nutritional deficits and correcting them contributes significantly to improved outcomes for older surgical patients. This has been particularly clearly shown in patients with femoral neck fractures.[12,13]

Rehabilitation planning

Early mobilisation improves patients' perceptions and orientation as well as shortening hospital stay. There are but a few clinical situations where strict bed rest needs to be enforced. Furthermore, in orthopaedic patients, the benefits of postoperative exercise and balance training in reducing falls and facilitating discharge have been substantiated in a recent systematic review.[14]

The surgical episode as an opportunity for enhancing life quality

For a significant proportion of elderly patients, a surgical procedure represents the first medical contact the patient has made for some time, if not the first ever. For others it affords the opportunity to work in liaison with the general practitioner to review and stabilise therapy for coexisting disease in a supervised environment.

The whole episode should ideally be one of holistic care, with evaluation of and provision for all the health needs of the patient. Examples of beneficial parallel interventions range from the simple, such as reviewing medication, to the more complex, such as getting hypertension under control and preventing its contribution to the progression of dementia.[15] The aim should be to enhance the quality of life where possible. In this context, the anaesthetist's role is significant and complementary.

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 47)

7. Patients with cognitive impairment require less postoperative analgesia than other patients.
8. Older patients have fewer alveoli than younger adults.

New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Amprenavir

Agenerase (Glaxo Wellcome)

150 mg capsules, and 240 mL bottles containing 15 mg/mL oral solution

Approved indication: HIV-1

Australian Medicines Handbook Section 5.3.5

Amprenavir is the fifth protease inhibitor to be approved for use in Australia. It can be used to treat HIV infection in combination with other antiretroviral drugs, such as zidovudine and lamivudine. By inhibiting the protease in HIV-1, amprenavir results in the production of non-infectious virions.

Patients take amprenavir twice a day. As the dose is 20 mg/kg the patients need to take several capsules. The oral solution is

less bioavailable than the capsules, so the doses are not equivalent. Although absorption is affected by food, amprenavir can be taken with or without food. The volume of distribution is large, but amprenavir does not greatly penetrate the blood brain barrier. Concentrations in cerebrospinal fluid are less than 1% of the plasma concentration.

Amprenavir is eliminated by hepatic metabolism and has a half-life of 7-11 hours. The metabolism of amprenavir involves cytochrome CYP3A4. It therefore has many potential interactions including those with other drugs used to treat HIV. Patients taking amprenavir should not be given drugs such as midazolam, triazolam, ergot derivatives and rifampicin.

Clinical trials show that adding amprenavir to a combination of zidovudine and lamivudine in previously untreated patients is more efficacious than the combination alone. Almost 60% of patients will have concentrations of viral RNA less than 400 copies/mL after 16 weeks of treatment. An open label extension of this study resulted in 43% of the patients being at or below the target concentration after 48 weeks.[1]

In patients who have previously had treatment, but not with a protease inhibitor, 30% will have less than 400 copies/mL after 48 weeks. If amprenavir is given to patients who have already been treated with a protease inhibitor, 34% will have less than 200 copies/mL after 24 weeks of taking the dual protease inhibitor regimen. The response rate is reduced if the patients have previously taken a non-nucleoside reverse transcriptase inhibitor.

Adverse effects are common and include nausea, vomiting and diarrhoea. Some patients will develop rashes. These usually resolve spontaneously, but the Stevens-Johnstone syndrome has been reported. Other uncommon adverse effects include lipodystrophy, hyperlipidaemia and diabetes mellitus.

The capsule formulation contains vitamin E, so patients are advised not to take supplements of vitamin E. The oral solution is not suitable for young children and pregnant women because it contains the potentially toxic propylene glycol. This formulation is also contraindicated in patients with hepatic or renal impairment.

In patients who have not previously had a protease inhibitor as part of their treatment, indinavir may be better tolerated and have greater efficacy than amprenavir. However, it is only approved for patients who have previously been treated with a protease inhibitor. HIV can become resistant to protease inhibitors, however the profile of resistance to amprenavir differs from that of other protease inhibitors. It may therefore have a role in 'salvage therapy' when resistance to other protease inhibitors has developed.

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Azelastine

AZEP (Sigma)

0.1% nasal spray

Approved indication: allergic rhinitis

Australian Medicines Handbook Section 9.4.3

When seasonal or perennial rhinitis is severe enough to require drug treatment, a topical antihistamine is an alternative to topical nasal corticosteroids. Azelastine is an H_1-receptor antagonist which has been approved for use in patients over five years old.

Patients spray a dose of azelastine into each nostril twice a day. Within 15 minutes this starts to relieve nasal symptoms induced by histamine or allergens. The effect of a dose can last for up to 12 hours. Part of each dose is absorbed. This is then extensively metabolised with most of the metabolites being excreted in the faeces. The major metabolite, desmethylazelastine, is also an H_1-receptor antagonist. It has a half-life of 56 hours so there is a potential for accumulation with twice-daily doses.

In studies of seasonal allergic rhinitis, azelastine was as effective as oral terfenadine at reducing symptoms such as rhinorrhoea, nasal irritation and sneezing. Similar results were observed in patients with perennial allergic rhinitis.

Most of the adverse effects occur in the nose. They include stinging, itching, sneezing and epistaxis. Some patients will develop an altered taste sensation and possibly nausea.

While azelastine may have a more rapid effect, it is not more effective than nasal corticosteroids. In a placebo-controlled trial budesonide had a significantly greater effect on the symptoms of perennial allergic rhinitis.[1] A short study (two weeks) found that beclomethasone produced a greater improvement in the overall symptoms of seasonal allergic rhinitis.[2]

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Gadoteridol

Prohance (Bracco)

279.3 mg/mL in 5, 10, 15 and 20 mL vials and 5, 10, 15 and 17 mL syringes

Approved indication: magnetic resonance imaging

Gadoteridol adds to the choice of contrast agents for use in magnetic resonance imaging. It is a non-ionic complex of gadolinium with a low molecular weight. Gadoteridol does not cross the blood-brain barrier, but if the barrier is damaged gadoteridol will penetrate into lesions such as tumours. It also highlights areas of increased vascularity so it has been used to improve the delimitation of lesions elsewhere in the body.

Apart from its paramagnetic effects, gadoteridol has no pharmacological activity in the body. After intravenous injection, most of the dose is excreted unchanged in the urine within 24 hours. There is little information about the effect of renal impairment on the clearance of gadoteridol. Severe renal impairment is a contraindication.

Adverse reactions are uncommon, but prescribers need to be equipped to deal with anaphylactoid reactions. The more frequent adverse effects of gadoteridol include nausea, altered taste, headache and pain at the injection site.

Gadoteridol has been available in Europe and the USA for several years. It does not appear to have any significant advantages over similar products.

Lanreotide

Somatuline LA (Ipsen)

glass vials containing 40 mg as powder (only 30 mg is available for the patient due to losses of the active ingredient during sterilisation, resuspension and administration)

Approved indication: acromegaly

Australian Medicines Handbook Section 10.6.4

Somatostatin is a peptide which inhibits the secretion of growth hormone. Synthetic analogues of somatostatin, such as octreotide and lanreotide, can therefore be used in the treatment of acromegaly which results from an excessive concentration of growth hormone.

Lanreotide is indicated for patients whose concentrations of growth hormone remain high despite surgery and/or radiotherapy. It is also indicated for patients who are refractory to treatment with a dopamine agonist.

A modified-release formulation allows lanreotide to be initially given every 14 days. After reconstitution it is injected intramuscularly. There is a rapid release, followed by a prolonged release from the microparticles in the formulation. The half-life of this formulation is approximately five days. Although the product is injected its bioavailability is 57%.

A European study involving 125 patients compared injections of 30 mg lanreotide every 10–14 days with monthly injections of 20 mg of modified-release octreotide. The growth hormone concentration was reduced significantly more by octreotide than by lanreotide and more patients reached the target concentrations.[1]

The most frequent adverse effects of lanreotide are reactions at the injection site and gastrointestinal upsets. As lanreotide may reduce gall bladder motility, patients should have an ultrasound scan before treatment and every six months during treatment.

Although more than half the patients treated with lanreotide will respond satisfactorily, some need injections more frequently than every 14 days. Lanreotide may be less effective than octreotide.

REFERENCE

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Linezolid

Zyvox (Pharmacia)

600 mg film-coated tablets

granules for oral suspension (20 mg/mL)

infusion bags containing 600 mg/300 mL

Approved indication: specified infections

Australian Medicines Handbook Section 5.1

The oxazolidinones are a new class of antibiotic. They are likely to have a role in the treatment of infections caused by resistant organisms.

Linezolid is the first drug of the class to be approved in Australia. Its inhibition of bacterial protein synthesis makes it bacteriostatic against staphylococci and enterococci, and bactericidal against most streptococci. Linezolid can be used to treat methicillin-resistant staphylococci and vancomycin-resistant enterococci. It is not active against *Haemophilus influenzae*, *Pseudomonas aeruginoia*, *Neisseria* or *Enterobacteriaceae*. *Legionella* and *Moraxella catarrhalis* are only intermediately susceptible to linezolid.

When taken by mouth, linezolid is almost completely absorbed. It has a half-life of 5-7 hours and is mainly eliminated by metabolism. As linezolid weakly inhibits monoamine oxidase there is a potential for interactions with tyramine and sympathomimetic drugs such as pseudoephedrine.

Adverse effects are common; 70% of the patients in one study had an adverse event.[1] The most frequent problems are headache, nausea, diarrhoea and candidiasis. Liver function is commonly disturbed and some patients develop myelosuppression. The haemoglobin and platelet count should be checked in any patient who takes linezolid for more than two weeks. Patients are also at risk of pseudomembranous colitis.

Some of the trials investigating the efficacy of linezolid have not been published. One published study was a double-blind comparison with vancomycin for the treatment of 396 patients with nosocomial pneumonia. Approximately 18% of the inpatients given linezolid died compared with 25% of the vancomycin group. None of the deaths in the linezolid group were due to a lack of response. The cure rate was 53% for linezolid and 52% for vancomycin.[1]

Although linezolid has been studied in soft tissue infections and community-acquired pneumonia, as well as in nosocomial pneumonia, it is not approved for general use in these conditions. As linezolid is unlikely to have cross-resistance with other antibiotics, because of its different mechanism of action, it should be reserved for organisms which are resistant to other antibiotics. As linezolid has oral formulations it may have a practical advantage over quinupristin/dalfopristin (see 'New drugs' Aust Prescr 2000;23:65), which is approved for the intravenous treatment of resistant organisms, but the two drugs have not been compared in clinical trials.

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Meloxicam

Mobic (Boehringer Ingelheim)

7.5 mg and 15 mg tablets

Approved indication: osteoarthritis

Australian Medicines Handbook Section 15.1

The new cyclo-oxygenase inhibitors are being promoted as drugs which inhibit the COX-2 enzyme more than the COX-1 enzyme. Although meloxicam is in a different class of non-steroidal anti-inflammatory drugs, it also inhibits COX-2 more than COX-1 (see 'COX-2 inhibitors' Aust Prescr 2000;23:30-2).

Patients take meloxicam once a day. It is absorbed slowly and has a half-life of 15-20 hours. Most of the dose is metabolised and this involves cytochrome P450 2C9 and 3A4. Although CYP2C9 predominates, caution is needed if an inhibitor of CYP3A4 is prescribed concurrently with meloxicam. It is contraindicated in patients taking drugs, such as sulfamethoxazole, which inhibit CYP2C9.

In clinical trials meloxicam has been as effective as sustained-release diclofenac in relieving the symptoms of osteoarthritis. For short-term treatment, meloxicam was as effective as piroxicam.

If taken for more than six months, meloxicam is associated with gastrointestinal adverse effects in more than 20% of patients. Common problems include diarrhoea, dyspepsia and nausea. Although the overall incidence may be less than for similar drugs, there is no clear reduction in serious adverse effects such as bleeding or perforation of peptic ulcers.

Correction

Daivonex (Aust Prescr 2001;24:158)

There was a typographical error in the New Formulations section of New drugs, regarding calcipotriol scalp solution (CSL). The brand name is Daivonex, not Diavonex.

Answers to self-test questions

1. False
2. True
3. False
4. False
5. False
6. True
7. False
8. True

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