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clinical initiatives, research and current updates in treatment

Staff at Newcastle Private Oncology Centre utilising the Dignicap scalp cooling system®

Scalp Cooling in the Management of Chemotherapy-Induced Alopecia

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Chemotherapy-induced alopecia (CIA) is a common and distressing side effect of many chemotherapy drugs. Well known chemotherapy agents with high potential to induce alopecia include anthracyclines (doxorubicin and epirubicin), taxanes (docetaxel, paclitaxel, cabazitaxel), cyclophosphamide, irinotecan and etoposide.[1]

Following the first dose of chemotherapy hair loss usually starts 1-3 weeks later.[1] Current anthracycline and taxane-based regimens often develop severe enough CIA to warrant the use of a wig or other head covering.[2] However, with the introduction of scalp cooling at the initiation of chemotherapy, the severity of CIA may be decreased.[3] When scalp cooling is used in the setting of breast cancer, it has been shown to be effective in more than 50% of CIA cases.[2]

Scalp cooling is thought to work in two ways. Firstly, by inducing vasoconstriction, there is decreased drug exposure to the scalp during peak concentration of the chemotherapy infusion. Secondly, there is a reduction of metabolism at the hair follicle and this leads to reduced drug uptake and action.[1] Both mechanisms simply decrease the overall effect of the drug on the hair follicles and increase their chance of surviving the course of chemotherapy.

Traditional scalp cooling involved the use of gel-containing caps, frozen to below -25°C. However, these caps were uncomfortable due to their bulkiness and weight, they were poor temperature regulators and needed to be frequently changed due to thaw effects.[4] Newer technology has led to the development of refrigerated units. A tight fitting silicone cap connected to a cooling and control system is fitted onto the patients scalp at room temperature. Cooling is initiated before chemotherapy, continues throughout and for a period afterwards. The length of time the cap remains in-situ after the infusion should equate to the half-life of the chemotherapy agent being administered, the active metabolites and the duration of the infusion.[1] Patients report refrigerated scalp cooling as being generally well tolerated with the most common side effect reported as a headache, which can be prevented by the use of paracetamol.[1]

Since the use of scalp cooling has been established as safe, well tolerated and effective its use should be considered for patients whose chemotherapy is likely to cause CIA. Currently, the technology has been utilised widely overseas[1] and there are a growing number of chemotherapy clinics in Australia now offering this preventative therapy.

Medication Safety in Postoperative Pain Management

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Acute postsurgical pain is related to the type of surgery performed and the degree of tissue damage.[1] The pain may be somatic, visceral, neuropathic or mixed in nature.[2] Good postoperative pain control results in fewer medical complications, enhanced patient comfort and satisfaction.[1,3,4] Concurrent use of analgesics with different actions improves pain control and decreases the dosage requirements for individual agents.[5,6]

Selection of Appropriate Post-operative Analgesia

Paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) are effective in managing mild-moderate acute pain.[2] NSAIDs are useful as the sole analgesic after minor surgical procedures and may have a significant opioid-sparing effect after major surgery. Unless contraindicated, all patients should receive an around-the-clock regimen of NSAIDs or paracetamol.[6] A moderate-severe acute pain state usually necessitates further addition of an opioid analgesic.[2,6,8]

Oral opioid administration is preferred in mild-moderate pain states.[2] This dosage route has high patient acceptability, can be easily continued in the outpatient setting and is equally effective as parenteral opioid formulations when dosed appropriately.[2] However it has slower onset and requires a functioning gastrointestinal tract.[2] Intravenous (IV) opioid analgesia is the mainstay of treatment for severe acute pain following surgery.[2] This dosage route provides rapid and reliable drug absorption.[6,8] Doses can be given as boluses, continuously infused or patient-administered via a patient-controlled analgesia (PCA) device.[2] Close monitoring is required because IV opioids have a greater risk of causing respiratory depression, a rare but serious adverse effect.[2] (Table 1)

Safe Opioid Use

Opioid analgesics have been implicated in a number of medication incidents causing death, and are therefore recognised internationally as a high-risk medicine (listed under "N" for narcotics in the "A PINCH" medication safety acronym).[12]

In a recent overseas review of fatal opioid medication incidents, four major themes were identified: opioid overdose, overlapping drug toxicities, people using opioids not intended for them, and incidents involving HYDROmorphone, an opioid 5 times more potent than morphine.[13]

Factors contributing to opioid overdose:[6, 13, 14]

- initiation of inappropriately high doses (including use of fentanyl transdermal patches in opioid-naïve patients or for treatment of acute pain),
- concomitant use of ceased drug orders,
- incorrect drug pump programming,
- inappropriate manipulation of dosage forms (e.g. crushing SR formulations),
- prescribing multiple opioids via different routes, and
- the routine administration of "as required" doses.

Concomitant use of multiple medicines with similar toxicity profiles e.g. central nervous system depressants (e.g. benzodiazepines, anticonvulsants, sleeping agents, general anaesthetics and alcohol), with or without comorbid disease states (such as renal or hepatic failure), has also resulted in patient casualty.[13]

Preventing adverse events with opioids requires a multifaceted approach addressing the safe practices for prescribing, storage, dispensing, administration, monitoring and reversal of opioids, as well as staff and patient education.[11]

Opioid conversion tables should be used to guide dosing, with modification in response to the patient's clinical condition and previous exposure to opioids.

Safeguards have been successfully implemented in hospitals worldwide to reduce mix-ups between HYDROmorphone and morphine. Many hospitals have removed high concentration HYDROmorphone formulations from patient care areas, utilise the Tall Man lettering system to distinguish these look-alike sound-alike medications and have integrated independent double-checks into workplace policy.[15] Confusion between immediate release (IR) and sustained-release (SR) formulations can be minimised by prescribing both generic and brand names and by ticking the SR box on the National Inpatient Medication Chart where appropriate.

An accurate and complete medication history upon patient admission and transfer is the basis for which therapeutic decisions can be made.[18] The extent of a patient's opioid naivety/tolerance directs choice of treatment. Patients may be inadvertently overdosed if their prescriber is unaware of applied opioid patches. As patients often think of "medications" as traditional oral solid dose forms, it is important to ask direct questions regarding specific dose forms such as patches to guarantee a complete medication history. The Medication History Checklist on the National Medication Management Plan supports

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Table 1: Opioid side effects (Adapted from Reference 9)

Common	Occasional	Rare
drowsiness/dizziness (initially)	dry mouth	respiratory depression (potentially fatal)
nausea and vomiting	itch	psychological dependence *(uncommon if no history of substance misuse)*
constipation (ongoing)	confusion/hallucinations	

Current Maintenance Therapy in Atrial Fibrillation

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Atrial fibrillation (AF) is the leading risk factor for ischaemic stroke increasing the risk in these patients by up to 5 times.[1] Therefore, it is imperative to understand the appropriate use of anticoagulants, rate and rhythm control strategies in patients with AF.

Anticoagulation Therapy

In non-valvular AF, the patient's risk of stroke must be assessed using the CHA2DS2-VASc score[4] evaluating age, sex, blood pressure, other comorbidities and stroke risk factors to determine their annual stroke risk percentage based on a score between 0 and 9. Patients who score zero are classified as low risk and do not require any anti-thrombotic therapy. A score of one requires the clinical judgement of the physician on whether to begin anticoagulation, while a score of two and above indicates definite use of anticoagulant therapy.[1,4] Major bleeding risk must also be assessed using the HAS-BLED score, which also considers age, hypertension, prior stroke, as well as other haemorrhagic risk factors. HAS-BLED scores ≥3 (range 0-9) indicate a high bleeding risk, necessitating caution and regular review, with attempts to correct the potentially reversible risk factors for bleeding, such as alcohol intake and use of certain medications, e.g. NSAIDs.[4]

It is important to note that patients with paroxysmal or persistent AF are at similar risk of developing a thromboembolic occlusion to patients with permanent AF and should be treated in the same way.[2] Anti-platelets such as aspirin play a minute role in the prevention of ischaemic stroke and increase the risk of bleeding hence cannot be used as an alternative to anti-coagulants.[3] Patients with valvular AF must be treated with warfarin as studies have not yet been conclusive on the use of novel oral anti-coagulants (NOACs).[1] In non-valvular AF, warfarin and NOACs have similar efficacy in preventing ischaemic stroke giving patients more control over their choice of anti-coagulant.[5] NOACs have a rapid onset, do not require INR blood monitoring, have shorter half-lives, and less food and drug interactions. However in severe renal and liver impairment, warfarin is preferred.[4] The lack of NOAC reversal agents has proven to be a strong deterrent against the use of NOACs.[6]

Rate Control Therapy

Rate control should be offered as first line treatment except for AF with a reversible cause, heart failure thought to be caused by AF or new onset AF.[7] Rate control in AF improves symptoms, quality of life and reduces morbidity. For some patients it is acceptable to obtain appropriate rate control while continuing not to be in sinus rhythm.[8] Metoprolol, atenolol, nondihydropyridine calcium channel blockers (verapamil, diltiazem), digoxin and certain antiarrhythmics such as amiodarone and sotalol are effective in achieving rate control. In choosing the most appropriate agent, the physician must take into account the patient's severity of symptoms, haemodynamic status and other comorbidities such as heart failure and other precipitants of AF.[8]

Studies show that beta blockers are the most effective in achieving rate control and should be considered first line treatment. If beta blockers are contraindicated, nondihydropyridine calcium channel blockers are preferred.[9] Although patients with left ventricular dysfunctional heart failure should avoid calcium channel blockers due to their negative inotropic effects which may further depress myocardial function. Digoxin, normally third line, can be used adjunctively with beta blockers or calcium channel blockers to improve rate control.[8] Due to its positive inotropic effects, digoxin can also increase the force of contraction needed in heart failure patients.

Rhythm Control Therapy

Rhythm control becomes a viable option if symptoms persist with rate control or in patients who can be easily

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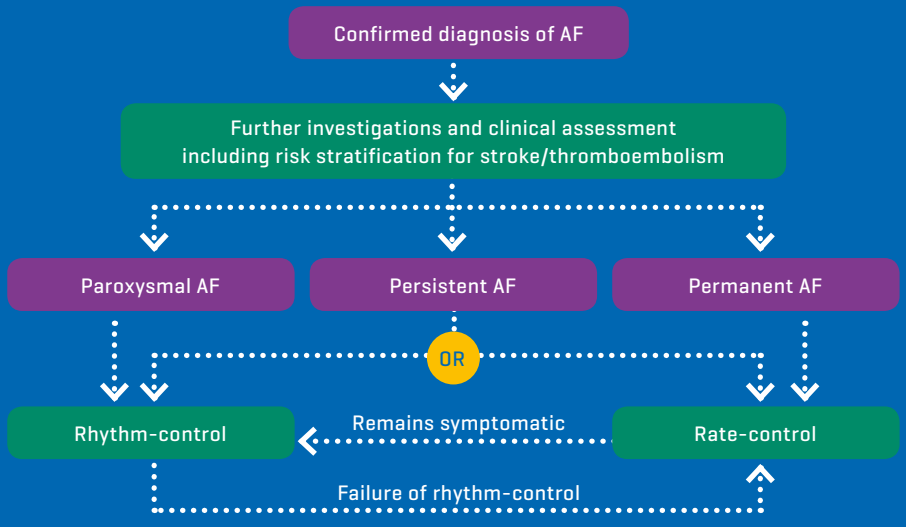
Figure 1. Treatment strategy decision tree for confirmed diagnosis of AF[14]



What's New

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Thyroxine

Sanja Mirkov, Pharmacy Practice Unit

Eltroxin® brand of thyroxine sodium tablets is now available on the PBS. As Eltroxin® is not bioequivalent with other thyroxine brands Eutroxsig® or Oroxine®, do not interchange Eltroxin® with Eutroxsig®/ Oroxine® unless a decision has been made to switch the products. Switching between the different brands of thyroxine requires monitoring of TSH levels and dose adjustment may be required. When taking medication history, confirm and document both thyroxine generic and brand name on the medication chart.[1]

Storage requirements for Eltroxin® tablets are different to those of Eutroxsig®/ Oroxine® tablets which are stored in the fridge. Contrary to this, Eltroxin® tablets are stored at room temperature (below 25°C) in original bottle protected from light.[1]

Eltroxin® tablets are available in six different strengths: 25, 50, 75, 100, 125 and 200 micrograms.[1] Select the Eltroxin® tablet strength carefully when prescribing, dispensing or administering tablets.

As thyroxine sodium dose is in micrograms, write "micrograms" or "microg" to avoid misreading "mcg" as "mg" or include both i.e. "0.1mg = 100 micrograms" when prescribing thyroxine tablets. Do not use the dangerous abbreviation "mcg".[2]

Thyroxine has been identified as a look-alike, sound-alike medication: levothyroxine (a term used more commonly overseas) and L-thyroxine (T4) have been confused as liothyronine (T3), Lanoxin® (digoxin) and lamotrigine[3-5] and thyroxine 100mcg was confused with thiamine 100mg.[6]

The table below summarises the adverse events reported in the literature associated with misinterpreting thyroxine prescriptions due to the use of dangerous abbreviation "mcg", misreading decimal points and its look-alike, sound-alike features: [3,4,7]

Intended (Prescribed as)	Dispensed	Outcome
Thyroxine 25mcg	Thyroxine 0.25mg	Hospitalised
Thyroxine 25mcg oral	Thyroxine 25mg IV*	Death
Thyroxine 0.25mg	Thyroxine 0.025mg	Prolonged hospitalisation
L-thyroxine	Liothyronine	Elevated T3 levels

*Not marketed in Australia

Medication safety in postoperative pain management

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such practice. Furthermore, a full body skin assessment of patient prior to administering a new opioid may also be considered, to eliminate the risk of undetected opioid patches.

Patient education is an important tool in empowering patients to detect and prevent medication errors. A pain management plan at discharge may be a useful consideration for some patients.[6] This could include a list of all analgesics with dosage instructions, estimated duration of therapy, medicines information and instructions for monitoring and managing side effects.[6] By adopting a patient-centred approach to care, practitioners can help improve patient outcomes and decrease the incidence of medication safety mishaps.

Current Maintenance Therapy in Atrial Fibrillation

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converted and maintained in sinus rhythm such as younger patients or those having their first episode of AF.[8] Antiarrhythmic therapy has similar efficacy with rate control however has a greater rate of hospitalisation.[10] For maintenance of sinus rhythm after cardioversion, flecainide, sotalol and amiodarone are all effective. The choice of antiarrhythmic therapy is dependent on patient comorbidities and adverse effect profiles of individual medications.[1,11,12] Patients with significant left ventricular hypertrophy and coronary artery disease should avoid flecainide due to its negative inotropic effects and increased mortality in patients with ischaemic heart disease.[1] Sotalol causes QT prolongation and should be monitored closely when combined with other drugs that prolong QT. Sotalol is also renally excreted and should be used with caution in those with chronic kidney disease.[11] Amiodarone has been shown to be the most effective antiarrthymic however is deemed second line as a result of its significant adverse effects which may be slow to resolve due to its long half-life of up to 110 days.[12] Amiodarone is known to inhibit cytochrome P450 enzymes CYP3A4, CYP2C9 and p-glycoprotein, affecting the metabolism and excretion of many drugs and its ability to cause QT prolongation, pulmonary toxicity, thyroid dysfunction and photosensitivity reactions.[13]

The UK National Institute for Health and Care Excellence (NICE) guidelines (Figure 1, page 3) outlines the treatment decision tree in patients with confirmed diagnosis of AF.[14]

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