Part V

Whats New In Therapeutics (WNIT) Survey

Innovations
Discontinued drugs
More information please
Drugs for Alzheimer's disease

WNIT Survey

This annual survey helps to identify trends in drug use. Until 2002 the survey was completed by those actually attending the Advanced Courses. Now, by hosting it on **palliativedrugs.com**, it is possible to obtain a more international perspective. This year, there were 102 respondents; 46 from the UK and 56 from other countries. Doctors accounted for about 2/3, nurses for 1/4, and pharmacists for the rest.

The results of the survey are summarised below, and will be posted on the website in due course. The names of those who completed the survey are confidential. However, if you are attending one of the Advanced Courses and have reported a change in prescribing, we hope you will want to share your experiences with other participants.

1. **What is your professional role? Please select one:**
   Doctor Nurse Pharmacist Other

2. **List up to 3 new drugs that you have introduced into your palliative care practice in the last 12 months.**
   Please do not include 'one-off, never-again' treatments.

   Drug name Indication Replacement for what? Comment

3. **List up to 3 drugs that you have discontinued using in your palliative care practice in the last 12 months, and which do not feature in Question 2.**

   Drug name Original indication Reason for discontinuation?

4. **What drugs have you heard about, but not used, and would like more information about?**
   List up to three drugs.

Question 2: Innovations

Innovations are listed in alphabetical order (Tables 2.1 & 2.2). In the 'Rest of the World' table, only those items which did not feature in the UK list are included.

Table 2.1 Innovations during the last 12 months (UK)

In	*Out*
Alfentanil, nasal spray	Fentanyl injection, OTFC, morphine tablets
Buprenorphine [Transtec]	(Fentanyl [Durogesic])
Celecoxib	Other NSAIDs in elderly or concurrent with corticosteroids
Clonazepam	
Dexamethasone	*'as analgesic'*
Epoetin	Blood transfusions
Fentanyl lozenge/OTFC	Other opioid
Fentanyl SL	Morphine solution [Oramorph]
Glycopyrronium	Hyoscine
Heliox	
Ketamine	
Ketorolac	Diclofenac
Lidocaine in Lutrol	Morphine in Purilon
Lignocaine SC	*'for neuropathic pain'*
Lofepramine	Amitriptyline
Macrogols [Movicol]	Traditional laxatives
Methadone	Ketamine and other opioid/other opioids
Methylphenidate	SSRIs
Mirtazapine	Citalopram
Nystatin	Fluconazole → 2nd line
Ondansetron	*'anti-emetic', 'antipruritic (3rd line)'*
Olanzapine dispersible	Haloperidol
Oral Balance gel	
Oxycodone	Fentanyl, hydromorphone, (methadone), morphine
Oxycodone injection	(Diamorphine injections)
Paroxetine 5mg	*'for pruritus, with mixed response'*
Phenoxymethylpenicillin (Pen V)	*'intractable SD site problems'*
Pilocarpine	Glandosane
Risperidone	Thioridazine, (haloperidol)
Sucralfate suspension	Adrenaline soaked dressings
Tramadol	*'in selected patients'*
Venlafaxine	*'additional adjuvant analgesic'*
Zoledronic acid	Pamidronate

Table 2.2 Innovations during the last 12 months (Rest of world)

In	*Out*
Baclofen	Chlorpromazine, haloperidol (for hiccup)
Carbamazepine	Haloperidol (for aggression)
Cimetidine	Medroxyprogesterone (cancer-related sweating)
Clonazepam	
Fentanyl [Durogesic]	Morphine
Fentanyl, intranasal	*'when SC not effective because of gross oedema'*
Frusemide, nebulised	Saline
Gabapentin	Other anti-epileptics (for neuropathic pain)
Hydromorphine [Dilaudid]	Morphine
Levabalbuterol	Albuterol
Levomepromazine	Haloperidol, chlorpromazine, NSAID
Lidocaine, inhaled	*'for cough'*
Megestrol acetate	*'hot flashes in prostate cancer'*
Methadone, topical	
Morphine, nebulised	*'for dyspnoea'*
Morphine, topical	
Octreotide	Hyoscine
Oxcarbazepine	Carbamazepine
Quetiapine	Haloperidol, olanzapine, risperidone
Rofecoxib [Vioxx]	
Sufentanil CSCI	Fentanyl CSCI
Trazodone	Benzodiazepines

Discontinued drugs

Drugs are listed here only if they did not feature in Question 2

Table 3.1 Discontinued drugs (UK)

Dextromoramide	*'no longer manufactured'*
Fluconazole	
Hydromorphone	*'morphine, fentanyl, oxycodone better'*
Hyoscine hydrobromide	*'glycopyrronium more effective'*
Magnesium hydroxide mixture	*'change of doctors'*
Oxetacaine suspension [Mucaine]	*'no longer manufactured'*
Phenytoin	*'because of side effects'*
Thioridazine	*'dangerous cardiac side effects'*
Tramadol	*'excess side effects'*

Table 3.2 Discontinued drugs (Rest of World)[a]

Amitriptyline (for neuropathic pain)	
Atropine	*'use hyoscine or glycopyrronium'*
Carbamazepine	*'toxicity'*
Codeine	
Codeine and paracetamol/acetaminophen	
Co-proxamol (dextropropoxyphene + paracetamol/acetaminophen)	*'low efficacy and potential for adverse reactions'*
Cyclizine	*'greater use of levomepromazine'*
Dihydrocodeine	*'not available'*
Dimenhydrinate [Gravol]	*'useless'*
Fentanyl lozenges/OTFC	*'difficult for patients to use'*
Glycopyrronium	*'expensive and hysocine butylbromide just as good'*
Ketamine	*'poor evidence to support ongoing use'*
Lorazepam	*'prefer diazepam (longer acting) or chlorpromazine'*
Octreotide	*'too expensive'*
Pethidine/meperidine	*'not recommended in literature'*
Prochlorperazine	*'too many toxic reactions'*
Sufentanil	*'prescribing difficulties and cost'*
Trimethobenzamide	*'less effective anti-emetic than placebo'*

a. only those not listed under UK included here

Question 4: More information, please!

There is never time to cover all these requests. However, sometimes the answer is available in the respective monograph in *Palliative Care Formulary 2* or *www.palliativedrugs.com*.
If a monograph probably deals adequately with the request, two asterisks (**) have been inserted before the drug name.
When the respective monograph probably does not deal adequately with a more specific request, the entry is marked with only one asterisk (*).

Box United Kingdom

*Alfentanil, SL
Atropine, for mouth care
**Buprenorphine [Transtec]
Buspirone
**Cannabinoids
**Epoetin, darbepoetin
Fosphenytoin IV, for neuropathic pain
Gelclair
**Glycopyrronium, PO
Ibandronate
*Ketamine, PO, **topical**
Lidocaine, patch
**Methadone, *see also Newsletter February 2004*
**Methylphenidate
*Midazolam, **intranasal**
**Mirtazapine
**Olanzapine, *SC not available*
*Oxycodone, SR [Oxycontin], **SC, CSCI**
Paracetamol + tramadol
Rifampicin
**Thalidomide, efficacy in sweating?
Valdecoxib
**Zoledronic acid

Box Rest of the World[a]

Alzheimer's disease drugs for patients with brain tumours
**Cyclizine
**Diamorphine
Donepezil
Furosemide inhalation
**Levomepromazine
Memantidine
**Morphine, topical for wounds
**Nabilone
Silver dressings for wounds
**Tramadol
**Venlafaxine

a. The items listed here include only those not covered by the UK list.

Drugs for Alzheimer's disease

Main source of information: The Maudsley Prescribing Guidelines 2003 (7th edition; Martin Dunitz, London).

Acetylcholinesterase inhibitors
Four are licensed in the UK:

- tacrine = poorly tolerated → superseded
- donepezil = selective for acetylcholinesterase (AChE)
- galantamine = selective for acetylcholinesterase (AChE)
- rivastigmine = affects AChE and butyrylcholinesterase (BuChE).

The latter 3 drugs appear to be comparable in efficacy and tolerability but, so far, no head-to-head studies have been published.
Withdrawal from trials = 16-29%.
Common undesirable effects: nausea, vomiting, diarrhoea, insomnia.

Results demonstrate 3 groups of patients:

- *non-responders* (continue to decline)
- *non-decliners* (remain the same)
- *improvers* (>4 points on ADAS-cog over 6 months).

Table Anticholinesterases in Alzheimer's disease

Drug	*Starting dose*	*Typical maintenance dose*	*Cost of 1 month's treatment*
Donepezil	5mg daily	10mg daily	£103
Galantamine	4mg b.d.	12mg b.d.	£90
Rivastigmine	1.5mg b.d.	6mg b.d.	£67

Box Summary of NICE guidance on anticholinesterases

Anticholinesterase drugs may be prescribed for those with Alzheimer's disease with a MMSE score of >12 points.

Diagnosis must be made in a specialist clinic.

Assessments of cognitive functioning and activities of daily living should be made before starting drug treatment.

Only specialists should initiate treatment.

Only those likely to comply with drug treatment should be considered.

Further assessments should be made 2-4 months after starting treatment. If MMSE scores indicated no deterioration or improvement and there is evidence of global or functional improvement then treatment should continue.

Those remaining on drug treatment should be assessed at 6-monthly intervals. Anticholinesterases should not normally be used in patients where MMSE scores fall below 12 points.

Slatkin NE, Rhiner M, Bolton TM.
Donepezil in the treatment of opioid-induced sedation: report of six cases.
Journal of Pain and Symptom Management 2001; 21: 425-438.

Donepezil, an oral acetylcholinesterase inhibitor approved for the treatment of Alzheimer's disease, was given to 6 cancer pain patients having sedation related to the analgesic use of opioids. Each patient was taking more than 200 mg of oral morphine equivalents per day, and several were receiving complex analgesic regimens consisting of multiple adjuvant medications. Sedation improved at least moderately in 5 of the patients and mildly in 1 after they began taking donepezil. Patients reported a decrease in episodes of spontaneous sleeping during the day, fewer myoclonic twitches, improved daily function and greater social interaction. Several also reported improved sleep at night. Analgesia was not compromised by the use of donepezil, and in some cases it appeared improved. Donepezil may be a valuable alternative to psychostimulants in the treatment of opioid-induced sedation. A prospective controlled trial comparing the treatment effects of psychostimulants and donepezil on patients having opioid-induced sedation is underway.

Slatkin N, Rhiner M. Treatment of opioid-induced delirium with acetylcholinesterase inhibitors: a case report. *Journal of Pain and Symptom Management* 2004; 27: 268-273

A 55-year-old woman with advanced ovarian cancer and severe pain developed hypoactive delirium after an increase in her opioid dosage. Myoclonus and delirium improved dramatically with the intravenous injection of the acetylcholinesterase inhibitor physostigmine, and this improvement was maintained during the administration of donepezil, an oral medication with similar pharmacodynamic properties. Evidence for a disorder of cholinergic neurotransmission in opioid-induced delirium is discussed, as is the rationale for treatment with acetylcholinesterase inhibitors and other cholinomimetic agents.

Memantine

Licensed in the UK for the treatment of moderately severe to severe Alzheimer's disease.
It acts as an antagonist at N-methyl-D-aspartate (NMDA) receptors, an action which, in theory, may be neuroprotective and thus disease-modifying (Danysz et al 1999).
Memantine appears to be well tolerated but clinical experience is limited.
Trials in severe dementia (Winblad & Poritis 1999) and vascular dementia (Orgogozo et al 2002) suggest an advantage over placebo of around 2 points on the ADAS-cog scale and NNTs (improvement) of 4-10. Improvement was also seen in other domains of functioning.

Common undesirable effects: halluncinations, dizziness, delirium.

Starting dose: 5mg o.d.
Typical maintenance dose: 20mg o.d. (£79 for 1 month's supply)

References

Danysz W et al. Neuroprotective and symptomatological action of memantine relevant for Alzheimer's Disease – a unified glutamatergic hypothesis on the mechanism of action. *Neurotoxicity Research* 1999; 2: 85-97.

Orgogozo J-M et al Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). *Stroke* 2002; 33: 1834-1839.

Winblad B, Poritis N. Memantine in severe dementia: results of the 9M-Nest stucdy (benefif and efficacy in severely demented patients during treatment with memantine). *International Journal of Geriatric Psychiatry* 1999; 14: 135-146.