Optimum management of atrial fibrillation in the Intensive Care Unit

Clinical Problem

A 61 year old man, PD, presented to the Intensive Care Unit (ICU) after angiography and intra arterial thrombolysis of an occluded Y graft limb. He had no history of atrial fibrillation (AF). He subsequently developed compartment syndrome of the affected leg and had to return to theatre for fasciotomies and stenting of the graft. Despite the surgical complications he remained cardiovascularly stable and required minimal respiratory support, successfully being extubated after the general anaesthesia for the second operation.

His discharge was being planned when he developed a resistant fast AF at a rate of 140-160 beats per minute (bpm).

Management

Multiple medications were tried including potassium replacement, magnesium, metoprolol, bisoprolol and digoxin. DC cardioversion was discussed, as the patient was already anticoagulated for surgical reasons. This was discounted for two reasons, he was well and showed no evidence of compromise and it was felt it would reoccur. Amiodarone was discussed but the patient had no central access and it was therefore not used.

Ultimately further dosing of beta blockers resulted in cardioversion to a sinus rhythm rate of 80 bpm. He was then discharged from the ICU.

This case highlighted the lack of clarity as to appropriate management of AF in ICU. Different doctors treating PD on different days had conflicting opinions as to the most appropriate strategy. This is an issue that I have previously noted on ICU and also between cardiologists.

I have therefore chosen this case to explore the evidence base behind the management of AF in ICU and to attempt to generate an appropriate strategy for future patients.

Discussion

There are two related questions to consider in this case summary. Firstly whether we should aim for rhythm control or rate control and secondly what is the most appropriate technique to use both initially and as a second line option. I will consider patients appropriate to a District General Hospital ICU, i.e. not post cardiothoracic surgery as this represents a very different patient group. I will
focus on management of the AF itself and not subsequent stroke risk management.

Atrial fibrillation is a condition where coordinated electrical and mechanical action of the atria is lost, consequently the atrial kick is absent and ventricular filling is impaired. This combined with an often rapid ventricular response leads to impaired cardiac efficiency. In critically ill patients the loss of cardiac output and/or increased cardiac oxygen demand can have significant deleterious effects.

AF is common in the ICU population, with approximately 15% of medical ICU patients having periods of AF\(^1\). There are many potential triggers amongst the ICU population. There is also the added complexity of assessing whether fast AF represents an appropriate tachycardic response to stress and illness allowing the patient to maintain their cardiac output or a primary cardiac pathology that is actually impairing their cardiac output.

**Rate versus rhythm control**

In patients who are haemodynamically compromised, with evidence of cardiac ischaemia, shock or cardiac failure it is generally accepted that rhythm control with electrical cardioversion (ECV) should be the aim\(^2\). This has understandably not been the subject of a randomised controlled trial. Delineating what part of a critically ill patient’s haemodynamic compromise is due to fast AF may not be straightforward however. It is probably acceptable to state that a sudden rise in vasopressor requirements, drop in blood pressure or signs of cardiac ischaemia in the context of a new fast AF should prompt consideration of ECV.

Patients who are not significantly compromised are less straightforward. Rhythm control success rates are poor with a large retrospective observational study of medical and non-cardiac surgical ICU patients\(^3\) showing pharmacological cardioversion success rates of 87% for new onset AF but with 42% reverting back into AF thereafter. ECV was successful in only 27% of patients. This study was not a randomised trial but it was large (348 patients) and multi centre.

There is no data on rate versus rhythm control in this patient population. Non-ICU studies have shown similar outcomes with a trend to favouring rate control\(^4\). It is impossible to extrapolate to the ICU population, the loss of cardiac efficiency of even rate controlled AF has to be balanced against the poor success rates of rhythm control highlighted above.

If rhythm control is chosen it would appear that pharmacological methods may be preferable. Only one trial\(^3\) applicable to the patient population was found.

**Choice of drug**

Academically rigorous evidence is scarce. There are five randomised controlled trials, none against placebo, none recent.
Chapman and colleagues assessed 24 ICU patients with a new onset atrial tachycardia without significant haemodynamic compromise (excluded if systolic blood pressure (BP) less than 80mmHg). After correction of magnesium and potassium they were randomised to procainamide or amiodarone. Both groups showed sinus rhythm in 70% of patients at 12 hours, BP unaffected by either drug. This study is small, with poor randomisation (hospital number odd/even) and no blinding.

Moran and colleagues compared amiodarone and magnesium in 42 patients with atrial tachycardias. Magnesium target was 1.4 to 2.0 mmol/l. Rhythm control after two hours was statistically significantly better in the magnesium group. Rate control was similar. This was a pragmatic but small trial. Randomisation was reasonable but no blinding and the presentation of the results makes it difficult to assess whether they have been accurately analysed.

Amiodarone was also compared with diltiazem in a trial by Delle Karth et al. 60 medical ICU patients with SVT (57 of which were AF) were randomised to diltiazem or amiodarone. Both groups had similar rates of rhythm and rate control but significant hypotension leading to drug discontinuation was found in 30% of the diltiazem patients. Unclear randomisation and blinding.

Barranco and colleagues compared flecainide and verapamil in a study that included patients with AF and atrial flutter (AFl). 30 patients were enrolled in total, 15 had flutter/fibrillation, the rest had multi focal atrial ectopics or a supraventricular tachycardia. Flecainide showed a 70% success rate in the AF/AFl group and verapamil a 25% success rate. Again a very small study with a lack of clarity on randomisation and blinding.

The final RCT was a study by Balser et al. This studied esmolol versus diltiazem in post operative non cardiac surgical ICU patients with an SVT. Notably patients on inotropes were excluded. When considering all SVT’s there was a difference in rhythm control at two hours, in favour of esmolol. When the AF only subgroup was analysed the statistical significance was lost but the trend remained. Between 30 and 40% of patients had significant hypotension in both groups. Trial was open label and randomisation unclear again.

Ibutilide is a class III antiarrhythmic whose use has been studied. Whilst seeming effective it has not been subjected to any randomised controlled trials and significant (>10%) rates of ventricular tachycardia are reported.
Perhaps surprisingly digoxin has not been the subject of an RCT in critically ill patients either. There are a number of problems with its use on ICU. It has a slow onset of action and is considered much less effective in hyperadrenergic states, it also can accumulate and cause toxic side effects in renal impairment\(^1\).

In summary there is an inadequate amount of data to make an assessment of the relative merits of different drugs. The trials are all small and of low to medium academic rigour. Several mention the difficulty of not being able to have a placebo arm on ethical grounds. A formal systematic review undertaken in 2008\(^1\) found “Using the current published literature, we cannot recommend a standard treatment for atrial fibrillation in noncardiac critically ill adult patients”.

Mengalvio Sleeswijk has published multiple papers and reviews on the topic of AF on ICU. He has proposed a management protocol\(^1\) which appears logical and as evidence based as is possible. This starts with magnesium at 0.037 g/kg in 15 minutes then 0.025 g/kg/hr. Non responders, defined as persistent AF at a rate >100bpm, at one hour receive amiodarone (300mg then 1200mg/24hrs). 16 of 29 patients studied responded to magnesium alone, 13 required amiodarone. 24 hour response rate was 90%. He proposes ibutilide as rescue treatment where this protocol fails, this was not used in any of the 29 patients.

Lessons Learnt

This remains an area of study with no clear answers. A pragmatic summary of the evidence would be that a pharmacological approach should be favoured unless there is significant haemodynamic compromise. Choosing drugs that achieve rate control whilst also potentially restoring sinus rhythm side steps the question of rate versus rhythm. Whilst in theory restoring the atrial kick is helpful a normalised rate tends to achieve our aims in my clinical experience. Furthermore, evidence outside of ICU does not support rhythm control over rate control.

An evidence based choice of drug is not possible. My impression from reviewing the trials listed above is that both calcium channel blockers and beta blockers bring with them a substantial risk of hypotension. Flecanide is not appropriate in patients with structural heart disease, which discounts many of our patients. Procainamide is an old drug with a risk of pro-arrhythmic effects and QTc prolongation, ibutilide appears to have similar issues. Magnesium and amiodarone both seem to have some evidence of efficacy with lower discontinuation rates, there is also the benefit of clinical familiarity. As such I would favour these drugs. I think the Sleeswijk protocol has merit.

There is a genuine need for further, high quality, RCT’s in this area. Placebo controlled studies are not feasible. Magnesium and amiodarone versus beta blockers would be of interest, particularly in view of the recent questions around beta blockers and improved outcome in sepsis\(^2\).
References