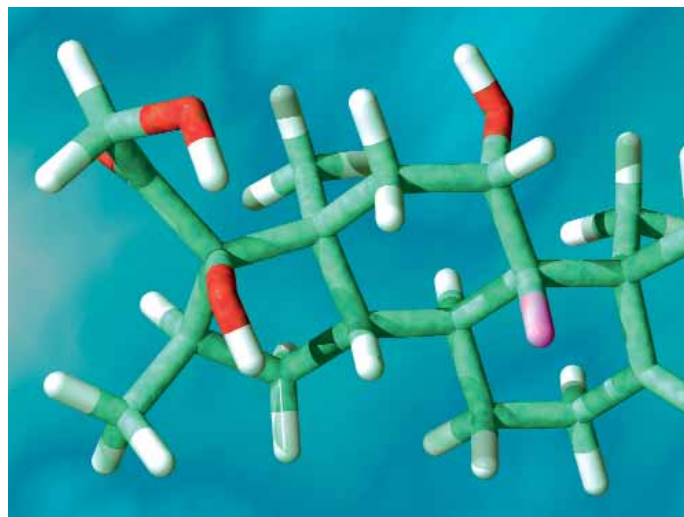


# Urological emergencies

## — pharmacological treatment

By Charlotte Battersby, MRPharmS, and Kevin Thomas, FRCS(Urol)

Prompt treatment of urological emergencies can relieve the symptoms quickly and effectively in some cases, and prevent permanent damage in others. This article looks at the pharmacological treatment of acute urinary retention, renal colic and spinal cord compression



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A dexamethasone molecule: used in the treatment of spinal cord compression

**T**reatment of urological emergencies requires a multidisciplinary approach. Treatment usually depends on the cause of the condition, so prompt investigation and diagnosis is important, as described in the first part of this feature (p325).

### Acute urinary retention

Acute urinary retention (AUR) is the painful inability to pass urine, for which there are several possible causes. Although many cases require surgical intervention (eg, those caused by strictures or neurogenic bladders), some can be treated effectively with drugs.

AUR can often occur after a patient has undergone surgery. Many factors influence the incidence of post-operative AUR, including predisposing BPH, the patient's current medicines, constipation or nerve damage.

The majority of patients admitted to hospital with AUR are catheterised to reduce the immediate discomfort. Catheterisation is often accompanied by treatment with alfuzosin, as described in Panel 1. Once the initial discomfort has been

alleviated, the cause of AUR needs to be determined and treated.

**Urinary tract infections** AUR can be caused by urinary tract infections (UTIs). After the patient has been catheterised, a urine sample is routinely analysed to determine whether an infection is present. Most hospitals have standard protocols for treating a UTI (eg, trimethoprim or cefalexin for uncomplicated UTIs, ciprofloxacin for complicated UTIs).

**Current medicines** A full drug history should be taken from the patient after admission, to allow any possible drug-related cause for AUR to be identified. Several classes of drug can cause AUR as a side effect and examples of these are listed in Panel 2 (p334). The duration of treatment for each drug should also be determined, since recently started drugs are more likely to be associated with the current hospital admission. If a causative agent is identified, it should be replaced or stopped wherever possible.

**Constipation** AUR is frequently associated with constipation in both men and women, although the reason for this is not well understood. A full drug history will help establish if there is a pharmacological cause for the constipation (eg, opioids). Patients must be thoroughly examined for the

presence of impacted faeces, since this complication will need to be treated first. Laxative enemas are typically used to clear any blockage caused by impaction or chronic constipation.

If constipation is confirmed, regular laxatives are started and may need to be taken continuously to prevent recurrence.

**Benign prostatic hyperplasia** Some patients will be admitted to hospital having experienced symptoms of AUR that have been gradually worsening over days or weeks. These symptoms are described on

### Panel 1: Use of alfuzosin post-catheterisation

Alfuzosin is licensed for use in patients aged 65 years or over who have been catheterised, to help them pass urine during their trial without a catheter (TWOC).

The dose is 10 mg daily (as a modified release tablet taken after food) from the first day of catheterisation. Treatment should continue for two to three days during catheterisation, and for one day after the catheter is removed.

No benefit has been shown for continuing treatment beyond four days, or in patients under 65 years.

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## Panel 2: Drugs that can cause acute urinary retention

- Anticholinergics
- Antidepressants
- Decongestants
- Antispasmodics
- Opioids
- NSAIDs
- Amphetamines
- Adrenaline
- Alcohol

p325. A slow onset of symptoms indicates that benign prostatic hyperplasia (BPH) could be the cause of AUR. This occurs when hyperplasia of the prostate causes a physical blockage of the bladder outlet. The prostate grows naturally over time in male patients, so the risk of BPH increases with age.

Once the patient has been catheterised and is in a stable condition, prostate specific antigen is measured (see p327) and a digital rectal examination is performed to determine if the patient has an enlarged prostate.

First-line treatment of BPH involves alpha-adrenoceptor blocking drugs (alpha-blockers).<sup>1</sup> There are many alpha-receptor subtypes in the body, so the potential for side effects is high when non-specific alpha-blockers are used. Using a selective alpha<sub>1</sub>-receptor blocker (eg, tamsulosin) achieves maximum blockade of receptors in the prostatic capsule, smooth muscle and bladder neck, while minimising side effects. This reduces pressure in the bladder, relieves symptoms and improves the chance of the patient passing urine after the catheter is removed. Panel 3 lists the selective alpha<sub>1</sub>-receptor blockers currently available in the UK.

When BPH is diagnosed, the alpha-blocker can be continued after the catheter is removed to relieve any ongoing symptoms.

The first dose of an alpha-blocker should be given at night, due to its hypotensive effect. Other potential side effects include ejaculatory disturbances and floppy iris syndrome — a phenomenon observed during cataract surgery in some patients who are, or have previously been, treated with tamsulosin. Initiating any alpha-blocker in patients scheduled for cataract surgery is not recommended because there have been isolated cases of floppy iris syndrome with other alpha-blockers, so the possibility of this being a class effect cannot be ruled out.

If alpha-blockers do not produce an adequate response, or if the patient's trial without a catheter (TWOC) fails, a 5-alpha-reductase inhibitor can be used, either to supplement or replace the alpha-blocker.<sup>3</sup>

Prostatic growth depends on the presence of dihydrotestosterone — an androgen that

is converted from the inactive testosterone by the enzyme 5-alpha-reductase. The prostate requires dihydrotestosterone to maintain its size and continue to grow. If levels of dihydrotestosterone are reduced, the prostate will decrease in size. 5-alpha-reductase inhibitors are divided into type I (which convert testosterone in the skin) and type II (specific for the prostate). The two 5-alpha-reductase inhibitors currently licensed in the UK are dutasteride and finasteride.

Finasteride, a type I 5-alpha-reductase inhibitor, takes about three months to produce an adequate response, although it may take six months for a response to be measurable. Dutasteride inhibits both type I and type II 5-alpha-reductase, so is believed to have a more rapid response. Patients usually undergo up to three TWOC attempts. Introduction of a 5-alpha-reductase inhibitor may help to achieve

success after the first TWOC has failed, thus preventing the need to undergo surgery.

The MTOPS study showed that concomitant use of alpha-blockers and 5-alpha-reductase inhibitors is beneficial.<sup>4</sup> In this study, doxazosin and finasteride in combination reduced the risk of overall BPH progression significantly more than either drug alone. The study also showed that the combination of the two therapies and finasteride alone reduced the long-term risk of AUR and the need for invasive surgery.

## — Acute renal colic

Passing ureteric calculi (kidney stones) can cause sudden, severe suprapubic pain known as acute renal colic (ARC). Patients suffering with ARC are often restless and unable to lie flat. When they are admitted to hospital, pain

## Panel 3: Doses and precautions for selective alpha<sub>1</sub> blockers<sup>2</sup>

Alpha blocker	Dose	Precautions for use
Alfuzosin	10mg (slow release) <i>od</i> 2.5mg <i>bd</i> if patient is over 65 years or regularly takes antihypertensives	Dose reductions required for patients with renal or hepatic impairment
Tamsulosin	400µg <i>od</i>	No dose adjustment needed in renal impairment, or in mild to moderate hepatic impairment. Contraindicated in severe hepatic impairment
Doxazosin	1mg <i>od</i> Increase by 1–2mg every one to two weeks according to response to a maximum of 8mg. Usual maintenance dose is 2–4mg <i>od</i>	Caution in patients with hepatic impairment
Indoramin	20mg <i>bd</i> Increase by 20mg every two weeks according to response up to a maximum of 100mg daily. In elderly patients, 20mg <i>on</i> may be adequate	Contraindicated in heart failure and in patients taking monoamine oxidase inhibitors. Use with caution in patients with hepatic or renal impairment, or in patients with Parkinson's disease
Terazosin	1mg <i>od</i> Increase by 1mg every one to two weeks according to response to a maximum of 10mg	No dose adjustment required for patients with renal or hepatic impairment
Prazosin	500µg <i>bd</i> Give for three to five days according to response. Usual maintenance dose (and maximum dose) 2mg <i>bd</i>	May cause collapse due to hypotensive effect (first dose effect). First dose should be given on retiring to bed. Patients should be advised to lie down if symptoms such as dizziness, fatigue or sweating develop, and remain lying down until symptoms have abated.

control is administered before any further investigations take place.

**Analgesia** Several studies have reviewed pain relief for patients with ARC. Many compare the use of non-steroidal anti-inflammatory drugs (NSAIDs) or opioids alone with a combination of both, but have shown mixed results. The decision often comes down to the consultant's preference.

A recent Cochrane review showed that single bolus doses of opioids or NSAIDs provided pain relief to patients with ARC. However, patients receiving NSAIDs achieved greater reduction in pain scores and were less likely to require further analgesia in the short term.<sup>5</sup> In addition, opioids (especially pethidine) were associated with a greater risk of vomiting than NSAIDs. Therefore, NSAIDs are the first-line analgesic for treating ARC, with opioids (other than pethidine) only being used if the patient has a contraindication to NSAIDs. Diclofenac is the NSAID of choice, administered as an injection or a suppository.

**Stone passage** Often, patients suffering from ARC will pass the stone (or stones) without medical intervention. If they do not, alpha-blockers or calcium channel blockers can be used to aid this process and prevent the need for surgical intervention such as stenting.<sup>6</sup> However, evidence for the use of these agents is sparse and no products have been licensed for this indication.

Prednisolone may be used to help reduce inflammation around the site of the stone, thus helping its removal from the urethra.

Allopurinol is licensed for the prophylaxis of calcium oxalate renal stones and is used to prevent recurrence.

## — Spinal cord compression

Spinal cord compression (SCC) is a recognised complication of metastatic cancer. It can have a substantial negative effect on quality of life and survival. SCC most commonly develops in patients with advanced stage disease but can be the presenting feature or first sign of metastatic disease.<sup>7</sup> Approximately 50 per cent of spinal metastases are due to breast, lung and prostate cancers. About 90 per cent of prostatic metastases involve the spine, especially the lumbar region.

The signs and symptoms of SCC are described on p329. Early detection and treatment of the condition is essential, because patients experiencing SCC can deteriorate rapidly towards complete paraplegia. Bladder dysfunction, including urinary retention, is one of the symptoms that can present during SCC.<sup>8</sup> Once diagnosed, treatment with corticosteroids, along with analgesics if required, should be started promptly.

**Corticosteroids** There is good evidence to support the use of corticosteroids in patients with newly diagnosed SCC and a history of cancer. Patients with no history of cancer presenting with an undiagnosed spinal mass, especially younger patients, should avoid corticosteroids until a diagnosis is confirmed. This is because these drugs have an oncolytic effect on some tumours, especially thymomas and lymphomas, which may delay diagnosis.<sup>9</sup> The corticosteroid of choice is dexamethasone, although the optimal dose is unclear, since several are recommended in the literature.

Initially a high loading dose should be given as a bolus. The recommended dose varies from 16mg to 100mg, and seems to depend on the severity of the lesion. Doses of dexamethasone at the high end of this range have an increased risk of side effects, which may outweigh the potential benefit, so the decision is up to the consultant.

Following the loading dose, treatment is maintained at 4–24mg daily, either orally or intravenously, in divided doses. Some studies state this should be given four times a day.<sup>10,11</sup> The maintenance dose should then be tapered down over about 14 days.<sup>9</sup>

It is important to remember that doses given later than 6pm can cause insomnia, and prolonged use may lead to steroid withdrawal symptoms.

Many decisions on corticosteroid treatment of SCC are made according to the consultant's preference or experience. After a patient has received dexamethasone treatment, he or she may go on to receive radiotherapy or surgery to the spinal cord.

**Analgesia** NSAIDs can be used to reduce the inflammation and pain associated with SCC. If the pain is severe or pain relief with NSAIDs is not sufficient, opioids can be used.

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## — Summary

The treatment of AUR, ARC and SCC requires accurate diagnosis. Once established, the symptoms can be treated quickly and effectively. In AUR, the most suitable treatment option is only chosen once the cause is established.

In ARC, adequate pain relief is of paramount importance until the stone or stones are excreted. Some drugs can be used to help expel the stones, although there is little evidence for this use.

SCC can have severe and potentially fatal consequences if not treated quickly and correctly. The diagnosis must be accurate and subsequent treatment swift. This usually involves a bolus dose of dexamethasone followed by a tapering maintenance dose. Pain control may be required, depending on the nature of the patient's symptoms.

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