (EPA) + Docosahexaenoic acid (DHA) and ≥2 g Alpha Linolenic Acid (ALA) daily 	<ul style="list-style-type: none"> Encourage patients to follow the Heart Foundation's 'Enjoy Healthy Eating' messages which encourage patients to choose: <ul style="list-style-type: none"> Mainly plant-based foods – vegetables, fruits and legumes, and grain-based foods (preferably wholegrain) such as bread, pasta, noodles and rice Moderate amounts of lean meats, poultry, fish and reduced fat dairy products Moderate amounts of polyunsaturated and monounsaturated fats Advise patients to consume approximately 1 g of combined EPA and DHA per day (through a variety of oily fish and fish oil capsule supplements), as well as ≥2 g of ALA daily
Alcohol	
Goal: <ul style="list-style-type: none"> Low risk alcohol consumption 	<ul style="list-style-type: none"> Assess patient medications for potential interactions with alcohol and advise as appropriate Encourage patients with hypertension who drink alcohol to limit intake to no more than 2 standard drinks per day for men and 1 standard drink per day for women
Physical Activity	
Goal: <ul style="list-style-type: none"> Progress, over time, to the recommended goal of at least 30 minutes of moderate intensity physical activity on most, if not, all days of the week (minimum of 150 minutes/week) Can be accumulated in shorter bouts of 10 minutes duration Minimum activity may be reduced for those with advanced heart disease 	<ul style="list-style-type: none"> Assess patient's physical activity habits together with severity of disease and comorbidities Discuss physical activity needs/capabilities/barriers and encourage the patient to be active Begin at low intensity and gradually increase duration and intensity over several weeks working towards specific goals Note that vigorous physical activity is generally not encouraged for people with CHD Refer to a cardiac rehabilitation program and/or exercise physiologist where appropriate
Healthy weight	
Goal: <ul style="list-style-type: none"> Waist measurement: Male ≤94 cm; Female ≤80 cm BMI 18.5–24.9 kg/m² 	<ul style="list-style-type: none"> Assess and continue to monitor both waist circumference and Body Mass Index (BMI). (BMI = weight (kg)/height (m)²) Set immediate, achievable goals Encourage healthy eating and regular physical activity

Figure 1. 'Will you recognise your heart attack?' leaflet

Where can I find more information?

More heart health information can be found at: www.heartfoundation.com.au, or consumers can call Heartline on 1300 36 27 87. A 'Will you recognise your heart attack?' information fact sheet can be accessed at: www.heartfoundation.org.au/SiteCollectionDocuments/WS_Consumer%20fact%20sheet_FINAL_LR.pdf

Case scenario continued

Simon should be advised about the benefits of taking his new medications and encouraged to take them regularly. He should also be offered information on the management of modifiable risk factors and strongly encouraged to attempt to reduce his risk through measures such as smoking cessation and weight loss. He should be instructed on what to do in the event of chest pain, how to effectively administer his GTN spray, and advised on the warning signs of a heart attack.

Key learning points

Angina is a symptom of coronary heart disease, a condition which is responsible for the deaths of many Australians. Pharmacists can play an important role in reducing the impact of coronary heart disease in the community through encouraging all

patients presenting with any form of chest pain to consult their doctor for investigation.

Encouragement to modify lifestyle-related risk factors, counselling patients on the correct and effective use of GTN spray and raising awareness of how to recognise the signs of a heart attack and what to do in such an event are also key roles a pharmacist can play.

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Questions

A score of 4 out of 5 attracts 1 CPD credit.

- Which of the following statements about unstable angina is **true**?
 - It can cause recurring or prolonged angina attacks at rest.
 - It rarely occurs unless the myocardial oxygen demand is increased.
 - It often has increased responsiveness to sublingual nitrates.
 - Attacks are usually infrequent.
- Which of the following statements about short-acting nitrates is **true**?
 - Short-acting nitrates can be used to prevent exercise-induced angina.
 - If the pain or discomfort does not go away with the first dose, the patient can repeat the dose of GTN spray every 10 minutes up to a maximum of four sprays.
 - The sublingual GTN tablets are a more appropriate option for those with infrequent angina.
 - Sublingual nitrates are suitable for relief of chronic stable angina attacks, and not for unstable angina.
- Which of the following combinations of medications would be **most** appropriate for a newly diagnosed angina patient, provided there are no contraindications to recommended first-line therapies:
 - Aspirin 100 mg, atorvastatin 40 mg, perindopril/indapamide 5 mg/1.25 mg.
 - Aspirin 100 mg, atorvastatin 40 mg, metoprolol 50 mg.
 - Atorvastatin 40 mg, metoprolol 100mg, verapamil 180 mg.
 - Aspirin 100 mg, atorvastatin 40mg, verapamil 180 mg.
- Which of the following statements about risk factor modification is **true**?
 - Patients with hypertension who drink alcohol should limit their intake to no more than 3 standard drinks per day for men and 2 standard drinks per day for women.
 - Males should aim for a waist measurement of less than or equal to 98 cm, and females should aim for less than or equal to 88 cm.
 - Patients with coronary heart disease should be encouraged to perform regular vigorous physical activity.
 - Patients should consume approximately 1 g of combined EPA and DHA per day as well as at least 2 g of ALA.
- Which of the following symptoms is the **least** likely to indicate a heart attack?
 - Severe pressure in the arms and back.
 - Tightness across the chest.
 - Tingling in the hands and feet.
 - Pain in the neck and jaw.