bestpractice

Issue 10

December 2007

DR SEUSS

SMART

GLUCOSE METERS

EYE MEDICATIONS

SMOKING CESSATION

bpac nz
better medicine

Best Practice Journal (BPJ)

ISSN 1177-5645

BPJ is published and owned by bpac^{nz}

Level 8 10 George Street, Dunedin, New Zealand.

BPJ, Issue 10, December 2007

Bpac^{nz} is an independent organisation that promotes health care interventions which meet patients' needs and are evidence based, cost effective and suitable for the New Zealand context.

We develop and distribute evidence based resources which describe, facilitate and help overcome the barriers to best practice.

Bpac^{nz} has four shareholders:

Procare Health, South Link Health, IPAC and The University of Otago.

Bpac^{nz} is currently funded through contracts with PHARMAC and DHBNZ.

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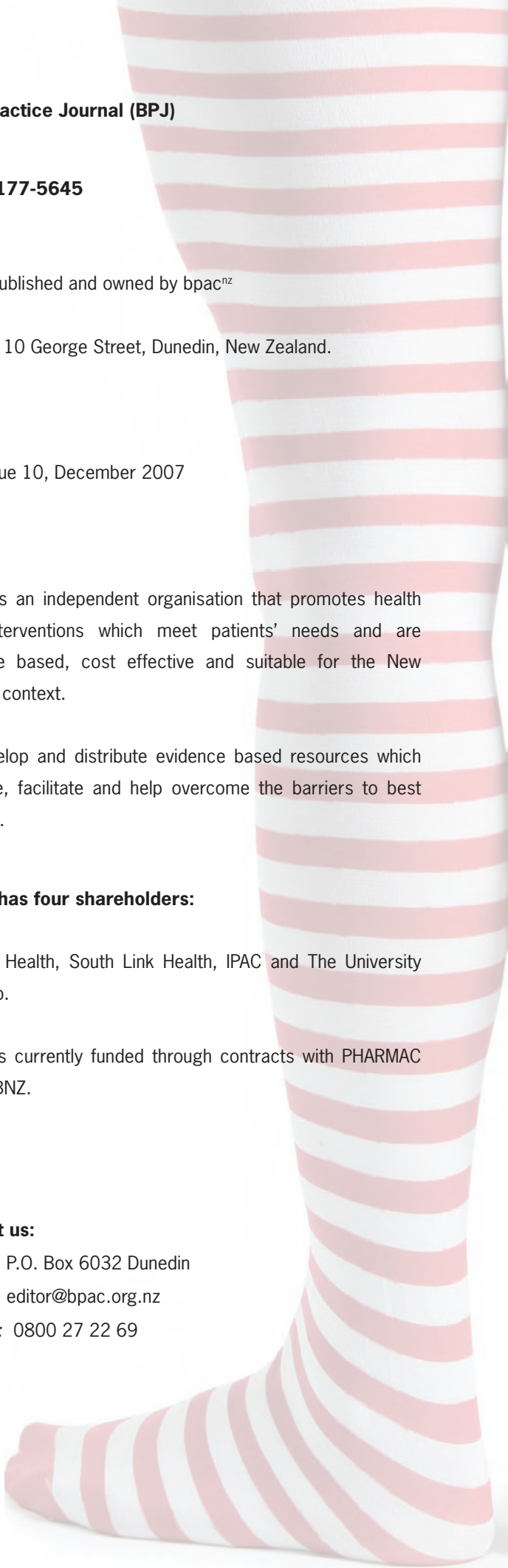

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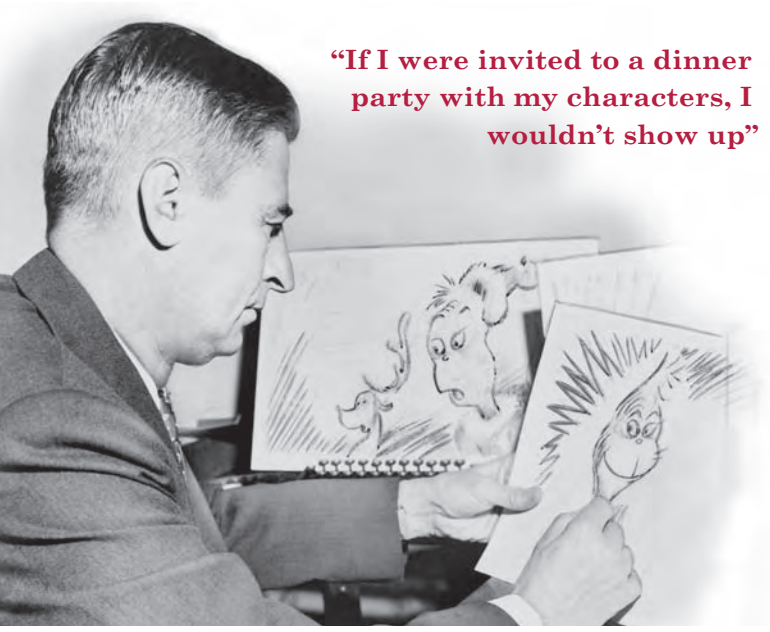
UPFRONT

The doctor who wasn't

"How did it get so late so soon? Its night before its afternoon. December is here before its June. My goodness how the time has flewn. How did it get so late so soon?" – Dr Seuss

Theodor Seuss Geisel (1904–1991), better known as Dr Seuss, is one of the most famous and well loved children's authors of all time. He is perhaps one of the first names that come to mind when thinking of a list of famous doctors…but is he? In actual fact, Theodor Geisel was not a doctor at all. His father always hoped that he would earn a doctorate at Oxford and his pen-name was an acknowledgement of this.



"If I were invited to a dinner party with my characters, I wouldn't show up"

In the 1950s, illiteracy among school children was a significant problem in the USA. A report concluded that children were not learning to read because their books were boring. Dr Seuss decided to come up with a list of 220 words which he felt were the most important and he used these words to write an entire book – *The Cat in the Hat*. As the result of a bet several years later, Seuss composed a work using a mere 50 words – the result was *Green Eggs and Ham*. Dr Seuss understood that a message is best received when delivered in a concise and straight forward manner.

"Sometimes the questions are complicated and the answers are simple." – Dr Seuss

One of the most important lessons we have learned at bpac this year is that our messages need to be concise. Health professionals are obliged to stay on top of latest research, patients are increasingly more informed and demanding of service, paperwork has evolved into a mountain and there is precious little time to achieve this all. It is our job to collect the evidence, call in the experts, reach a conclusion and pass on this information and guidance to our clinicians in a concise and easily readable format.

When evaluating the impact of our programmes, we consistently receive feedback both when our messages are concise; *"**It was very useful and contained excellent, clear guidelines**"* and when, perhaps, we need to be a little less wordy; *"**Try and avoid over repetition in the space of three or four pages, we are not thick - twice is adequate!**"*

Time is important. Many of our readers complain that there is simply too much information and not enough time to read it all; ***"It is a pity with the time constraints of running a busy practice that much of this good material goes unread. Unfortunately everyone that sends their bit of paper is so convinced of its importance that the good stuff gets drowned by the irrelevant minutiae"***. We work hard to select topics and deliver messages that are important to our audience; ***"Fantastic read, really helpful, as always bpac provide a great user friendly service. bpac publications seem to understand what GPs need and the limited time we have to update ourselves"***.

"You have brains in your head. You have feet in your shoes. You can steer yourself in any direction you choose. You're on your own. And you know what you know. You are the guy who'll decide where to go." – Oh, the Places You'll Go, Dr Seuss, 1990

GPs and health professionals must take a pragmatic approach to interpreting the medical evidence and applying it at both a practice and patient level; ***"There is academia and "real life" - what I say when I am answering a quiz & what I do when***

time is short and patients are being querulous & 'difficult' can be different....! Not because I INTEND them to be so, but sometimes it seems just easiest to take the road of least resistance".

We know that "real practice" often takes precedence over the best, most up to date, evidence based information and expert opinion. One of our major themes for 2008 is embracing the pragmatic approach of our New Zealand primary health care clinicians.

"Unless someone like you cares a whole awful lot, nothing is going to get better. It's not." – The Lorax, Dr Seuss, 1971

We provide the information; GPs, nurses and pharmacists make the difference in patient outcomes. ***"Good campaign - just got to change the thinking of the patients now!!"***

So far this year we have seen an increase in monitoring for adverse effects and metabolic disturbances in people taking lithium, a reduction in the use of antibiotics for "winter ills" in children and a reduction in the use of codeine for acute migraine. No doubt there have been many more changes, all with the common outcome of better patient care.

"Often it is only those who were motivated to read your information, and then motivated or willing to change, that take it on board". We may not have changed the world, but what we have done matters to individual patients and the clinicians who care for them.

"Today was good. Today was fun. Tomorrow is another one." – Dr Seuss

We are only as good as our last issue; ***"I found this to be the least useful of the campaigns, mainly because it did not tell me anything I didn't already know".***

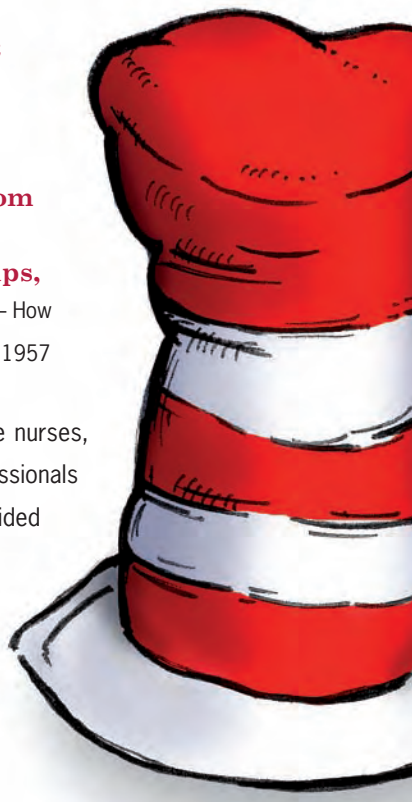
Perhaps one of the most frequent comments we receive is that information needs to be reinforced, in order to be remembered; ***"Very relevant to day to day general practice, follow up messages strongly encouraged"***. We produce four theme issues and four responsive journals each year. This allows us to rapidly respond to topical issues and update information from previous programmes.

"And will you succeed? Yes indeed, yes indeed! Ninety-eight and three-quarters percent guaranteed!" – Oh, the Places You'll Go, Dr Seuss, 1990

We have had a great year here at BestPractice and almost all our feedback has been positive; ***"excellent as it stimulates thought and review of one's practice"*** and when its not; ***"I cannot recall anything about the programme"*** we do care and we do make changes.

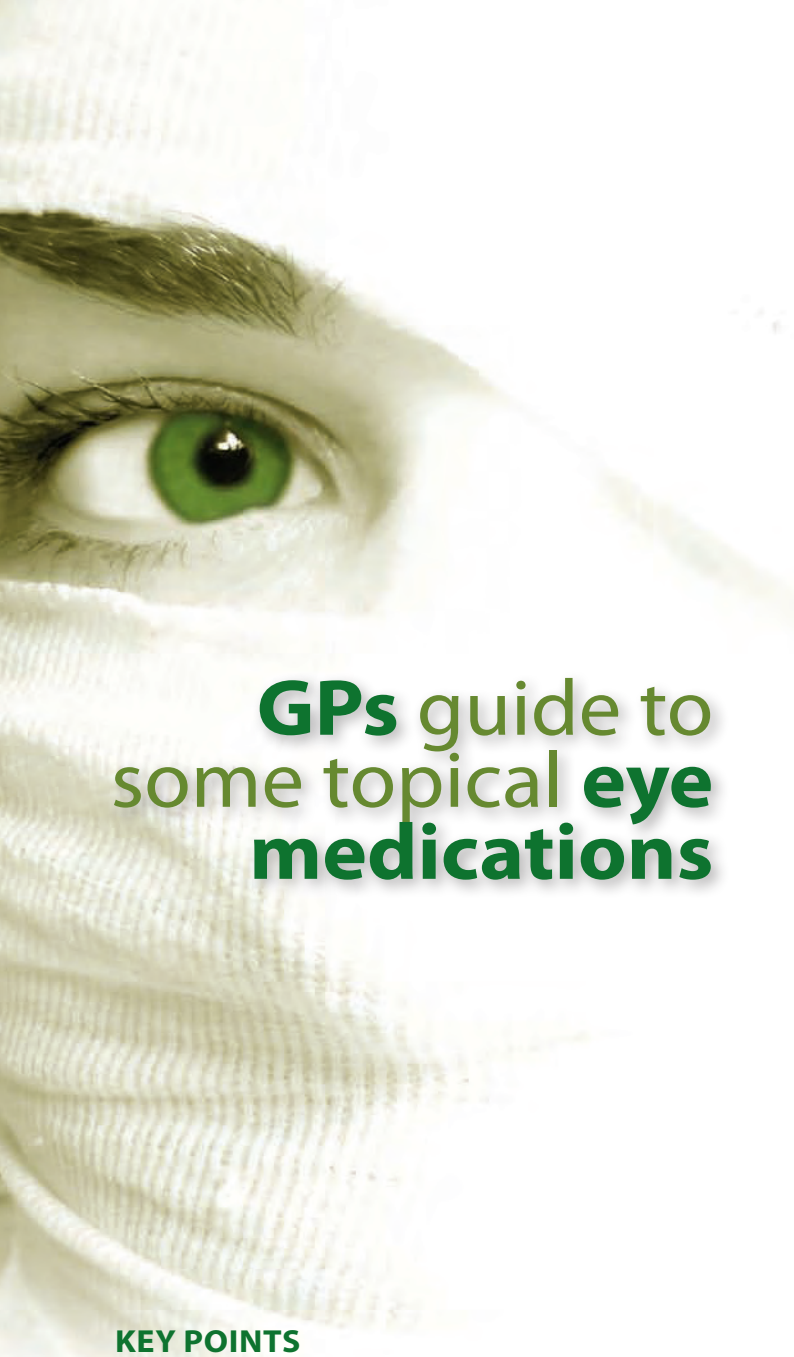
We aim to provide clear, well-researched guidance that is practical and relevant to the needs of primary care and constantly evolving in response to our audience. Together we hope we are achieving this goal; ***"I will try harder. I will try harder. I will try harder. I will try harder. I will try harder..."***

"And the Grinch, with his Grinch-feet ice cold in the snow,
stood puzzling and puzzling, how could it be so? It came without ribbons.
It came without tags. It came without packages, boxes or bags.
And he puzzled and puzzled 'till his puzzler was sore.
Then the Grinch thought of something he hadn't before.
What if Christmas, he thought, doesn't come from a store.
What if Christmas, perhaps, means a little bit more." – How the Grinch Stole Christmas, Dr Seuss, 1957



Thank you to all the GPs, practice nurses, pharmacists and other health professionals who read our journals, provided feedback and made a difference this year.

Merry Christmas from the team at bpac.



GPs guide to some topical eye medications

KEY POINTS

- ***Specialist prescribing restrictions have been removed from some topical eye treatments***
- ***Although general practitioners can now initiate some topical eye treatments, it does not mean they should***
- ***Significant corneal disease, intraocular inflammation and glaucoma still require specialist diagnosis and management***
- ***Primary care will still be involved in the ongoing support and education of people with these conditions and the continuation of the medications used to treat them***

EYE MEDICATIONS ARE OFTEN USED IN HIGH RISK SITUATIONS REQUIRING SPECIALIST SKILLS

Some eye medications are used when there is high risk of visual loss and their misuse can increase this risk. Initiation and monitoring often require specialist expertise as well as the availability and ability to use specialist equipment. For example:

- Slit-lamp examination is needed for accurate diagnosis and monitoring of intraocular inflammation, such as iritis and keratitis and ulceration of the cornea.
- Accurate diagnosis and monitoring for adequacy of treatment of glaucoma requires accurate detailed assessment of intraocular pressure, the optic disk and visual fields.
- Accurate distinction between infective and non-infective inflammatory conditions is essential because medications, such as steroid drops, used for some conditions, will make others much worse.
- Use of steroid drops for more than ten days requires, monitoring for steroid-induced glaucoma.

PRIMARY CARE ROLE STILL IMPORTANT

Although primary care is not equipped to initiate and monitor treatment for these conditions, it still plays a valuable role. People will still look to primary care for support, education and continuation of treatment. Clinicians, particularly prescribers, need to understand the actions of these medications and how to avoid and identify possible adverse effects. For example:

- Some topical preparations, e.g. beta blockers, if sufficiently absorbed, may cause systemic effects.
- Unless medically indicated, soft contact lenses should not be used for the duration of treatment with eye drops and ointments.[1]
- However, it is safe to replace contact lenses 15 minutes after use of some drops.
- Application of gentle pressure to the tear duct after instilling drops increases exposure of the anterior eye tissues to the treatment and reduces systemic absorption. This is especially advisable in children.[2]

eye medications

ANTIVIRAL

Acyclovir 3% ointment [Zovirax]

Acyclovir eye ointment is indicated for treatment of herpes simplex (HSV) keratitis and dendritic ulceration of the corneal epithelium.

Viruses other than HSV may cause dendritic ulceration and slit lamp microscopy and laboratory examination of a corneal scrape is recommended for accurate diagnosis.

Recommened dose is a 1cm ribbon of ointment, applied five times daily inside the lower eyelid and continued for at least three days after apparent healing. Contact lenses should not be used during this time.

Stinging is common after application but is usually transient. Occurrence of superficial punctate keratopathy is also quite common but treatment can be continued and the keratopathy expected to heal.

ANTIBACTERIALS

Ciprofloxacin, gentamicin and tobramicin eye drops are not first line treatments for common conjunctival or adnexal eye infections and their use should be strictly guided by laboratory identification and determination of the antibiotic sensitivities of pathogens.

Ciprofloxacin 0.3% drops [Ciloxan]

Indicated for bacterial keratitis (infected corneal ulcers), severe bacterial conjunctivitis and blepharitis due to susceptible bacteria. Ciprofloxacin is active against a wide range of gram-positive and gram-negative bacteria. Laboratory identification and sensitivity testing is advised. Superinfection with resistant bacteria can occur.

The recommended dose for treating corneal lesions with ciprofloxacin eye drops is 1–2 drops, used at 15 minute intervals for the first six hours.[3] Local burning discomfort, white precipitate and foreign body sensation may occur.

Ciprofloxacin is not recommeded for use in children under one-year-old and contraindicated in case of hypersensitivity to other quinolones.

Gentamicin 0.3% drops [Genoptic]

Indicated for bacterial keratitis, conjunctivitis and blepharitis, meibomian gland and lacrimal/tear duct infections (dacrocystitis).

Gentamicin is effective against a wide range of gram-negative and gram-positive bacteria. There is increasing Strep. pneumoniae resistance.

Caution applies to use in pregnancy due to risk of foetal nephrotoxicity and ototoxicity.

Recommended dose is 1–2 drops four hourly. Transient irritation may occur.

Tobramicin 0.3% drops and ointment [Tobrex]

Indications are as for gentamicin and the antibacterial activity is similar. Resistance to one may confer resistance to the other.

Adverse events include local ocular toxicity and delayed corneal wound healing. Tobramicin eye drops may be inactivated by systemic beta-lactam antibiotics. Antiemetics can mask ototoxic effects of tobramicin.

Caution applies to use in pregnancy due to the possibility of foetal nephrotoxicity and ototoxicity.

Recommended dose is 1–2 drops four hourly for 7–10 days.

CORTICOSTEROID DROPS & OINTMENTS

Corticosteroid eye treatments pose four main dangers:[4]

- Undiagnosed red eye and risk of uncontrolled infection
- Steroid-induced glaucoma in susceptible individuals
- Steroid- induced cataract and atrophy of the cornea and sclera from prolonged use
- Steroid and antibiotic combinations should not be prescribed as empiric treatments for an undiagnosed red eye, which may be caused by HSV and may be difficult to diagnose.[5] Their use for any reason requires close supervision.

In general, the cautions outlined below apply to all corticosteroid eye drops.

Steroid use is contraindicated in Herpes simplex keratitis and in untreated other viral and bacterial eye infections – there is risk for progressive corneal injury and globe perforation.

Steroid use may cause recrudescence of quiescent herpes simplex virus and access to frequent slit lamp examination is mandatory.

Intensive and prolonged use of topical steroids should be avoided but some chronic recurrent inflammatory conditions such as iritis or iridocyclitis may necessitate such use - obtain specialist advice.

Topical steroids are not effective in Sjogren's keratoconjunctivitis.

If used for more than ten days, intraocular pressure needs to be monitored in case of steroid glaucoma in susceptible individuals – this can be difficult in children.

Persistent corneal ulceration as a result of fungal keratopathy may be associated with long-term topical steroid use.

Topical steroids are also used in selected infective conditions, including herpes zoster keratitis and after trauma including thermal, chemical or radiation injury, after weighing the risk against the benefit of reduction of inflammation. In these situations, specialist involvement is strongly advised.[6]

In the general practice setting, topical steroids are best avoided after removal of a foreign body – a simple ocular lubricant or antibiotic ointment is useful and mostly sufficient in this context.

Dexamethasone 0.1% drops and ointment [Maxidex]

Dexamethasone is a potent corticosteroid used for non-infective inflammatory and allergic conditions affecting the anterior eye.

Recommended treatment is to instil drops four to six times daily (soft contact lenses can be replaced 15 minutes after use of drops) or a ribbon of ointment four times daily.

Safety and effectiveness in children has not been established.[7]

Fluoromethalone 0.1% drops [Flucon]

Fluoromethalone is indicated for inflammation of anterior eye tissues. It is contraindicated in Herpes simplex keratitis and untreated other infections of the eye.

Safety in pregnancy and safety and efficacy in children under two-years-old has not been established.[8]

Recommended dose is 1–2 drops two to four times daily.

Prednisolone drops [Pred Forte, Pred Mild, Minims Prednisolone]

Preparations available are prednisolone acetate in Pred Forte 1.0% or Pred Mild 0.12% and prednisolone sodium phosphate in Minims Prednisolone 0.5%.

Prednisolone is indicated for non-infective inflammatory anterior eye conditions.

Safe use in pregnancy, breast feeding and children is not established.[9]

Recommended dose is 1 drop two to four times daily. Brief burning or stinging may occur.

NON-STEROIDAL ANTIINFLAMMATORY DROPS

Diclofenac sodium eye drops 0.1% [Voltaren][10]

Diclofenac drops are used to reduce inflammatory response to cataract, squint and trabecular surgeries, and to relieve pain and photophobia after corneal surgery or accidental corneal trauma.

Diclofenac drops are contraindicated in people with Aspirin/ NSAID sensitive asthma, urticaria or acute rhinitis.

Do not use in the third trimester of pregnancy – there is risk of premature closure of the ductus arteriosus. Paediatric experience is limited, so caution applies to use in children.

Transient burning, itching, blurring of vision and punctate keratopathy can occur. As with steroid drops, non-steroidal antiinflammatory drops can mask infection.

Recommended dose is 1 drop four to six hourly. Contact lenses can be replaced 15 minutes after use.

INTRAOCULAR PRESSURE REDUCTION WITH TOPICAL EYE TREATMENTS

Specialist prescribing authority has been removed from several topical agents used in the treatment of ocular hypertension and chronic open-angle glaucoma. However we recommend that they continue to be used under specialist supervision. Initiation and monitoring often require specialist expertise as well as the availability and ability to use specialist equipment. Prescribing eye drops for glaucoma treatment in between specialist reviews continues to be an appropriate role for GPs.

Glaucoma affects 1% of people over 40 years of age and open-angle glaucoma is the most common form (80%). Gradual obstruction occurs in the trabecular meshwork so that the rise of intraocular pressure (IOP) is often slow and asymptomatic despite significant loss of visual field. Viewed through an ophthalmoscope the optic disc is depressed or cupped because of loss of nerve fibres.

Note: the topical eye drugs mentioned here are discussed in relation to ocular hypertension and chronic open-angle glaucoma and not in relation to acute angle-closure glaucoma. Acute angle-closure glaucoma is a medical emergency. A shallow anterior chamber creates an abnormally narrow angle between the cornea and the base of the iris. The iris seals off the trabecular meshwork and blocks the outflow of aqueous from the anterior chamber.[11] IOP is usually > 40mm Hg.[12] An urgent specialist opinion is essential.

Topical beta blockers

These are first-line agents for lowering IOP in ocular hypertension and chronic open-angle glaucoma. They probably lower IOP by reducing the rate of production of the aqueous.[13] They are used alongside miotic agents, sympathomimetic agents and carbonic anhydrase inhibitors to get full control of IOP in chronic open-angle ocular hypertension and glaucoma.

Because topical beta blockers, such as betaxolol, levobunolol and timolol, do not have miotic action, they have the advantage of not causing the blurred vision and poor night vision associated with miosis.[14]

They can cause problems related to systemic absorption, which can be reduced by applying gentle pressure on the nasolacrimal duct for two minutes after use.

Betaxolol is cardio-selective (blocks only beta-1 receptors) and in clinical studies the eye drops have minimal effect on pulmonary and cardiovascular parameters. However, some patients may be affected.[15]

Levobunolol and timolol are not cardio-selective (they block both beta-1 and beta-2 receptors) so their systemic absorption poses more potential risk to pulmonary and cardiovascular function.

A strong caution or contraindication applies to use of these three drugs in people with bradycardia, heart block, cardiac failure, airways disease or history of anaphylaxis.[16]

General management of severe adverse systemic effects is adrenaline.

Ophthalmic beta-blockers can mask hypoglycaemia in diabetes and also some clinical signs of thyrotoxicosis.[17]

Gradual withdrawal should be considered prior to general anaesthesia to protect sympathetic/adrenergic cardiac responses.[18]

Avoid use in pregnancy near parturition – foetal and neonatal bradycardia can occur.[19]

Note that beta-blockers are prohibited in some sports by the world anti-doping agency (WADA).[20]

Betaxolol eye drops [Betoptic 0.5% and Betoptic S 0.25%] Betaxolol lowers intraocular pressure within 30 minutes of use. Twice daily use keeps the IOP below 22mm Hg in most patients.[21]

Levobunolol eye drops [Levobunolol 0.5%[22] , Betagan 0.25%[23]]
IOP falls within an hour of use and by 6-8 mm Hg over several weeks. Twice daily use effects long-term control in most cases.

Timolol eye drops [Apo-Timopt 0.25%, Timoptol 0.25%, Timoptol-XE 0.25%, Nyogel 0.1%]
Recommended treatment starts with one drop of 0.25% solution twice daily. IOP reduction occurs after 20 minutes. Viscous drops or gel enable once daily treatment.

Local reactions may occur with any one of these agents.

Carbonic anhydrase inhibitors reduce IOP by reducing aqueous production in the ciliary body.[24]

Dorzolamide eye drops 2%[25] [Trusopt]
Dorzolamide is a carbonic anhydrase inhibitor that can be used as monotherapy (one drop three times daily) or as adjunctive therapy with an ophthalmic beta-blocker (one drop twice daily).

Dorzolamide has a structure similar to sulphonamide and therefore has potential for sulphonamide-like adverse effects.

Its use is contra-indicated in pregnancy, lactation and in renal impairment. Local eye reactions and a bitter taste may be experienced. Headache, dizziness and nausea may also occur.

Separate administration from other eye drops by at least ten minutes.

Dorzolamide combined with Timolol
Dorzolamide is combined with timolol in Cosopt eye drops.[26]

This may be used when monotherapy is not sufficient to lower IOP below 22mm Hg.

Contraindications and cautions are similar to those for individual components.

Alpha-2 agonists reduce the rate of production of aqueous in the ciliary body by alpha-mediated vasoconstriction of afferent ciliary blood vessels. However, they are also mydriatic and are not for recommened for use in patients with risk of angle-closure, unless an iridectomy has been done.

Brimonidine eye drops 0.2%[27] [Alphagan]
Brimonidine is a selective alpha-2 agonist that can be used to reduce IOP in patients for whom beta-blockers are not appropriate. It can also be used as adjunctive therapy when IOP is poorly controlled.

Caution is necessary in severe cardiovascular or cerebrovascular disease, pregnancy and breast feeding.

Drowsiness may occur and pose a risk to driving.

Local ocular reactions may occur.

Brimonidine is combined with timolol in Combigan, which may be considered when monotherapy fails to lower IOP below 22mm Hg. Contraindications and cautions are those that apply to the individual components.

Direct-acting parasympathomimetic drops

These have cholinergic effects i.e. they constrict the pupil and cause contraction of the ciliary muscle. Contraction of the ciliary muscle stretches the trabecular meshwork and improves the outflow of aqueous.

Pilocarpine eye drops 2%[28] [Minims Pilocarpine Nitrate][29]
Pilocarpine is a tertiary amine and can diffuse through the cornea into the aqueous. There is dimming of vision and poor night vision because of pupillary constriction.

Pupillary constriction is contraindicated in acute iritis and in case of risk for retinal detachment.

Caution applies to use in asthma, pregnancy and lactation.

The contraction of ciliary muscle causes myopia in young

patients. Irritant eye reactions occur and frontal headache can be problematic if there is ciliary muscle spasm.

Recommended dose is 1–2 drops two to four times daily.

Changing drops being used to treat ocular hypertension

If changing from one beta blocker to another, use the final daily dose of the old agent and start the new agent the very next day. If a beta blocker is being substituted for a non-betablocker, the beta blocker is added to the non-beta blocker for one day and the non-beta blocker stopped the next day.[30]

Prostaglandin analogues

Prostaglandin analogues are believed to reduce IOP by increasing the outflow of aqueous humor.

Travaprost eye drops 0.004% [Travatan]
The reduction in IOP starts after approximately two hours and is maintained for at least 24 hours.

Recommended dose is one drop instilled in the affected eye(s) daily with optimal effect if this is administered in the evening.

Travaprost is contraindicated for pregnant women and those attempting to become pregnant.

Travatan eye drops may gradually change the eye colour by increasing the number of pigment granules. The changes may be permanent and the long term consequences of this are not yet known. Darkening of the skin around the eye has also been reported.

Reference Notes

1. BNF 53, Mar 2007, 11.9, p568
2. Medsafe data sheet: Prednisolone sodium phosphate, Oct 2006
3. see Medsafe dose data or BNF or MIMS
4. BNF 53, March 2007, 11.4.1, p555
5. BNF 53, Mar 2007, 11.3.1, p553
6. Medsafe data sheet: Maxidex, Jul 1999
7. Medsafe data sheet: Maxidex, Jul 1999
8. Medsafe data sheet: Fluorometholone Aug 2002
9. Medsafe data sheet: Pred Forte, Sept 2005
10. Medsafe data sheet: Voltaren Ophtha, Apr 2007
11. BNF 53, 11.6, p559
12. Chern, Kenneth C; Emergency Ophthalmology. McGraw-Hill 2002
13. BNF 53, 11.6, p559
14. Medsafe data sheet: Betaxolol Oct 2001; Levobunolol Jan 2000; Timolol Apr 2000, Feb 2005
15. Medsafe data sheet: Apo-Betaxolol Oct 2001
16. Medsafe data sheet: Apo-Betaxolol Oct 2001and Betoptic Mar 1999; Levobunolol Jan 2000 and Betagan Aug 2002; Apo-Timopt Apr 2000 and Nyogel Feb 2005
17. Medsafe data sheet: Apo-Betaxolol Oct 2001
18. Medsafe data sheet: Apo-Betaxolol Oct 2001
19. Medsafe data sheet: Apo-Betaxolol Oct 2001; Betoptic Mar 1999
20. WADA Prohibited List 2005
21. Medsafe data sheet: Apo-Betaxolol Oct 2001
22. Medsafe data sheet: Levobunolol Jan 2000
23. Medsafe data sheet: Betagan Aug 2002
24. BNF 53, 11.6, p562
25. BNF 53, 11.6, p563
26. Medsafe data sheet: Cosopt Jun 2006
27. BNF 53, 11.6, p561-2
28. Neal M J; Medical pharmacology at a Glance. 4th Ed. Blackwell Science 2002
29. Medsafe data sheet: Minims Pilocarpine Nitrate Oct 2006
30. Medsafe data sheet: Apo-Timopt Apr 2006

Self monitoring in DIABETES

Self monitoring of blood glucose is an important component of diabetes management for some people. But, which people?

Any component of a treatment plan that is both invasive and expensive needs to result in an improved clinical outcome.[1] Gathering information about blood glucose levels is only useful when it can be used to improve clinical outcomes.

Clinical outcomes in diabetes are improved when glycaemic control is improved. Measurement of the concentration of glycated haemoglobin (HbA1c) is the most appropriate and accurate way to monitor glycaemic control. When then, does self monitoring of blood glucose provide additional benefit?

TYPE 1 DIABETES

Self monitoring of blood glucose (SMBG) is mandatory for people with type 1 diabetes. The information gained is essential for patients to adjust the type and amount of food and exercise, document hypo and hyperglycaemia and select appropriate dosages of insulin. People with type 1 diabetes usually test three to four times a day and are educated to act on the result to bring about improved control (i.e. a lower HbA1c result).

TYPE 2 DIABETES

Self monitoring is required for people with type 2 diabetes on insulin

Advice regarding the use of SMBG for people with type 2 diabetes treated with insulin is essentially the same as for people with type 1 diabetes. These people however, may be on insulin regimens with less frequent dosing, and so may only need to test twice a day.

Advice for people with type 2 diabetes who are not using insulin needs individual consideration (includes those on oral medication)

There is no doubt that for the vast majority of people with diabetes, measurement of the concentration of glycated haemoglobin (HbA1c) remains the most appropriate and accurate way to monitor glycaemic control.

Evidence of benefit for SMBG in non-insulin treated type 2 diabetes

There is now an abundance of published research in this area. However the designs of the studies, the outcomes and ultimately the conclusions reached, have varied widely.[2] There is still a lack of consensus.[3,4] A conclusion reached in a recent commentary article was that for people with non-insulin treated type 2 diabetes, SMBG "is an expensive and popular procedure without an evidence base".[5] The author suggests that the only way to answer the question of whether to advocate routine SBMG would be through "properly designed, randomised clinical trials."

Do the guidelines help us?

The current New Zealand guideline states that "self-monitoring of blood glucose is well-established in clinical practice, but the literature in this area is limited and difficult to assess".[6] The recommendation is that SMBG "should be considered in conjunction with appropriate therapy as a part of integrated self-care. The purpose of blood glucose self-monitoring should be clear and agreed with the person with diabetes." A similar recommendation is included in the NICE guideline.[7] However, a new draft of this guideline is under consultation at present.[8]

When does SMBG produce benefit for people with non-insulin type 2 diabetes?

The key message is that the aim of using SMBG is to improve glycaemic control, i.e. a lower HbA1c, and to ultimately reduce long term complications. Measuring blood glucose gives immediate information for the patient, but to give any benefit, this information must be acted upon.[9]

If HbA1c is already satisfactory without SMBG, adding it may not be associated with any further improvement.[2]

Therapeutic benefit is more likely to be obtained when:

- There are special circumstances such as new diagnosis, starting or changing medication, illness, pregnancy and frequent hypoglycaemia[10]
- The patient knows how and when to test and how to interpret or act on the results[2]
- Patient education is individually tailored and ongoing[11]
- Patients are "sufficiently literate and numerate"[10]
- Patients are motivated to make changes to diet or lifestyle[2,10]
- A clear goal is negotiated and agreed with patients[11]
- There is an understanding of the relationship between SMBG and HbA1c results[11]

When used appropriately, SMBG can increase disease awareness and compliance[10], it can empower[9,12] and reassure.[11]

Conversely, the continual reminder of less than ideal control can lead to uncertainty, frustration, guilt and high levels of anxiety.[9,11] If GPs and practice nurses take little notice of self monitoring results and don't use the readings as a chance for further education, it tends to reinforce the idea that test results are not important.[11] The patient will often become discouraged and lose motivation. GPs can end up spending a lot of time dealing with the anxiety arising from unexpected or poor results.

In patients who are receiving no benefit from SMBG, it is appropriate to stop.

The recent Diabetes Glycaemic Education and Monitoring (DiGEM) trial has concluded that "routine self monitoring of blood glucose for patients with reasonably controlled non-insulin treated type 2 diabetes seems to offer, at best, small advantages, is not well accepted, and the cost, effort and time involved in the procedures may be better directed to supporting other health related behaviours."[13] It is thought that studies such as this may encourage clinicians to talk to their patients about the usefulness of SMBG and give them "confidence to discontinue it if it is providing no benefit."[14]

A pragmatic approach to the use of SMBG is recommended

If we are faced then with contradictory evidence and very broad recommendations, how do we make choices that will benefit our patients? The decision comes down to an individual patient level and relies upon the doctor and patient reaching agreement on the best course of action.

Andrew Moore, the editor of Bandolier, has been involved in a systematic review of the current evidence.[10] He states that:

"It is sobering to remember that where doctors make their own decisions, the results have been terrific, especially in clinical outcomes with major consequence. They did it by deciding which patients with type 2 diabetes would benefit from self-monitoring and prescribing self-monitoring in those patients. Simple, really". [16]

Further reading

For more information on the DiGEM trial, refer to the following articles in the BMJ (requires subscription)

http://www.bmj.com/cgi/content/full/335/7611/132

http://www.bmj.com/cgi/content/full/335/7611/105

The issue of cost

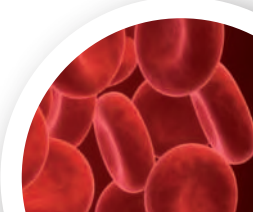
Healthcare providers worldwide are struggling with the difficulties of who should get the healthcare dollars. A huge multi-billion dollar industry has developed to supply meters and strips and there is ongoing spending, with companies trying to produce increasingly fast and easy to use devices.[15]

The largest group of people using SMBG are those with non-insulin treated type 2 diabetes. The routine use of SMBG in this group can have a major cost impact and the expense can be justified only if it leads to savings in the future.[15]

Who to test and why to test have become major issues. In the United Kingdom, some primary care organisations now restrict access to blood testing strips causing debate between doctors, patients and suppliers. Diabetes UK (a charity for people with diabetes) has launched a national online campaign to try and reintroduce unrestricted access to home blood glucose testing equipment.[3] Similar financial dilemmas face those working in primary health care in New Zealand.

References

1. Davidson MB. Counterpoint: Self-Monitoring of Blood Glucose in Type 2 Diabetic Patients not Receiving Insulin: A waste of money. Diabetes Care 2005;28(6):1531-35
2. Self-monitoring of blood glucose in diabetes. Drug Ther Bull 2007;45:65-70
3. Diabetes UK website. The charity for people with diabetes. Available from http://www.diabetes.org.uk Accessed October 2007
4. Consensus statement on self-monitoring in diabetes: Institute of Health Economics, Alberta, Canada, November 14-16,2006. Int J Technol Assess Health Care 2007;23(1):146-151
5. Davidson MB. The dilemma of self-monitoring of blood glucose. Diabetologia 2007;50(3):497-499
6. New Zealand Guideline Group Management of Type 2 Diabetes. 2003. Available from http://www.nzgg.org.nz/guidelines Accessed October 2007
7. National Institute for Health and Clinical Excellence (NICE) Guideline for Type 2 diabetes – Management of blood glucose. 2002 Available from http://www.nice.org.uk/guidance Accessed October 2007
8. NICE: Self-monitor in type 2 diabetes. Pulse. Oct 3, 2007. pg 3
9. Martin S, Schneider B, Heinemann L et al. Self-monitoring of blood glucose in type 2 diabetes and long-term outcome: an epidemiological cohort study. Diabetologia 2006;49:271-8
10. McGeoch G, Derry S, Moore RA. Self-monitoring of blood glucose in type-2 diabetes: what is the evidence? Diabetes Metab Res Rev 2007; 23(6):423-440
11. Peel E, Douglas M, Lawton J. Self monitoring of blood glucose in type 2 diabetes: longitudinal qualitative study of patients' perspectives. BMJ 2007;335:493-96
12. Mirza SA. Don't take my parachute away! BMJ Rapid Response published online 26th July 2007. Available from http://resources.bmj.com Accessed October 2007
13. Farmer A, Wade A, Goyder E et al. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. BMJ 2007;335:132-35
14. Heller SR. Self monitoring of blood glucose in type 2 diabetes. BMJ 2007;335:105-6
15. Ipp E, Aquino RL, Christenson P. Point: Self-Monitoring of Blood Glucose in Type 2 Diabetic Patients not Receiving Insulin: The sanguine approach. Diabetes Care. 2005;28(6):1528-1531
16. Moore RA, Derry S, McGeoch G. In which patient is monitoring useful? BMJ Rapid Response published online 5th July 2007. Available from http://resources.bmj.com Accessed October 2007



GLUCOSE METERS

– different meters, different results

The way that blood glucose results are presented varies depending on the type of meter used. There is a danger that these variations could be falsely attributed to poor control.

WHOLE BLOOD VERSUS PLASMA GLUCOSE

Plasma glucose results measure approximately 15% higher than whole blood glucose results. This is often called the 'matrix effect' and is due to the higher protein and lipid content of red cells than the liquid portion of the blood. This results in glucose (which is water soluble) being unequally distributed between the intracellular and the extracellular space.

VARIATION IN THE WAY BLOOD GLUCOSE METERS REPORT RESULTS

The difference is significant because glucose meters currently available in New Zealand report results as either whole blood or as a "plasma equivalent" while laboratory results are reported as plasma results.

The "plasma equivalent" result is calculated from the whole blood glucose reading using an equation built into the glucose meter. This allows GPs and patients to easily compare laboratory test results with glucose results obtained at home. The International Federation of Clinical Chemistry and the American Diabetes Association has also recommended home glucose analysers should report results as "plasma equivalent".

If however, the meter is reporting results as "whole blood equivalent", both **GP and patient have to know that the whole blood equivalent result is approximately 15% lower than the plasma result,** and is therefore not directly comparable with results obtained from the laboratory.

Table 1 indicates the method of reporting for glucose meters currently available in New Zealand.

As of the 1 July 2008, PHARMAC will no longer be funding test strips for Accu-check Advantage, therefore patients currently using these meters will need to change to either the Abbott Optium Xceed or the Roche Accu-Chek Performa system. Following this change results throughout New Zealand will be consistently reported as "plasma equivalent".

Table 1: methods of reporting for glucose meters currently available in New Zealand.

Analyser	Reported as:
Abbott Optium Xceed	Plasma equivalent
Roche Accu-Chek Advantage	Whole blood equivalent
Roche Accu-Chek Performa	Plasma equivalent

GLUCOSE METERS – common problems

Probably the greatest concern when using glucose meters is false results. All users should be educated about factors contributing to false results.

The Office of In Vitro Diagnostics (OIVD), a service of the FDA, evaluates glucose meters. They evaluate long term safety and effectiveness of the analysers and how devices are used. OIVD, in consultation with manufacturers and users, have produced a table of common problems encountered when using glucose meters (Table 2).

Causes of false results may be patient/sample based or user/device based. Probably the most important advice for any user of a blood glucose meter is to question any result not consistent with the clinical picture. This needs to be investigated and, at a minimum, the test repeated.

Table 2: Common problems with glucose meter results.

Results	Problem	Recommendation
Falsely low results	Sensor strips not fully inserted into meter	Always be sure strip is fully inserted in meter
	Not enough blood applied to strip	Repeat test with a new sample
	Patient in shock	Treat appropriately. Venous sample should be sent immediately to a laboratory
	Squeezing fingertip too hard because blood is not flowing	Repeat test with a new sample from a new stick
	Polycythaemia/increased haematocrit	Venous sample should be sent to a laboratory
Falsely high results	Patient sample site (for example the fingertip) is contaminated with sugar	Always clean test site before sampling
	Patient is dehydrated	Treat appropriately. Venous sample should be sent immediately to a laboratory
	Anemia/decreased haematocrit	Venous sample should be sent to a laboratory
Variable results	Test strips/controls stored at temperature extremes	Store kit according to directions
	Sites other than fingertips	Results from alternative sites may not match finger stick results
	Test strips/controls damaged	Always inspect package for cracks, leaks, etc.
	Dirty meter	Even small amounts of blood, grease, or dirt on a meter's lens can alter the reading
Error codes	Batteries low on power	Change batteries and repeat sample collection
	Test will not complete	Check package details, calibration code, and expiry dates are all compatible

Further reading

FDA diabetes website: http://www.fda.gov/diabetes/

The Office of In Vitro Diagnostics: http://www.fda.gov/cdrh/oivd/labsafetytips.html#tip4

Brand change update:

Ritalin SR now available by Special Access

In response to concerns raised by Medsafe and the Centre for Adverse Reactions Monitoring (CARM), PHARMAC has agreed to allow patients, who experience serious adverse reactions while on Rubifen SR, to return to Ritalin SR under special access.

CHANGING FROM RITALIN TO RUBIFEN

In September 2006, PHARMAC announced that it would cease funding for Ritalin SR (long-acting methylphenidate), a decision mostly affecting children with Attention Deficit Hyperactivity Disorder (ADHD). Instead, Rubifen SR (also long-acting methylphenidate) would be funded, at first along with Ritalin SR, and then as the sole brand of methylphenidate from April 2007. Rubifen was not a new brand; the short acting form was already funded and used by more than 6000 people, at the time of this decision.[1]

Rubifen SR tablets and packaging appear different than that of Ritalin SR, however both brands are considered bioequivalent.

Refer to BPJ Special Edition, March 2007, for more details on the guidelines for medication bioequivalence in New Zealand

Reports begin to emerge of adverse effects following the change to Rubifen SR

CARM received 88 reports of adverse reactions between February and September 2007, when people began to change brands of methylphenidate. Around half of these people claimed a reduction in therapeutic effect with Rubifen SR. In addition, some people reported mood changes, irritability, aggressive or threatening behaviour and unusual psychiatric events shortly after changing to the new brand. This was of particular note in children aged under 17 years.[2]

These reports accounted for less than 2% of patients on methylphenidate SR and most reported adverse reactions occurred within a few days of the brand switch.[3] However, the rate may be higher due to under reporting.

PHARMAC allow a special access subsidy for Ritalin SR

As a result of these reports, Medsafe's Medicines Adverse Reactions Committee (MARC) recommended that PHARMAC make funded Ritalin SR available for patients who experienced serious side effects when they changed to Rubifen SR.[2]

On September 27th, 2007, it was announced that Ritalin SR would be funded for these people on application to PHARMAC on the Ritalin SR Special access form.[3]

NB: Ritalin SR Special Access funding is only being offered for people who had a prior prescription for Ritalin SR, not new patients who started on methylphenidate for the first time after the brand change had occurred.

DEALING WITH BRAND CHANGE

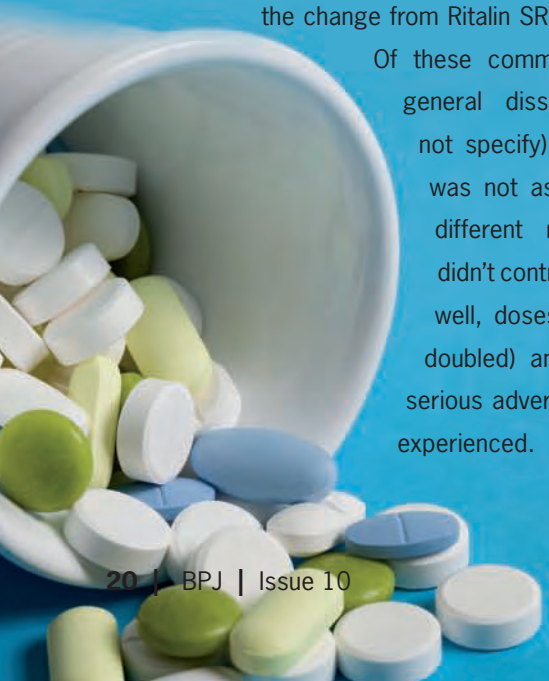
The issues surrounding a brand change become more complex when the drug in question is mainly used in the treatment of mental illness. Consideration must be given to the perception and attitudes of a person receiving treatment for ADHD, and their likely young age, and how this may affect the way they accept a change to their drug therapy, both physiologically and psychologically. One of the main barriers in changing brands of medication is perception of risk by the patient, their family and their caregivers. Studies have found that patients who receive information from their physician or pharmacist about generic substitution are more likely to accept the change.[7]

There is no physiological reason why switching between identical doses of the same drug should result in a different response, however it is unknown what effect drugs such as methylphenidate may have on behavioural responses to change.

Refer to BPJ Special edition, March 2007, for further information on changing to a generic drug

bpac receives anecdotal reports from pharmacists of adverse effects with Rubifen

While assessing pharmacist response to another brand change, we received several spontaneous reports of problems surrounding the change from Ritalin SR to Rubifen SR. Pharmacists were asked to describe any instances of dissatisfaction with brand change. Of the 220 pharmacists who responded, 23 specifically mentioned the change from Ritalin SR to Rubifen SR. Of these comments, 12 were general dissatisfaction (did not specify), ten claimed it was not as effective (e.g. different release profile, didn't control symptoms as well, doses needed to be doubled) and one claimed serious adverse effects were experienced.



IS THERE A PROBLEM WITH RUBIFEN SR?

No obvious cause can be isolated to explain the occurrence of the adverse reactions experienced by people changing from Ritalin SR to Rubifen SR. It is not unexpected that adverse effects are reported after a brand change. This can occur even when the brand does not actually change, for example in one study, nearly half the participants reported subjective differences between their own and study-supplied Ventolin inhalers.[4] Another study assessing acceptance of generic drugs (satisfaction, adverse effects), found significant differences between pharmacological classes of drugs, with less acceptance associated with substitution of drugs acting on the central nervous system.[5]

The brand change from Ritalin SR to Rubifen SR involved the slow release form of methylphenidate 20 mg. This is said to be equivalent to two doses of normal release methylphenidate 10 mg, given four to six hours apart. However there is a lack of evidence of comparisons between the normal and slow release forms. It is claimed that with the slow release form, the release of methylphenidate is slower and the maximum blood level is lower for a more consistent effect. It is theoretically possible that Ritalin SR and Rubifen SR could have different release profiles in some people however, when compared, they were considered to be bioequivalent forms of the same chemical.

Details of CARM reports

CARM has released further information on reports of adverse effects in 56 children who changed from Ritalin SR to Rubifen SR. Symptoms were experienced from a few hours to a few days after the change.[2]

- 75% reported loss of effect
- 55% reported unusual psychiatric events; mood disorders, irritability, hallucinations and suicidal ideations
- 55% reported aggressive and/or oppositional defiant behaviour

Reports of adverse effects in the literature

A literature search using Medline revealed no reports of adverse effects specifically attributable to Rubifen or methylphenidate brand change. It is known that methylphenidate use in children

can be associated with symptoms such as those reported, however this is very rare.[2] The only other country in which the Rubifen brand is marketed is Argentina.

Side effects that can commonly occur when treatment with methylphenidate is first commenced include; nervousness, insomnia, headache, decreased appetite, abdominal pain, nausea, vomiting and minor cardiovascular effects.[6]

An **overdose** of methylphenidate results in overstimulation of the central and sympathetic nervous system and symptoms may include; vomiting, agitation, tremor, hyperreflexia, muscle twitching, convulsions, euphoria, confusion, hallucinations, delirium, sweating, tachycardia and hypertension.[6]

IS IT SAFE TO USE RUBIFEN?

Medsafe has stated that it is satisfied that the two brands of methylphenidate SR are bioequivalent and that no safety issues have been identified at this point.[2] However it is investigating the Rubifen brand and conducting independent testing. AFT Pharmaceuticals, the manufacturer of Rubifen SR, has been asked to urgently provide further data about the quality and safety of their product.

SUMMARY OF ADVICE

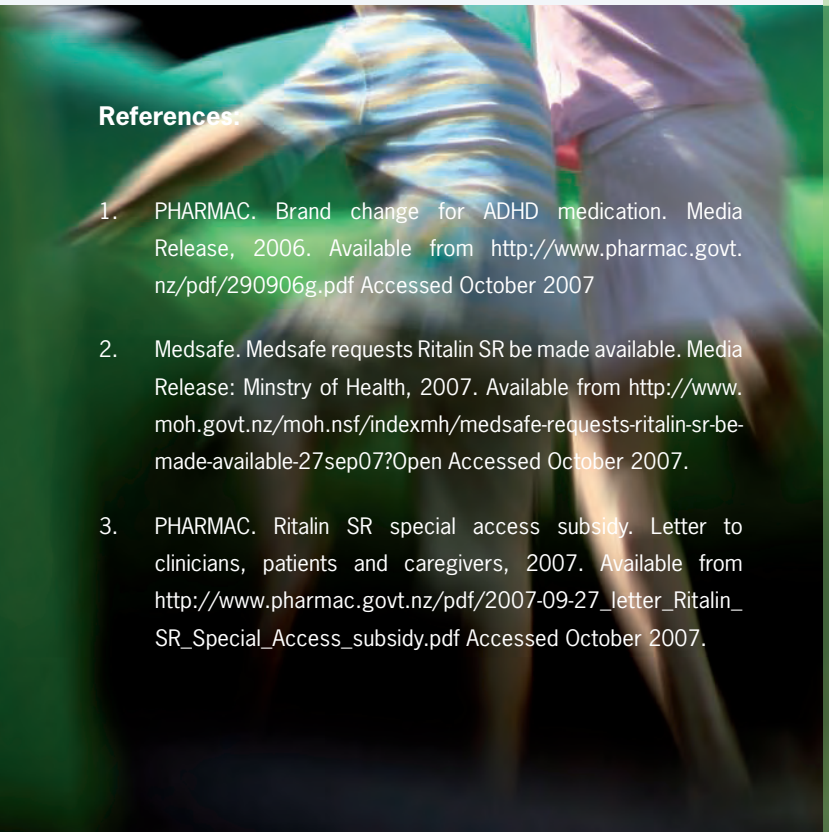
The majority of people using Rubifen SR will not experience any adverse effects in addition to ones previously experienced with Ritalin SR.

Anyone receiving a new prescription for Rubifen SR, as for any brand of methylphenidate, should be started at a low dose and increased slowly to allow monitoring of effect and side effects.

If a person previously on Ritalin SR, taking Rubifen SR for the first time experiences major mood changes (e.g. sadness, anxiety, agitation or aggression) or abnormal behaviour or thoughts, the following action is recommended:

- Rapid assessment is required by the specialist multidisciplinary team
- Alternative treatment options should be discussed with patient and family
- Adverse reactions should be reported to CARM
- Special Access funding for Ritalin SR can be applied for if all other treatment options are unsuccessful

Refer to BPJ Issue 3, February 2007, for further information on the management of people with ADHD



References:

1. PHARMAC. Brand change for ADHD medication. Media Release, 2006. Available from http://www.pharmac.govt.nz/pdf/290906g.pdf Accessed October 2007
2. Medsafe. Medsafe requests Ritalin SR be made available. Media Release: Minstry of Health, 2007. Available from http://www.moh.govt.nz/moh.nsf/indexmh/medsafe-requests-ritalin-sr-be-made-available-27sep07?Open Accessed October 2007.
3. PHARMAC. Ritalin SR special access subsidy. Letter to clinicians, patients and caregivers, 2007. Available from http://www.pharmac.govt.nz/pdf/2007-09-27_letter_Ritalin_SR_Special_Access_subsidy.pdf Accessed October 2007.
4. Williamson IJ, Reid A, Monie RD, Fennerty AG, Rimmer EM. Generic inhaled salbutamol. A randomised double-blind study. Postgrad Med 1997; 73:156-158.
5. Valles J, Barreiro M, Cereza G et al. A prospective multicenter study of the effect of patient education on acceptability of generic prescribing in general practice. Health Policy 2003;65:269-75.
6. Medsafe. Rubifen SR. Data sheet, 2006. Available from http://www.medsafe.govt.nz/profs/datasheet/r/rubifentabsrtab.htm Accessed October 2007
7. Kjoenniksen I, Lindbaek M, Granas A. Patients' attitudes towards and experiences of generic drug substitution in Norway. Pharm World Sci 2006;28:284-9.

A Māori/Pacific Nursing service in a mainstream PHO

A nursing service providing a range of activities targeted at Māori and Pacific whanau was introduced in November 2006 by Mornington PHO, a single practice mainstream PHO, operating through the Mornington Health Centre in Dunedin. At Mornington, 8.4% of the enrolled population of 15,654 self identify as Māori or Pacific. Analysis of data showed that Māori and Pacific patients were not making full use of the available services. The Māori/Pacific Nursing service was established in recognition of the need to address the health centre's obligations to this group, individually and collectively. Various measurable improvements are already evident and the GPs involved rate the service highly and report enhanced care for their patients. By sharing this experience, Mornington PHO hopes to encourage other PHOs and practices to consider implementing similar initiatives to improve the outcomes for their Māori and Pacific patients.

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A Māori/Pacific nursing service can be successfully implemented into mainstream general practice with measurable benefits. It complements and supports other practice activities and ensures increased uptake of services and better engagement with patients.

From a GP perspective good intentions and a willingness to provide culturally appropriate care are not enough. A more active approach is necessary to engage Māori and Pacific patients, facilitate their access to services and cultivate not merely compliance but keen participation in their own care.

There are a range of potential activities that PHOs can adopt to address population issues. The Māori/Pacific Nursing service embodies a dual approach to both the individual and the population. Activities may include:

- Screening
- Individual risk assessment
- Co-ordination of immunisation services
- Health promotion and education
- Counselling and skill development
- Social marketing
- Organisational development
- Community action for supportive environments
- Economic and regulatory activities

The service is provided in the context of He Korowai Oranga (the national Māori Health Strategy) and Whare Tapawha - embracing the four cornerstones of family health (taha whanau), physical health (taha tinana), mental health (taha hinengaro) and spiritual health (taha wairua). In particular, emphasis is placed on Te Ao Māori (Māori world-view), Te Reo Māori (Māori language), management of chronic disease states, access, screening, immunisation and mental health.

Most importantly, this service helps establish a trusting relationship with effective communication between GPs, other staff and Māori and Pacific patients and their whanau.

ACTIVITIES OF THE SERVICE

The Māori/Pacific nursing role is an outreach service with flexible hours of work that are tailored to meet the health needs of the whanau/family. Features of the service include:

- Clients come to the service by referral from clinic staff, whanau or other health and social providers. Initial contact occurs within two days and focuses on building a rapport and establishing priorities. Sometimes more pressing demands make patients unwilling to address health needs until, for example, help from the food bank has been arranged, or a financial crisis has been addressed.
- The service works in partnership with Māori providers and other health and social agencies providing whanau ora, tamariki ora, disease state management, healthy lifestyle promotion, smoking cessation, family violence and wellbeing, budget advice and food bank.
- The service co-ordinates with other Primary Care services such as the Outreach Immunisation service, which allows the opportunity for vaccinating children in an environment that is safe and comfortable.
- The service establishes contact with patients who are preparing for discharge from hospital and is involved in multidisciplinary hospital meetings, ensuring patients and whanau understand what is happening on discharge and what services will be put in place.
- Pharmacies are consulted to ensure medications are affordable and manageable. The client is helped to understand what medications are for and how they should be taken.
- The nurse often facilitates attendance at appointments and accompanies clients as a support person.
- The Māori/Pacific nurse has a leadership role; developing practice systems and fostering a team approach to reducing barriers to access.
- The service employs a bottom-up approach based on consultation with whanau, rather than a top-down planning process.

RESULTS

There have been measurable changes as a result of the Māori/Pacific Health Nurse service being established at this PHO.

- There has been an increase in the number of Māori and Pacific patients registered with the practice due to both increased enrolments and patients being re-allocated to their correct ethnicity.
- Māori and Pacific patients are attending the practice more frequently.
- 77% of patients seen by the Māori/Pacific nurse are Māori, with 43% from the most highly deprived areas (decile 9 or 10).
- 89% of Māori children are fully immunised by 18 months (compared to 65% for Otago and 49% for New Zealand). 100% of Pacific children are fully immunised by 18 months.
- The overall cervical screening rate is 80%, with 75% of high needs Māori and Pacific patients being screened. The nurse thinks that part of the reason these results have been achieved is that Māori patients prefer a Māori smear taker.
- There has been an increase in the uptake of Diabetes Annual Reviews.
- Uptake of the smoking cessation programme has increased by 50%.
- Mental health consultations have increased significantly.

SMART?

In view of the recent promotion of the SMART regimen, (Symbicort single inhaler Maintenance And Reliever Therapy) we thought we should review the use of inhalers containing a combination of a long acting beta agonist (LABA) and inhaled corticosteroid (ICS).

The SMART regimen is the use of budesonide/eformoterol combined (Symbicort) as a single inhaler for both maintenance and reliever therapy.

KEYPOINTS

- Using Symbicort for both maintenance and relief of asthma, is gaining acceptance around the world but when it should be introduced is not yet established.
- A combined LABA/ICS inhaler can be considered for maintenance therapy for patients whose asthma is not well controlled on separate LABA and ICS inhalers (Special Authority).
- The combined budesonide/eformoterol inhaler (Symbicort) can be considered for single inhaler maintenance and reliever therapy for adults with poorly controlled asthma characterised by frequent exacerbations while using a conventional regimen.
- The combined fluticasone/salmeterol inhaler (Seretide) should not be used for single inhaler maintenance and reliever therapy, because the LABA salmeterol has a slower onset of action than eformoterol. Salmeterol is not indicated for the immediate relief of acute asthma attacks.
- High dose symbicort inhalers containing budesonide/eformoterol 400/12 are not suitable for single inhaler maintenance and reliever therapy.
- People using SMART should not exceed six inhalations in one hour or twelve inhalations in any 24-hour period.
- SMART is not appropriate for young children, patients who tend to overuse reliever inhalers or patients with "problem asthma" (vocal cord dysfunction, respiratory symptoms due to obesity, anxiety-hyperventilation).

LABA THERAPY IN ASTHMA

LABA therapy improves symptom control and lung function and reduces the need for rescue medication in people with asthma which is poorly controlled on ICS. LABA therapy should be considered for people for whom regular use of standard dose ICS has failed to control asthma adequately.

Initial LABA therapy should not be commenced in patients with rapidly deteriorating asthma. It is not appropriate to commence LABA therapy for people not already on ICS.

Side effects of LABA therapy include fine tremor, palpitations, arrhythmias, tachycardia and paradoxical bronchospasm. Other side effects include anxiety, headache, muscle cramps, urticaria, angioedema, hypotension, hypokalaemia in high doses, and sleep and behavioural disturbance in children.

COMBINATION LABA / ICS INHALERS

Combination LABA / ICS inhalers are available under a special authority for subsidy when an adult with asthma remains poorly controlled on a dose of at least 800 micrograms per day of beclomethasone or budesonide, or 500 micrograms per day of fluticasone and a LABA, and the prescriber considers the patient would receive additional clinical benefit from switching to a combination product. The specified doses for children are lower than this.

SINGLE INHALER MAINTENANCE AND RELIEVER THERAPY (SMART)

SMART regimen being promoted in New Zealand

Single inhaler maintenance and reliever therapy (SMART) is being promoted for the management of asthma. The single inhaler (Symbicort) contains both budesonide and eformoterol. The highest dose Symbicort inhaler (400/12) is not included in SMART due to the risk of supra-therapeutic doses.

Combination inhalers containing salmeterol are not suitable for single inhaler therapy

Combination inhalers of salmeterol with an ICS, such as Seretide, are not suitable for single inhaler maintenance and reliever therapy. Salmeterol should not be used for the relief of acute asthma symptoms because it has a significantly slower onset of action than either eformoterol, salbutamol or terbutaline.

Single inhaler therapy available but when to use is not yet resolved

Using Symbicort for both maintenance and relief of asthma, is gaining acceptance around the world but when it should be introduced is not yet established.

BNF 54 lists single inhaler for maintenance and reliever therapy with Symbicort 100/6 or 200/6 for adults over the age of 18 years but this regimen is not mentioned in its asthma management tables. [1]

Results of trials encouraging

Clinical trials up until March 2007 demonstrate that by comparison with Seretide plus short acting beta agonist, single inhaler therapy with Symbicort:

- reduces the total number of observed asthma exacerbations
- increases the time elapsed before hospitalisation
- decreases the total amount of oral steroid used
- decreases the inhaled corticosteroid burden [2,3,4]

Fewer Exacerbations

In the COMPASS trial the SMART regimen resulted in a significant reduction in severe exacerbations of asthma in adults and adolescents (aged 12 years and older) in comparison with either equivalent maintenance dose fluticasone/salmeterol with a short acting beta agonist as required, or a maintenance dose budesonide/eformoterol at twice the SMART dose with a short acting beta agonist as required.[5]

Significant reductions in the number of severe exacerbations, and in the time elapsed before the first severe exacerbation, were also seen using the SMART regimen in the STAY and COSMOS trials.[2,3]

Comparable adverse events

Adverse event profiles were comparable in all of the treatment groups of the trials considered.[2,4,5]

Decreased corticosteroid burden

The average total dose of ICS/LABA used in the SMART regimen approximated to 0.75 of the dose administered in the other treatment groups. This corresponds to a lower amount of ICS administered, a lower drug load and a lower glucocorticosteroid burden.

How should general practitioners respond?

The dust has not yet settled on the results of these trials. They appear to be signaling a paradigm shift in asthma management. The role of ICS during worsening asthma is

under review. With the new combined single inhaler method, people are receiving additional ICS earlier in the onset of an exacerbation, in combination with a fast acting beta agonist. It is yet to be determined what each of the components contributes to the improved response.

GPs will no doubt respond with their usual pragmatic approach whilst specialist experts scrutinise the evidence and work out how this regimen fits into asthma management guidelines. In the meantime it may be appropriate to use the SMART regimen for adults, who are not under optimal control with a conventional regimen, especially if they are experiencing frequent exacerbations.

Cautions with the use of the symbicort single inhaler maintenance and reliever regimen

If this regimen is used the following cautions need to be observed.

- Search for aggravating factors for asthma such as inhaled allergens, smoking, anxiety etc.
- Doses should not exceed six inhalations at one time or twelve inhalations in any 24-hour period.
- Safety and efficacy has not been established for children under 12 years of age.
- Symbicort 400/12 is not suitable for the SMART regimen.
- Inhaled ICS can cause dose dependent side effects similar to those from non-inhaled ICS.
- Side effects of beta-agonists may include the advent of tolerance, paradoxical bronchoconstriction, or even increased airway inflammation if used to excess.
- The SMART regimen is not suitable for patients who are not sensitive to variations in airway flow, for patients who tend to overuse reliever inhalers or for those patients with "problem asthma" (vocal cord dysfunction, respiratory symptoms due to obesity, anxiety-hyperventilation) .

References:

1. British National Formulary 54. London. BMJ Publishing Group Ltd. 2007.
2. O'Byrne P, Bisgaard H, Godard P et al. Budesonide/Formoterol Combination Therapy as Both Maintenance and Releiver Medication in Asthma. Am J Respir Crit Care Med. 2005; 171 (2): 129-136.
3. Vogelmeier C, D'Urzo A, Pauwels R et al. Budesonide/formoterol maintenance and reliever therapy: an effective asthma treatment option? Eur Respir J 2005; 26: 819-828.
4. Rabe K, Atienza T, Magyar P et al. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomized controlled, double-blind study. Lancet 2006; 368(9537): 744-753.
5. Kuna P, Peters M, Manjra A et al. Effect of budesonide/formoterol maintenance and reliever therapy on asthma exacerbations. Int J Clin Pract 2007; 61 (5): 725-736.

COPD in primary care: reminder and update

Managing COPD continues to be a major feature of primary care, particularly in practices with a high proportion of Māori and Pacific peoples.

COPDX clinical practice guidelines provide a useful framework for the diagnosis and management of COPD.[1,2] Here is a reminder of the COPDX framework and an update of recent evidence on COPD management based on a 2007 report by the Canadian Thoracic Association.[3]

Smoking cessation is still the only intervention that slows deterioration in lung function. However, the roles of other interventions, such as long acting beta-2 agonists (LABAs), aminophylline, inhaled steroids and tiotropium, are evolving as new evidence becomes available.

Key Components of the COPDX plan

- **Confirm diagnosis** and assess severity by the use of spirometry and measurements of functional impairment
- **Optimise function** by relief of symptoms, increasing wellbeing and reducing the number and severity of exacerbations and complications
- **Prevent deterioration** by smoking cessation and reduction of exposure to other harmful inhaled fumes and particles
- **Develop support network and self management plan**
- **Manage eXacerbations** promptly and appropriately

CONFIRM DIAGNOSIS AND ADDRESS SEVERITY

Spirometry remains key to confirming the diagnosis and assessing the severity of COPD. There are no evidence-based criteria on which to select people for spirometry but the Canadian Lung Association's suggestions seem reasonable (Table 1).

OPTIMISE FUNCTION

Bronchodilators are useful for people with moderate to severe COPD

Bronchodilators currently form the mainstay of pharmacological therapy for people with moderate to severe COPD. They improve expiratory flow and lung emptying thereby reducing air trapping and hyperinflation. However there is little information available on their efficacy for people with mild COPD (FEV1 > 65% of predicted).

Short acting bronchodilators

Short acting bronchodilators, both the beta-2 agonists such as salbutamol and anti-cholinergics such as ipratropium, improve pulmonary function, dyspnoea and exercise performance in moderate to severe COPD. Individual responses to different classes are variable. Using both classes together often produces a superior response.

Tiotropium

The effects of daily tiotropium on pulmonary function, chronic activity-related dyspnoea and quality of life is more sustained than four times per day ipratropium and adherence may be

better. Short-term studies have shown it to be as effective, or more effective than LABAs, but long-term comparisons are not yet available.

N.B. Patients perscribed tiotropium should have their ipratropium discontinued. Combinations such as Combivent include ipratropium.

Long acting beta-2 agonists.

LABAs produce more sustained improvements in pulmonary function, chronic dyspnoea and quality of life than short acting bronchodilators in moderate to severe COPD. Their effect on exercise performance has not yet been consistently demonstrated.

LABA / tiotropium combinations

Combination of these two classes of long acting bronchodilators may improve pulmonary function in severe COPD.

Oral theophyllines

Oral theophyllines are relatively weak bronchodilators; they may offer some additional effects when added to inhaled bronchodilators in chronic COPD management. However, theophylline has significant adverse effects and drug interactions and changes in smoking habits can alter blood concentrations of theophylline.

Inhaled corticosteroids may reduce exacerbation rates

Inhaled corticosteroids (ICS) do not reduce the decline of lung function in COPD but may reduce the severity or frequency of exacerbations.

The place of ICS in combination with LABAs is still not clear. Salmeterol plus fluticasone does not appear to reduce mortality rates compared to placebo but the combination does appear to reduce exacerbation rates and improve lung function. Addition of this combination to tiotropium does not appear to reduce exacerbation rates but may improve lung function, quality of life and exacerbation rates.

Table 1 Canadian Lung Association suggestions for selection for spirometry

Offer spirometry to current or ex-smokers who are aged over 40 years and answer yes to any of the following questions.

1. Do you cough regularly?
2. Do you cough up phlegm regularly?
3. Do even simple chores make you short of breath?
4. Do you wheeze when you exert yourself or at night?
5. Do you get frequent colds that persist longer than those of other people?

Special Authority Criteria for Tiotroprium

In New Zealand, for special authority for subsidy of tiotropium, ALL of the following criteria must be met:

1. To be used for the long-term maintenance treatment of bronchospasm and dyspnoea associated with COPD
2. In addition to standard treatment, the patient has trialled a dose of at least 40 micrograms ipratropium q.i.d for one month
3. Any of the following:

The patient's breathlessness according to the Medical Research Council (UK) dyspnoea scale is either:

   a. Grade 4 (stops for breath after walking about 100 metres or after a few minutes on the level) or;
   b. Grade 5 (too breathless to leave the house, or breathless when dressing or undressing)

4. Actual FEV1 (litres) < 0.6 × predicted FEV1 (litres)
5. Either:
   a. The patient is not a smoker (for reporting purposes only) or;
   b. The patient is a smoker and has been offered smoking cessation counselling
6. The patient has been offered annual influenza immunisation.

Opioids

Opioids may help relieve severe intractable dyspnoea and are the most effective dyspnoea relieving medication in end of life care.

Long-term oral corticosteroids not appropriate

Long-term treatment with oral corticosteroids is not appropriate for COPD as there is little evidence of benefit and substantial risk of systemic adverse effects.

Long term domiciliary oxygen therapy

Long-term continuous oxygen is beneficial for patients with stable COPD with severe hypoxaemia. However, there is no evidence to justify the widespread use of ambulatory oxygen or support the use of nocturnal oxygen to improve survival, sleep quality or quality of life for patient with isolated nocturnal desaturation.

Exercise and pulmonary rehabilitation

Pulmonary rehabilitation programmes are the most effective interventions for improving dyspnoea, exercise capacity and quality of life. These improvements are largely attributed to the exercise components of the programmes. Aerobic exercise of the lower limbs and strength training are both beneficial.

All people with COPD should be encouraged to maintain an active lifestyle and whenever possible, stable patients who remain dyspnoeic despite optimal medication, should be referred for pulmonary rehabilitation.

In 2006, Māori aged 45 years or over had a COPD hospitalisation rate four times that of non- Māori from the same age group. In addition, for this age group COPD mortality rates were over three times higher for Māori than for non-Māori. The relative risk increase was greatest for females for both hospitalisation and mortality rates. Māori females had a COPD hospitalisation rate almost five times that of non- Māori females.[4]

Māori have an increased smoking prevalence rate compared to non-Māori. See page 32.

Smoking cessation and reducing exposure to other inhaled noxious substances remain the only interventions which will slow the rate of deterioration of lung function in COPD (see page 32 for smoking cessation update).

Influenza immunisation reduces the risk of hospitalisation by approximately 40% in people with chronic respiratory disease.

The evidence for pneumococcal immunisation is less well established but is likely to be beneficial.

DEVELOP SUPPORT NETWORK AND SELF MANAGEMENT PLAN

Quality of life is improved for people with COPD who get good psychosocial support. Components of a COPD self-management plan should include:

- Reminder of day to day medications
- Nutritional advice with supplementation for some people
- Lifestyle tips to improve functional status and avoid exacerbations
- Early recognition of exacerbations
- Prompt response to exacerbations, including self-medication

Management of exacerbations

A wide range of comorbidities may confuse the diagnosis of exacerbations of COPD. Once a confident diagnosis has been made, most exacerbations can be managed at home.

Inhaled bronchodilators

Giving short acting inhaled beta2 agonists plus ipratropium is recommended in an acute exacerbation to relieve dyspnoea by improving airway function and reducing hyperinflation.

Oral corticosteroids

Oral prednisone at an individualised dose of approximately 40mg daily for seven to 14 days has good evidence of

efficacy in moderate to severe acute exacerbations of COPD. They are more effective if given early and people who have exacerbations should maintain a home supply.

Oral antibiotics

Oral antibiotics are beneficial in acute exacerbations of COPD and, as with prednisone, people who have exacerbations should maintain a home supply.

For simple exacerbations (increased cough, sputum, purulence and dyspnoea) in people without risk factors, first choice antibiotics are amoxycillin, doxycycline or erythromycin.

If the exacerbation is complicated by risk factors (see Table 2), amoxycillin/ clavulanic acid or another suitable antibiotic, such as a fluoroquinolone, are more appropriate.

Aminophylline

Aminophylline is no longer recommended for acute COPD exacerbations. It produces no clinically significant benefit and significantly increases nausea.[2]

CONCLUSION

COPD is likely to remain a major problem in primary care for some years to come. Tobacco smoking is the most common cause of COPD and around 23% of New Zealanders smoke tobacco. The prevalence is higher among Māori (46%) and Pacific peoples (36%).

Primary care clinicians can help by focusing on the framework of the COPDX plan, initiating therapy using Table 3 as a guide and tailoring care for individual patients based on their response to treatment, the number and severity of any exacerbations and any degree of reversibility. The evidence is often confusing and is continually evolving. However, the message that smoking cessation confers a greater health benefit than any other intervention for people with, or at risk of COPD is a message we should never tire of promoting.

Table 2 Risk factors in COPD exacerbation

- FEV1 <50% predicted
- Greater than four exacerbations per year
- Ischaemic heart disease
- Use of home oxygen
- Chronic oral corticosteroid use
- Antibiotic use in previous three months

References

1. McKenzie D, Frith P, Burdon J, Town G. The COPDX Plan: Australian and New Zealand guidelines for the management of chronic obstructive pulmonary disease 22003 Med J Aust 2003; 178 (6 suppl): S1-S40

2. Abramson J, Crockett A, Frith P, McDonald C. COPDX: an update of guidelines for the management of chronic pulmonary disease with a review of recent evidence. Med J Aust 2006; 184: 342-345

3. O'Donnell D, Aaron S, Bourbeau J et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease – 2007 update. Can Respir J 2007;14(Suppl B):5B-32B

4. Tatau kahukura - Māori Health Chart Book 2006. Available from http://www.maorihealth.govt.nz/moh.nsf/by+unid/CE9CA594D388BE4FCC25714600729978?Open Accessed October 2007

Table 3 Guide to initial therapy for COPD*

<table>
<tr><th>At risk</th><th>Mild</th><th>Moderate</th><th>Severe</th><th>Very Severe</th></tr>
<tr><td rowspan="4"></td><td rowspan="3"></td><td rowspan="2"></td><td></td><td>Oxygen therapy may be indicated</td></tr>
<tr><td colspan="2">Trial of inhaled steroids
Possibly theophylline</td></tr>
<tr><td colspan="3">Regular short acting beta agonist or ipratropium or both
Tiotropium if not responding to short acting bronchodilators
LABA if not responding to or intolerant of tiotropium
Pulmonary rehabilitation</td></tr>
<tr><td colspan="3">Intermittent short acting beta agonist or ipratropium
Exercise and lifestyle modification</td></tr>
<tr><td colspan="5">Smoking cessation (NRT ± support)
Regular questions about coughs, colds, sputum, dyspnoea and wheeze</td></tr>
</table>

*Tailor therapy to response and number and severity of exacerbations.

Update of New Zealand smoking cessation guideline

The recently overhauled New Zealand smoking cessation guideline is well presented and contains important new messages. The guideline has been delivered to all practices and we advise clinicians to take a look.

The guideline is structured around a new memory aid and takes a fresh look at the evidence on methods for assisting smoking cessation. The most effective approach to smoking cessation is judged to be a combination of multi-session face-to-face or telephone support in combination with medication.

In addition, the guideline discusses the problem of assisting smoking cessation for people from population groups who are at particular risk including: Māori, Pacific people, Asian people, children, adolescents, pregnant or breastfeeding women and people with mental illness.

ABC FOR SMOKING CESSATION

Ask	Ask about and document smoking status
Brief advice	Provide brief advice at least once per year to all people who smoke* Personalise the advice Acknowledge it may take several attempts to quit Document that the advice was given
Cessation support	Prescibe medication (usually NRT) Provide support such as Quitline or Aukati Kai Paipa

* NNT =40 for abstinence at six months when advised by doctor.

CESSATION SUPPORT

Primary care has a central role in increasing the number of quit attempts, which is the key to increasing quit rates. The emerging evidence seems to be that this role should be "broad" rather than "deep" – very brief advice to a lot of smokers is better than intensive advice to a few. Ensuring that patients are provided with NRT and shown how to use it is a good investment of time – any additional follow-up by primary care may be of lesser value and is resource intensive.

The basic principles of support are:

- Set a quit date
- Prescribe medication
- Emphasise the importance of complete abstinence
- Provide at least four support sessions

Medications

Nicotine replacement therapy (NRT) is safe and effective

Key points presented in the guideline are:

- NRT is safe and effective (NNT=14 for abstention at six months).
- The choice of NRT product can be guided by individual preference.
- Combining two NRT products (for example, patch and gum) increases abstinence rates.
- NRT should be taken for at least eight weeks.
- People who need NRT for longer than eight weeks (for example, people who are highly dependent) can continue to use NRT.
- NRT can be used to encourage reduction prior to quitting.
- People with cardiovascular disease can use NRT. However, if they have experienced a serious cardiovascular event (e.g. MI or stroke) in the past two weeks or have a poorly controlled disease, treatment should be discussed with a physician. Intermittent NRT products, for example, gum, inhaler, microtabs or lozenges are recommended rather than the longer-acting patches for such people.
- Pregnant women can use NRT after discussion of the risks and benefits. Intermittent NRT should be used in preference to patches.
- Young people (12–18 years of age) who are dependent on nicotine can use NRT if it is believed that the NRT may help. However, it is not recommended for occasional smokers, such as those who smoke on weekends only.

Nortriptyline, as effective as NRT

Nortriptyline is approximately as effective as NRT for smoking cessation (NNT=11 for abstinence at six months). There is no evidence that it is any more effective when combined with other smoking cessation medications.

Nortriptyline needs to be used with caution in people with cardiovascular disease and the other well known problems of the tricyclics need to be considered. There is insufficient evidence to recommend its use in adolescents or pregnant women.

Bupropion, as effective as NRT

Bupropion appears to be as effective as nortriptyline and has less potential for serious side effects. It is safe when used by people with stable cardiovascular or respiratory disease but has some contraindications, such as seizure disorders, CNS tumour, bulimia or anorexia nervosa, abrupt alcohol or sedative withdrawal, MAOI use and lactation. In addition, there is a wide range of precautions.

Bupropion is not currently subsidised in New Zealand.

Varenicline is effective

Varenicline is effective (NNT=8 for abstention at six months). It binds to nicotine receptors in the brain, reducing the severity of tobacco withdrawal symptoms and reducing the rewarding effects of nicotine.

Although it appears to have a good safety profile, adverse event data from general use are not yet available. There is insufficient evidence for its use in adolescents, pregnant women or people with unstable cardiovascular disease.

Varenicline is not currently subsidised in New Zealand.

Face-to face support

Face-to-face support increases abstinence rates at six months (NNT=20). Both individual and group sessions are effective.

Telephone support

Multiple telephone calls for proactive telephone support increase long-term abstinence rates and the addition of telephone support to medication increases smoking cessation rates above those of medication alone. Quitline works.

There appears to be no additional benefit from adding telephone support to multiple session face-to-face support.

Māori smokers want to quit and try to quit.

Smoking is a significant contributor to ethnic and socio-economic health inequalities. Parental smoking is a key risk factor for children and young people starting. Students with two parents who smoke are much more likely to be smokers (33%) than if only one (19%) or neither parent smokes (8%).

Māori smokers want to quit and try to quit. They are just as likely as non-Māori smokers to have made a quit attempt in the past year.

Most quit attempts in Māori, just as in the general population, end in relapse. The average smoker will make around 14 quit attempts before quitting successfully long term. The key is to encourage and support another quit attempt as soon as possible.

The focus should be on getting more smokers making more quit attempts

Health care professionals and health care providers have both the mandate to prompt quitting – most smokers want to quit – and the evidence, by way of the updated guidelines, of what to do.

Advice to stop smoking is often overlooked as an essential part of care for smokers. Nicotine replacement therapy doubles the likelihood of a quit attempt being successful. Regardless of the circumstances, adding support increases this likelihood.

Encourage Māori smokers to quit by providing NRT and promoting a variety of support options including those that take a whānau based, Māori specific approach in a Māori setting – such as Aukati Kai Paipa.

Peter Ellison, Māori Health Advisor, bpac.

"Your smoking is the main influence on whether your children will smoke or not. So if you quit, you will not only improve your health but also the health of your children and your children's children."

PRIORITY GROUPS

Interventions are equally effective for Māori who smoke

Interventions that work in the general population (cessation support plus medication) are equally effective in Māori. For example Māori who call Quitline are just as likely to stop smoking as non-Māori callers and bupropion has been trialled and found effective for Māori.

Smoking rates for Māori are high, with 46% of over 15 year olds smoking and approximately 60% of Māori women between the ages of 15 and 39 years smoking.

Some Māori may be more likely to undertake smoking cessation programmes if they are informed that culturally appropriate services are available. For example Aukati Kai Paipa is a smoking cessation approach developed by Māori for Māori and the Quitline service offers the support of Māori Quit Advisers.

Like Māori, Pacific people and those of Indian ethnicity are at increased risk of cardiovascular disease. There is likely to be higher uptake of smoking cessation interventions if they are presented in a culturally appropriate way.

Pregnancy and breast feeding

When pregnant women stop smoking, there are benefits to mother and child.

The benefits of using oral NRT for smoking cessation in pregnancy and breastfeeding outweigh any potential adverse effects of nicotine on the infant. There is a wide range of toxins in tobacco smoke that are harmful to both mother and child, whereas NRT used intermittently, such as by gum, inhaler, microtab or lozenge, results in a very low level of nicotine exposure to the foetus or breastfeeding infant.

Children and young people

Although there is limited evidence about smoking cessation in children and young people, NRT is less harmful than smoking and can be used along with cessation support, if it is likely to benefit that individual.

People with mental illness

People with mental illness often have not been advised to stop smoking but are likely to benefit from smoking cessation. Caution is required around medication dosage as tobacco smoke speeds up the metabolism of some drugs used to treat mental illness.

Bupropion has been shown to be effective, at least in the short term, for this population group and appears to have a good safety profile.

ALTERNATIVE SMOKING CESSATION REMEDIES

Evidence of lack of effectiveness

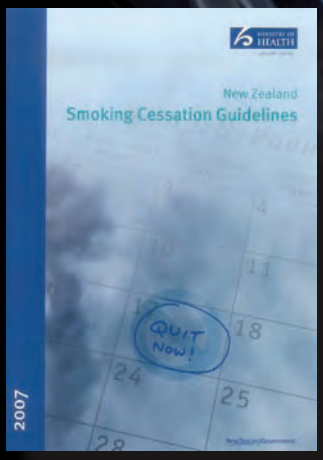
There is evidence that the following interventions are no more effective than placebos which provide the same amount of time and attention to the participant.

- Hypnosis
- Acupuncture
- Acupressure
- Laser therapy
- Electro stimulation
- Incentives

Insufficient evidence

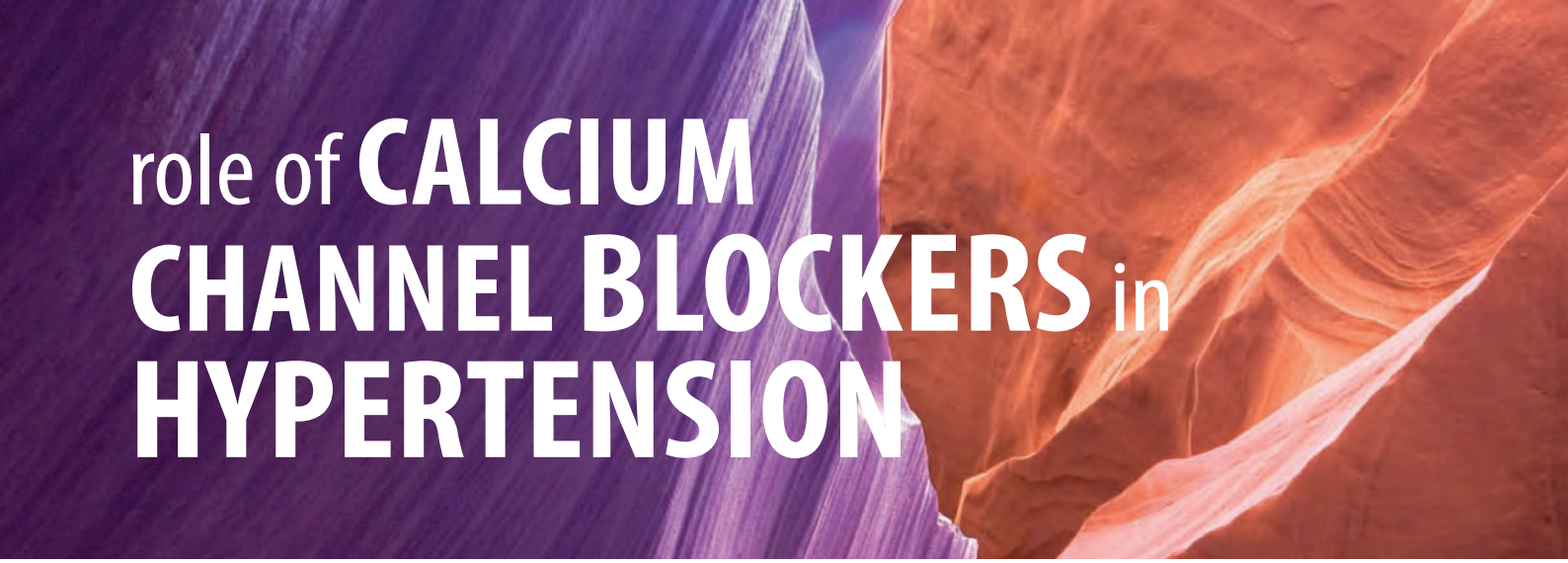
There is insufficient evidence on the following methods to be able to draw a conclusion on their effectiveness or lack of it.

- Allen Carr's method
- Nicobrevin
- Nicobloc
- St John's wort
- Lobeline



Guideline reference: Ministry of Health. 2007. New Zealand Smoking Cessation Guidelines. Wellington: Ministry of Health. August 2007.

Available from http://www.moh.govt.nz/moh.nsf/indexmh/nz-smoking-cessation-guidelines?Open



role of CALCIUM CHANNEL BLOCKERS in HYPERTENSION

KEY POINTS

- Thiazides are appropriate initial therapy for most people with hypertension.
- Choice of other antihypertensives is decided by individual patient factors.
- Factors which potentially favour use of calcium channel blockers include arrhythmia (verapamil only), angina, older age and high risk of stroke.
- Factors which may weigh against the use of calcium channel blockers include potential drug interactions, and diltiazem and verapamil are contraindicated in heart block and heart failure.
- Choice between the different calcium channel blockers depends on patient tolerability, co-morbidity and drug interactions.

Factors favouring use of calcium channel blockers:

- Hypertension with co-morbid angina
- Hypertension with co-morbid arrhythmia (verapamil only)
- Elderly people
- People with an increased risk of stroke
- Verapamil and diltiazem may be alternatives to beta blockers for secondary prevention post myocardial infarction if beta blockers are contraindicated or not tolerated.[2]

THIAZIDES ARE APPROPRIATE INITIAL THERAPY FOR MOST PEOPLE WITH HYPERTENSION

There is limited evidence of superiority of one antihypertensive over another but evidence suggests that for most patients, diuretics can be considered first, based on their effectiveness, safety and low cost.

CHOICE OF ADDITIONAL ANTIHYPERTENSIVES IS DECIDED BY INDIVIDUAL PATIENT FACTORS

Other agents may be chosen for individual patients based on concurrent medical conditions, patient tolerability and drug interactions. Indications for treatment with different antihypertensive agents are discussed in BPJ 6 (June 2007).

FACTORS FOR AND AGAINST THE USE OF CALCIUM CHANNEL BLOCKERS

Factors that potentially favour the use of calcium channel blockers include arrhythmia (verapamil only), angina, or high risk of stroke. Verapamil can also be used post myocardial infarction if beta blockers are contraindicated or not tolerated. In addition, calcium channel blockers may be more suitable than other agents for elderly people and those of African descent.[1]

There is some evidence of a superior protective effect of calcium channel blockers in people with a high risk of stroke when compared with other antihypertensives.[2]

Calcium channel blockers have a favourable effect for treating hypertension with co-existing angina. Verapamil may have a favourable effect when co-existing arrhythmia is present.

Age and ethnicity have less influence on the antihypertensive effect of calcium channel blockers compared with other agents (e.g. ACE inhibitors) and this may present a benefit for calcium channel blocker use in elderly patients.[2] The National Institute for Health and Clinical Excellence (NICE) issued an updated hypertension guideline in June 2006 which states that calcium channel blockers are a first line alternative to thiazide diuretics in hypertensive patients over 55 years.[3]

Factors, which may weigh against the use of calcium channel blockers include potential drug interactions, and diltiazem and verapamil are contraindicated in heart block and heart failure.

CHOICE BETWEEN CALCIUM CHANNEL BLOCKERS

Few studies have directly compared calcium channel blockers and choice may be largely based on patient tolerability, co-morbidity and interaction profile.

Calcium channel blockers vary in their site of action and therapeutic effect

All calcium channel blockers block the inward flow of calcium ions into cells in vascular smooth muscle, myocardial cells, and cells within the sino-atrial (SA) and atrioventricular (AV) nodes.

Dihydropyridines (amlodipine, felodipine, isradipine, and nifedipine) act mainly on vascular smooth muscle and have minimal effect on normal myocardial cells; therefore their main effect is vasodilation. Their minimal effect on the SA or AV nodes means they are not rate-limiting agents.

Isradipine and MIDAS study concerns.

The MIDAS study published in 1996 was designed to compare the effects of normal release (short acting) isradipine with hydrochlorothiazide on atherosclerosis progression in patients with hypertension. An incidental finding was the higher rate of major cardiovascular events in the isradipine group compared with the hydrochlorothiazide group (25/442 vs 14/441; P= 0.07). Apart from not reaching statistical significance other factors mitigate against concerns about the use of Dynacirc SRO for hypertension. Firstly, MIDAS was not designed to detect differences in clinical events or outcomes and these findings were incidental. Secondly in MIDAS, normal release isradipine (short acting) was given twice daily and in general short acting dihydropyridines (including nifedipine) have been associated with increased cardiovascular events in several trials and meta-analyses. Dynacirc SRO is formulated to provide a long duration of action similar to felodipine. Subsequent studies using longer-acting calcium channel blockers have shown better cardiovascular outcomes compared with shorter-acting agents.

The dihydropyridines are mainly used for hypertension and angina and common side effects are associated with vasodilatation, such as flushing, headache, and ankle swelling.

Benzothiazepines (diltiazem) and phenylalkylamines (verapamil) have less selective effect on vascular smooth muscle and have greater cardiac effects. They act on the myocardium to reduce contractility and heart rate and are used in angina and hypertension, but should not be used in heart failure. Verapamil has greater selectivity for cardiac tissue than diltiazem and therefore has more cardiac effects and is also used for arrhythmias.[4, 5, 6]

Choice of dihydropyridine may depend on patient preference

The dihydropyridines are similar in therapeutic effect and the choice between them may depend on patient preference. Long-acting preparations are preferred to short-acting agents which can cause reflex tachycardia and are not suitable for long term treatment of hypertension. Dihydropyridines are either formulated as long-acting preparations such as felodipine, isradipine or nifedipine or inherently long acting such as amlodipine.

Rate-limiting calcium channel blockers may be chosen based on co-morbid conditions

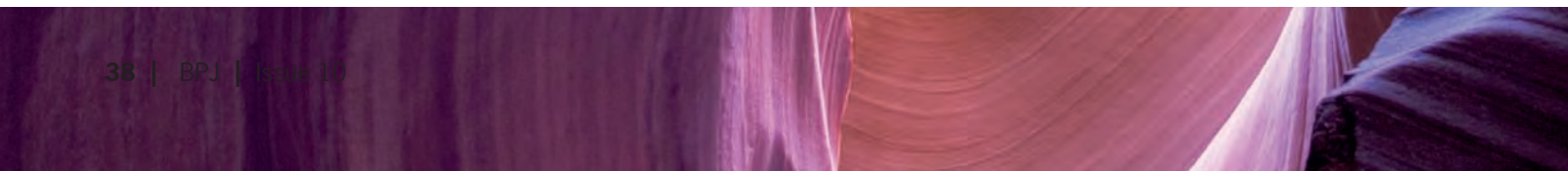
Verapamil and diltiazem are also indicated for use in hypertension and can be considered in patients who have co-existing conditions that would benefit from these agents such as verapamil in patients with co-existing arrhythmias. They are not appropriate in heart failure or heart block, although dihydropyridines can be used with these conditions.

Verapamil and diltiazem are also associated with a number of drug interactions. Co-administration with simvastatin may significantly increase the plasma concentration of simvastatin and potentiate the risk of statin-induced myopathy. Verapamil also significantly increases the plasma concentration of atorvastatin when used in combination. These reactions are less likely with the dihydropyridine group of calcium channel blockers and this should be considered when selecting a calcium channel blocker.

Review concurrent drug therapy when implementing any of the calcium channel blockers.

References

1. Grossman E, Messerli F. Calcium Antagonists. Prog Cardiovasc Dis 2004; 47 (1): 34-47
2. Epstein B, Vogel K, Palmer B. Dihydropyridine Calcium Channel Antagonists in the Management of Hypertension. Drugs 2007; 67 (9): 1309-1327
3. National Institute for Health and Clinical Excellence. Clinical Guideline: Hypertension: Management of hypertension in adults in primary care. June 2006. http://www.nice.org.uk/nicemedia/pdf/HypertensionGuide.pdf Accessed October 2007.
4. Australian Medicines Handbook. Australian Medicines Handbook Pty Ltd. July 2006
5. British National Formulary (BNF). BMJ Publishing Group and Royal Pharmaceutical Society of Great Britain. September 2007
6. Sweetman SC (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version, (Edition 2007).
7. Luscher T, Cosentino F. The Classification of Calcium Antagonists and their Selection in the Treatment of Hypertension. Drugs 2006; 55 (4): 509-517
8. Thomas S. Hypertension. In: Walker R, Whittlesea C, editors. Clinical Pharmacy and Therapeutics (4th Ed.) Edinburgh: Churchill Livingstone Elsevier, 2007: 265-279



COMPARISON OF CALCIUM CHANNEL BLOCKERS

Adapted from Lusher[7] and Thomas.[8]

Drugs	Group	Indications	Special considerations	Major adverse effects	Comments
Amlodipine **Felodipine** **Isradipine** **Nifedipine**	Dihydropyridines *Greater vascular than cardiac tissue selectivity*	Hypertension Angina (except isradipine which is only indicated for hypertension)	Less drug interactions with this group but some are significant including the interaction with grapefruit juice	Flushing Oedema Postural hypotension Headache	Similar efficacy to thiazides Recent studies suggest favourable effect in reducing stroke May be beneficial for elderly
Diltiazem	Benzothiazepine *Equal vascular and cardiac tissue selectivity*	Angina Hypertension	Contraindicated in heart block & heart failure	Bradycardia Heart block	Caution required when used in combination with beta-blocker
Verapamil	Phenylalkylamine *Vascular tissue selectivity less or equal to cardiac*	Angina Hypertension Arrhythmias Post MI if beta-blockers are unsuitable	Contraindicated in combination with a beta-blocker and in heart block & heart failure	Bradycardia Heart block Constipation	May be suitable for patients with ischaemic heart disease who are unable to tolerate beta-blockers

etc

evidence that counts

Benefits of Antidepressants Appear to Outweigh Risks in Children and Adolescents

Previous analyses showing an increased risk for suicidal ideation in children and adolescents taking antidepressants led the FDA to require a boxed warning on labels of all antidepressants. To further assess the risks and benefits of antidepressants, researchers conducted a meta-analysis of 27 clinical trials of antidepressant use (mostly SSRIs) in pediatric patients for major depressive disorder (MDD, 15 trials), obsessive-compulsive disorder (OCD, 6 trials), and other anxiety disorders (6 trials).

In pooled analyses, response rates in the drug and placebo groups were 61% versus 50% for patients with MDD, 52% versus 32% for patients with OCD, and 69% versus 39% for patients with other anxiety disorders. After minor statistical adjustments, the numbers needed to treat to benefit one patient were 10, 6, and 3 for MDD, OCD, and other anxiety disorders, respectively. The absolute difference in risk for suicidal ideation between antidepressant and placebo groups was 0.7% (number needed to harm, 143). No completed suicides occurred in any trial.

Comment:

These data provide a more balanced picture of the risks and benefits of antidepressant use in pediatric patients. The results support their use in children and adolescents by knowledgeable and experienced clinicians for appropriate diagnoses and with careful monitoring. The relatively greater efficacy in patients with anxiety disorders compared to those with MDD is worthy of further study.

— **Thomas L. Schwenk, MD**

Bridge JA et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: A meta-analysis of randomized controlled trials. JAMA 2007 Apr 18; 297:1683-96.

Effect of Soy Intake on Blood Pressure and Lipids

Dietary soy is one of several factors that might explain the lower incidence of coronary heart disease in Asian countries than in Western countries. In a randomized, crossover trial, 60 healthy postmenopausal women followed the National Cholesterol Education Program (NCEP) diet or the NCEP diet with 25 g of soy protein supplied as one half cup of unsalted soy nuts (i.e., roasted soy beans) daily while maintaining an equivalent total protein content. Each phase was continued for 8 weeks, and researchers assessed the effect of the diets upon lipids and blood pressure (BP). Patients with systolic BP ≥165 mm Hg or diastolic BP of ≥100 mm Hg were excluded from the trial.

Mean BP was lower with soy than without, both among hypertensive women (137/82 vs. 152/88 mm Hg) and normotensive women (110/67 vs. 116/69 mm Hg). The soy diet was significantly lower in total and saturated fat than the control diet. Nonetheless, among normotensive women, total, LDL, and HDL cholesterol levels did not differ across diets. Among hypertensive women, LDL decreased by 11%; total and HDL cholesterol levels did not differ significantly.

Comment:

In this small randomized crossover trial, adding soy protein to a diet showed impressive reductions in blood pressure; the magnitude of this effect was surprising and certainly requires confirmation. In contrast, the effect upon lipids was limited.

— **Jamaluddin Moloo, MD, MPH**

Welty FK et al. Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women. Arch Intern Med 2007 May 28; 167:1060-7.

Direct-to-Consumer Advertising of Prescription Drugs

Direct-to-consumer (DTC) advertising of prescription drugs is perhaps the most controversial form of pharmaceutical marketing in the U.S. Researchers from Pittsburgh gathered information on DTC advertising during the past decade.

Key findings were as follows:

- Total spending on DTC advertising in the U.S. increased from about $1 billion in 1996 to $4 billion in 2005; DTC advertising represented about 14% of drug company promotional expenditures in 2005.
- DTC advertising consumed about one third of the total marketing budgets for proton-pump inhibitors, statins, and erythropoietin in 2005.
- From 2002 to 2006, DTC advertising was the target of one third to one half of letters sent by the FDA to drug companies regarding violations in regulations on drug promotion. Most citations were for DTC advertising that minimized risks or exaggerated effectiveness.
- The authors suggest that the level of FDA staffing dedicated to review of DTC advertising has not kept pace with the recent increase in DTC advertising.

Comment:

Drug companies maintain that DTC advertising benefits patients because it increases awareness of drugs that might otherwise be underprescribed. In contrast, many clinicians believe that harmful effects (e.g., stimulating patient demand for unnecessary medications) outweigh any putative benefits. In my view, the big problem — both in DTC advertising and in drug promotion to physicians — is the manipulation of information in ways that subtly overstate the drug's benefits, indications, and target populations.

— **Allan S. Brett, MD**

Donohue JM et al. A decade of direct-to-consumer advertising of prescription drugs. **N Engl J Med** 2007 Aug 16; 357:673-81.

Possible New Treatment Strategy for Parkinson Disease

Like several other major neurodegenerative diseases, Parkinson disease (PD) is associated with aging. In PD, the protein α-synuclein causes aggregates called Lewy bodies and leads to the death of dopamine-containing cells in the substantia nigra. The human sirtuin genes play a role in aging (Journal Watch Jan 1 2006, p. 8). Therefore, a multi-institutional team asked whether the sirtuin genes might directly affect the pathogenesis of PD.

The team discovered two molecules that inhibit sirtuin 2 (SIRT2). They used those inhibitors, as well as the technique of RNA interference, to inhibit the activity of SIRT2 in human glioma cells that make α-synuclein, in rat neuronal cells that make α-synuclein, and in a fruit fly that develops loss of dopaminecontaining neurons, which causes a Parkinson-like disease. Inhibiting SIRT2 protected against α-synuclein–induced cell toxicity in the first two experiments and against dopaminergic cell death and Parkinson-like disease in the fruit fly.

Comment:

This study suggests a molecular link between aging and the pathogenesis of PD. It also suggests a new approach to treating PD, by inhibiting the action of the molecule SIRT2, thereby reducing the toxicity to dopamine-containing neurons by α-synuclein.

— **Anthony L. Komaroff, MD**

Outeiro TF et al. Sirtuin 2 inhibitors rescue α-synuclein–mediated toxicity in models of Parkinson's disease. Science 2007 Jul 27; 317:516-9.

Dillin A and Kelly JW. The yin-yang of sirtuins. Science 2007 Jul 27; 317:461-2.

etc

evidence that counts

Which Dressing for Venous Leg Ulcers?

Multilayer compression bandaging has become standard for treating venous leg ulcers, but it is unclear whether certain specific dressings (applied over the ulcer) are better than others. Moreover, many kinds of dressings are available at a wide range of costs.

This systematic review and metaanalysis updates our knowledge about the relative value of these bandages. Investigators reviewed 42 randomized controlled trials (3001 participants) that evaluated a total of four kinds of dressings: hydrocolloids, foams, alginates, and hydrogel. Eight trials (792 people) compared hydrocolloid with simple nonadherent dressings and found no difference in the rate of ulcer healing. Four trials (311 patients) compared hydrocolloid dressings with foam dressings and also found no difference in ulcer healing rates. None of the other comparisons showed any advantage of one dressing type over another.

Comment:

These studies were hampered by several problems, including small sample size and poor design. The most concrete finding is that colloid bandages perform no better than simple, nonadherent bandages. The authors recommend using cost as the most important determinant of bandage choice, given the lack of data supporting any single type.

— **Keith I. Marton, MD**

Palfreyman S et al. Dressings for venous leg ulcers: Systematic review and metaanalysis. BMJ 2007 Aug 4; 335:244.

What is the best treatment for a stye

Evidence-Based Answer

Warm compresses are recommended for the initial treatment of a stye. Antibiotic therapy is recommended only in the presence of a secondary bacterial infection. Additional treatments include eyelid hygiene, topical anti-inflammatory medications, and incision and curettage if conservative therapy fails (expert opinion). Topical antibiotics after incision and curettage are of no benefit. (based on 1 small RCT.)

No RCTs have been published on the effectiveness of treatments for a stye. Consensus recommendations suggest warm compress for 10 to 15 minutes several times a day to promote spontaneous rupture of the stye. Topical anti-inflammatory medications may be added, with inclusion of antibiotics if secondary infection is noted. Topical antibiotics may also be used if the stye is associated with significant blepharitis. Finally, for refractory cases – failing 1 month of conservative treatment – incision and curettage may be considered.[1,2]

One RCT investigated the effectiveness of a combined antibiotic ophthalmic solution (neomycin sulphate, polymyxin B sulphate, and gramicidin) after incision and curettage.[3] The study included patients with 5-mm styes that were at least 1 week old and not previously treated with antibiotics. Fourteen subjects were randomized to receive the topical antibiotic solution or artificial tears 4 times daily after surgery. The 2 groups were evaluated for pain and mass size on the third and seventh day after incisions and curettage. Investigators used a pain score in which patients gave a verbal rating of their pain

from 0 to 10 (0 for no pain and 10 signifying the maximum tolerable pain). At baseline, the mean pain score was 2.1 in the antibiotic group 2.8 in the placebo group (p=.34).

By the day 3, the pain score was 1.5 with antibiotics and 0.0 with placebo (p=.07). By day 7, the pain score for the antibiotic group was 0.7 and was again 0.0 for the placebo group (p=.32). Prior to treatment, the average mass sizes were 6.4 and 6.2 mm in the antibiotic and placebo groups, respectively (p=.08). By day 3, the mean sizes were 2.5 and 2.1 mm, respectively (p=.49). By day 7 the mean sizes were 1.4 and 1.7 mm (p=.63). Although no comparison reached statistical significance, less pain was reported with the use of artificial tears after surgery compared with the use of topical antibiotics.

— **Rebecca Abraham, MD**
— **Deepak Patel, MD, Assistant Director**
Flower Hospital Family Medicine Residency
Sylvania, Ohio

1. Pasternak A, Irish B. Ophthalmolgic infections in primary care. Clin Fam Pract 2004; 6:1–33.
2. Lederman C, Miller M. Hordeola and chalazia. Pediatr Rev 1999; 20:283-284.
3. Hirunwiwatkul P, Wachirasereechai K. Effectiveness of combined antibiotic ophthalmic solution in the treatment of hordeolum after incision and curettage: a randomized, placebo-controlled trial: a pilot study. J Med Assoc Thai 2005; 88:647-650.

Bandolier

Independent evidence-based thinking about health care

REMINDER - Bandolier has now ceased publishing its monthly print editions. The Bandolier website is now updated with new information

Newly written for Bandolier for October 07

This month Bandolier updates evidence about a number of acute pain interventions and the acute pain ladder. There is updated information on the following pain medications:

Celecoxib
Diclofenac
Dipyrone
Etoricoxib
Ibuprofen
Lumiracoxib
Naproxen

Bandolier has also updated its acute pain NNT League table.

Bandolier Knowledge. In this section of the website, Bandolier collects good quality evidence under a variety of different headings. They search for systematic reviews of treatments, of evidence about diagnosis, epidemiology or health economics, and abstract it.

Go to http://www.jr2.ox.ac.uk/bandolier

Snippets

CALCIUM SUPPLEMENTATION AND THE RISK OF MYOCARDIAL INFARCTION

The recent Auckland Calcium Study revealed an association of a daily one gram calcium supplement in elderly women with an increased risk of myocardial infarction. As a result, many doctors and patients have requested advice regarding the use of calcium supplements for the treatment and prevention of osteoporosis.

The data from the Auckland study have been presented at an Australasian and an American Meeting, but are not yet published. Three other recent studies of calcium supplementation in older women show similar trends, but do not reach statistical significance.

It is possible that high doses of calcium accelerate vascular calcification. There is no international consensus around the subject at present. While further research is being done in this area, the Greenlane Bone Clinic suggests the following:

- Daily one gram calcium supplementation be avoided for people over the age of 70 years and those known to have coronary heart disease.

It is likely that the association is mainly a problem for people with high risk of coronary heart disease. Calcium intake should probably be maintained at a total of approximately one gram per day (equivalent to four servings of dairy products). For instance, in a person consuming a dietary intake of ~0.5g, calcium supplementation should not exceed 0.5g.

There are very few data relating to the cardiovascular effects of calcium supplements in older men. What are available show similar non-significant adverse trends, so the same cautions suggested for older women may be appropriate.

- All people over age 70 years receive regular sunlight exposure or vitamin D supplementation.
- A total calcium intake of one gram per day should be advised for patients taking bisphosphonates for osteoporosis or Paget's disease, as there is a theoretical risk of mild hypocalcaemia. Higher intakes may be optimal in those under 70 years without coronary heart disease.
- Calcium supplements continue to be used, where indicated, for younger women.
- There is no reason on the basis of the Auckland Calcium Study, to advise reduced calcium intakes in children, adolescents or young and middle-aged adults.

Supplied by Professor Ian Reid, University of Auckland

USE OF eGFR FOR DRUG DOSE ADJUSTMENT

The new version of the BNF states:

"BNF 54 continues to provide drug dose adjustments based on creatinine clearance but also gives the advice that, in practice, for most drugs and for most patients of average build and height, the estimated glomerular filtration rate (eGFR calculated from a formula derived from the Modification of Diet in Renal Disease study) can be used to determine dose adjustments in place of creatinine clearance. However, for potentially toxic drugs with a small margin of safety and in some patients (e.g. those at both extremes of weight) the creatinine clearance should be used or the dose should be adjusted according to plasma-drug concentration and clinical response. Work is underway to remove the current BNF categorisation of renal impairment, which focuses on drug elimination, so that there is no confusion with the grading used to determine chronic kidney disease."

Comment

Creatinine Clearance is calculated from the Cockcroft Gault equation. The difference between this and eGFR was explained in BPJ 6. We agree that creatinine clearance and eGFR will be very similar in most people as described above but reiterate that significant differences may be observed in:

1. Ethnic groups for which the MDRD equation has not been validated (Māori, Pacific Island, Asian People) BPJ 6
2. Extremes of body size or muscle bulk
3. Combinations of the above factors
4. eGFR above 60 ml/min. This does not accurately reflect actual GFR and will not correlate well with creatinine clearance calculated by Cockcroft Gault. However, this is unlikely to affect drug prescribing

As more experience is gained in the interpretation of eGFR its utility in drug dose adjustment will become clearer.

Comments endorsed by Professor Rob Walker, University of Otago

Snippets

COMPULSIVE GAMBLING AND DOPAMINE AGONISTS

In BPJ 8 we discussed the drug management of Parkinson's Disease. The main therapies increase the availability of dopamine with levodopa or stimulate dopamine receptors with dopamine agonists such as bromocriptine, ropinirole, cabergoline and pergolide.

Recent cases described in the literature and from spontaneous reporting schemes suggest an association with pathological gambling, increased libido and hypersexuality.[1] Although rare, product information for these drugs includes, or is being updated to warn of, the potential for such effects especially at high doses. Patients or their carers are advised to report any unusual or atypical behaviour.

To some extent these unexpected events may be explained by the role of dopamine as the "reward chemical" and its role in addictive disorders.

PSYCHIATRIC REACTIONS WITH CORTICOSTEROIDS.

Systemic corticosteroids can cause a range of neuropsychiatric reactions from mood changes to psychoses.

The latest BNF carries a reminder about this reaction and the possible risk factors which include; high doses, tablet preparations and a history or family history of psychiatric illness. Psychiatric reactions occur in up to 6 % of people and include affective disorders, irritability, anxiety, sleep disorders, psychotic reactions, behavioural disturbances and cognitive dysfunction. Onset varies from a few days to weeks after starting treatment. Interestingly, reactions have also been reported on withdrawal of treatment.[2]

HEARING LOSS AND DRUGS FOR ERECTILE DYSFUNCTION

The FDA has recently announced a revision to the labeling of sildenafil (Viagra), tadalafil (Cialis) and vardenafil (Levitra) to warn more prominently of the potential risk of sudden hearing loss.

This warning is based on a total of 29 postmarketing reports of sudden hearing loss associated with these drugs, with or without tinnitus, vertigo or dizziness. A further trigger was a recent report of a man who developed bilateral, profound sensorineural hearing loss after taking sildenafil daily for 15 days. In most cases the hearing loss was one side only. In about a third of cases, the hearing loss was temporary.

The warning advises that if a there is a sudden loss of hearing while taking one of these drugs it should be stopped immediately and medical advice sought.[3]

WARNINGS FOR LUMIRACOXIB AND TERBINAFINE

The Medicines Adverse Reactions Committee (MARC) reminds all prescribers of the importance of monthly liver function monitoring in patients taking lumiracoxib (see BPJ 8 for more information). Any abnormal results should be forwarded to the Centre for Adverse Reactions Monitoring. Prescribers are also reminded to dispose of any 400mg sample stock they may have, and remove references to the 400mg strength from their computer.

Oral terbinafine is associated with serious hepatic and haematological reactions. MARC has concerns that oral terbinafine is often prescribed for conditions that are either clinically inappropriate or where the risk of harm outweighs the benefits. To maximise the safety and efficacy of oral terbinafine, prescribers should ensure that the infection is caused by susceptible fungal organisms before prescribing.[4]

References

1. MHRA. Drug Safety Update Vol 1 (1), August, 2007. Available from; http://www.mhra.gov.uk/mhra/drugsafetyupdate. (Accessed 28 October 2007)
2. MHRA. Drug Safety Update, Vol 1 (2), September, 2007. Available from; http://www.mhra.gov.uk/mhra/drugsafetyupdate. (Accessed 28 October 2007)
3. FDA News. October 18, 2007. Available from; http://www.fda.gov/bbs/topics/NEWS/2007/NEW01730.html (accessed, 28 October 2007)
4. Prescriber Update, Medsafe. Nov 2006. Available from; http://www.medsafe.govt.nz/profs/PUarticles/watchingbriefsNov06.htm#Terbinafine (accessed 28 October 2007)

Dear Dave

Dave and other members of the bpac[nz] team answer your clinical questions

BREAKTHROUGH BLEEDING

"I have a patient who has breakthrough bleeding on Estelle 35, when she has previously had no problems with this. She has also started fluoxetine 40mg recently. I noticed on the interactions list that it can interact with St John's Wort. Is the same true with fluoxetine? I have checked for other causes as well, but wondered if the fluoxetine could be to blame."

St John's Wort can interact with oestrogens (i.e the ethinyloestradiol component of Estelle 35) by inducing their metabolism and reducing plasma concentrations. This could lead to irregular menstrual bleeding. However, fluoxetine does not have the same effect and does not interact with oestrogens in this way.

I have looked into whether fluoxetine (and the SSRIs in general) can cause breakthrough bleeding or menstrual bleeding irregularities. A search of the product information and Medline via PubMed revealed nothing of relevance or interest.

Before discounting fluoxetine as a potential cause of this problem it is worth noting that SSRIs can cause bleeding disorders in general by virtue of their antiplatelet effect. A range of disorders have been reported from easy bruising, ecchymoses right through to gynaecological or GI haemorrhage. This may be an unlikely cause but it may be worth considering especially if your patient has other signs of bleeding such as bruising or bleeding gums.

CAMPHOR IN PREGNANCY

"I have a patient in early pregnancy who took camphor for a week to aid giving up smoking. This was recommended by the health shop. Is it safe? She has now stopped it."

Although camphor is not recommended in pregnancy it was presumably at a low dose for a short time and is unlikely to be harmful.

However, camphor is toxic and can cause death if taken in sufficient quantities.[1,2] A toxic dose in an adult would be about 2 g and 4 g or more may be a lethal dose [3]. Nicobrevin is one commercial smoking cessation product that contains 10mg of camphor. Camphor crosses the placenta however the rate and extent of transfer is unknown.[2]

Camphor is not recommended during pregnancy and there has been one reported case of fetal death when a pregnant woman had accidently ingested a toxic dose of camphor.[1,2]

See smoking cessation article (pg 32) for advice on smoking cessation therapy in pregnant women.

1. Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk. (6th Edition) Philadelphia: Lippincott Williams & Wilkins. 2002

2. Committee on Drugs: American Academy of Pediatrics. Camphor: Who Needs it?. Pediatrics 1978; 62(3): 404-406

3. Moffat AC, Osselton MD, Widdop B (eds), Clarke's Analysis of Drugs and Poisons. Pharmaceutical Press. Electronic version, (Edition 2006

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Correspondence

Aggression in medical practice

Dear Editor,

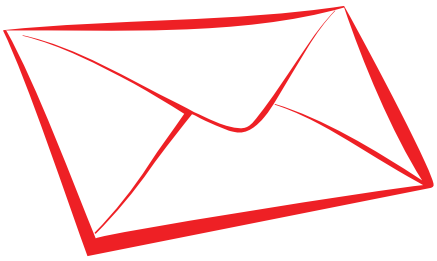
I found your recent publication "Laboratory Testing for Cardiovascular Risk" very useful. Unfortunately it was marred by the repeated use of the qualifier "aggressive", as in "aggressive management of lifestyle factors" (p12), "aggressive lifestyle intervention" (p15), "aggressive pharmacotherapy" (p17), "aggressive blood pressure control" (p23) etc.

If your panel of writers thinks this is a mere semantic quibble, then I beg them to consider how they would feel about having their GP "aggressively intervene" in their own lifestyle. Does this not smack of paternalism and medical hubris?

It seems to me that the notion of aggressive management is deeply inimical to a patient-centered approach to medical practice.

Ian Milne

Aggressive is often used in the literature to describe when an end point is pursued with vigour. But you are right, it does not sound nice – Editor



Send your letters to...

Correspondence, PO Box 6032, Dunedin
or email editor@bpac.org.nz

Medication use in the elderly

Dear Editor,

Just read your message re medication use by the elderly following discharge - yes this has been a problem in the past - I can remember several incidences where people have had to bring all their meds in to us so that we can sort it out. I think the problem is that they are sometimes confused while in hospital - they may receive a lot of verbal instructions for various reasons and as a consequence the medications are misused. I think a clear written chart is essential so mistakes are minimised. Often the discharge note is not faxed to us until days afterward.

Trish Metcalfe

Dear Editor,

My concern relates to those patients (and these are often the elderly) who are discharged from hospital with medication alterations. Often due to the urgency of discharge, patients are not given a new prescription and or medication card and then turn up at the doctor for a prescription prior to any discharge note which may not arrive for up to a week post discharge.

The elderly are especially vulnerable with medication changes as they are often unaware of them and may not even alert the doctors to the fact that they have seen a specialist since their last prescription. Thank goodness for vigilant pharmacists who contact us to discuss any anomalies between prescriptions.

Wendy Gill

Thanks for your feedback. These issues will be addressed in our next edition of BPJ – Dilemmas in prescribing for the elderly – Editor

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