CARDIAC SURGERY FOR THE NON CARDIAC ANAESTHETIST

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The "anaesthetic" administered to patients undergoing cardiac surgery has changed little in a decade. Yes, we have fiddled and adjusted around the fringes a little, but more or less it would be recognisable to most as similar to that which they saw in their registrar training. Perhaps the same could be said of anaesthesia in general. However, the ever aging population with its expanding list of co-morbidities brings the broader developments in medicine into sharper relief for anaesthetists. Likewise the drive for lower invasivity in surgical intervention pushes novelty and innovation daily into the theatre environ. The intent in this session is to examine a tiny corner of the changing world of medicine and surgery that relates particularly to cardiac anaesthesia, but will also impact on anaesthetists with more general focus. There will be a brief update on –

- Anticoagulant pharmacology
- Developments in 3D/4D echocardiography
- Developments in minimally invasive valve intervention

Anticoagulant Pharmacology

We all have some idea of how blood clots – it has something to do with platelets, a rent in the vessel wall, and coagulation factors. Everything has to pitch up in the right amount at the right time for holes to be plugged, and there are systems of checks and balances to make sure it doesn't happen in the wrong place at the wrong time. Further, most have come to grips with heparin and warfarin operating as "shotgun" inhibitors of this clotting process, and are nearly at ease with the fractionated heparins and their relatively greater inhibition of the formation of activated factor X. However the current drive is for cleaner, more predictable actions in the cascade which allow for weight or therapeutic purpose based dosing without the need for therapeutic effect monitoring. Simultaneously there is a drive for oral efficacy and long duration of action and a lesser drive for reversibility. The two targets receiving the most attention are Factor X and (pro)Thrombin – Factor II.

Anti Factor X Agents

Fondaparinux is a five unit sugar molecule that has the same structure as a pentameric saccharide sequence found in fractionated and unfractionated heparin. This sugar sequence functions as the binding site for endogenous antithrombin III which mediates its anti Xa effect. The shorter chain length in Fondaparinux, however, prevents the linkage of ATIII to thrombin and explains both the absence of a direct effect on thrombin formation and the restriction of effect to antiX. Unsurprisingly, its main serious side effect is bleeding and although a HITTs like thrombocytopaenia has been described, it is chemically unable to bind to platelet factor 4 precluding a commonality of mechanism. Indeed, case reports highlight its safe use in HITTs prone patients. Monitoring is generally not required, although Xa assays can be used. There is no licensed reversal agent. Nevertheless the universal haemostatic, factor VIIa has been shown to effectively reverse the anticoagulant effects.

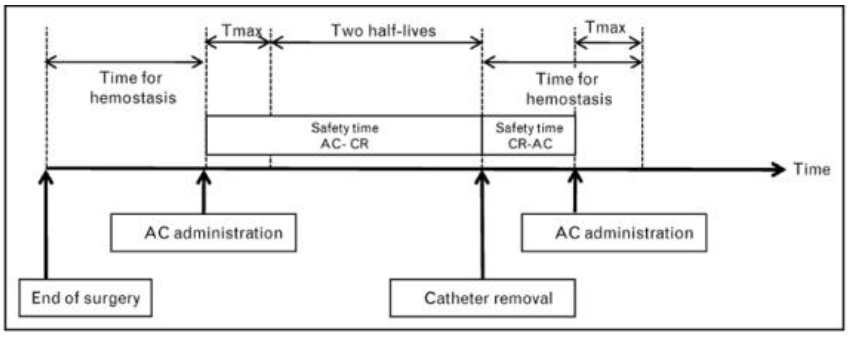
Idraparinux, is a similar pentasugar with additional negative charges attached. It binds ATIII somewhat more avidly and more or less just lasts longer. SSR 126517 is biotinylated Idraparinux – essentially Idraparinux welded to vitamin B7. This has the advantage that it can be reversed with the egg white derived protein avidin. IV avidin rapidly forms a high affinity stable complex with subsequent very rapid renal excretion. Rivaroxaban is chemically distinct. In structure it closely resembles the antibiotic linezolid, although it has no antibiotic activity. It is the first orally active Xa inhibitor, with approval in Europe and the US for VTE prophylaxis.

Thrombin Inhibitors

The second area of the coagulation cascade being targeted at present is direct and specific thrombin inhibition. Of the intravenous agents, many will know of hirudin, although its congener bivalirudin is more familiar to cardiac anaesthetists. When heparin is contraindicated or heparin effect monitoring is rendered unreliable due to underlying haematological disorders, then bivalirudin presents an alternative. However, of more general interest are the oral inhibitors of thrombin – Ximelagatran – withdrawn recently due to an unacceptable rate of liver failure, and Dabigatran – recently licensed in New Zealand. It has been touted as an alternative to heparins for VTE prophylaxis and is being extensively investigated as an alternative in stroke prophylaxis, and as an oral alternative to heparin in multiple settings from immediate treatment of VTE, acute coronary syndrome and in percutaneous coronary intervention. Sold as "Pradaxa," the prodrug Dabigatran etexilate, it is formulated with tartaric acid to facilitate absorption, but retains a bioavailability of only 5%. It has peak plasma levels at about an hour and a plasma half life of 8 hours – rising to 17 hours with repeat dosing. The peak effect mirrors plasma levels. APTT, INR, TT and ECT all provide some information about anticoagulant effect although only the latter is dose related. Nevertheless, predictability of dose effect relation renders monitoring largely unnecessary. There is no antagonist and no evidence based recommendations on how best to reverse its effect. However, FFP, prothrombinex-VF (human prothrombin complex) and recombinant factor VII would all likely be useful.

So with all these new agents flooding the market and the ever present fear of neuraxial haematoma in regional anaesthesia, we could be forgiven for developing somewhat of a complex. Most individuals enjoyed a comfortable consensus position on "when it is safe to do what" with neuraxial procedures in the presence of unfractionated heparin, which was hastily revised as LMW heparins eclipsed their predecessor. However it would seem that the future promises a much more extensive collection of pharmacologically diverse agents and the list will evolve and change more rapidly than in recent years. It will not be possible for most to recall the specific recommendations for each agent nor to develop a protocol for each new drug as it rolls into the market. Perhaps a better model to apply is that proposed by Llau and Ferrandis[1]. They propose that –

- The first dose of anticoagulant after neuraaxial anaesthesia should allow an interval of eight hours between the end of surgery and the peak effect of the drug.
- The removal of a catheter should be delayed for at least two half lives following peak effect (25% remaining).
- The next dose of anticoagulant after catheter removal should be an acceptable haemostasis time minus the time to peak effect of the agent concerned – a drug with a fast onset mandates a longer delay after catheter removal.



AC-CR, interval of time recommended between anticoagulant dose and catheter removal; CR-AC, interval of time recommended between catheter removal and next anticoagulant dose; Tmax, time to peak plasma level.

Llau and Ferrandis[1]

From this style of approach, complicated pharmacological data from almost any drug can be condensed into more practical and useable information. Of particular note with this current group of drugs are the very long half lives of some agents, that renders regional anaesthesia almost out of the question in any sort of useful time frame. If someone helpfully starts, for example Dabigatran post op as VTE prophylaxis, don't plan to remove the epidural catheter any time soon!

Developments in 3D/4D Echocardiography

Echocardiography and ultrasound in general continue to move ahead predominantly in the improvements to software and processing that make the images more understandable to us. I know that for many not used to looking at echo images, the majority of it looks like some sort of blizzard and a degree of suspended disbelief is required in image interpretation. Significant investment has been made over recent years into 3D echo and 3D echo displayed in real time – quaintly referred to as 4D. It has found a particular niche in the assessment of native and artificial valve function – particularly mitral valve as well as the monitoring of regional wall motion abnormalities, quantification of RV function, and examination of the interatrial septum. In general the images are just somewhat easier to appreciate. Taking the concept a step further is 4D echohology where the acquired images are processed and redisplayed in a virtual reality interactive hologram allowing the practitioner to manipulate the images by rotation and slicing in almost any plane. Depth perception facilitated by 3D glasses and image manipulation by a hand held tool lend the setup a rather futuristic aura.

Developments in Minimally Invasive Valve Intervention

One of the most rapidly developing areas of cardiac innovation is percutaneous valve intervention. This field is being driven furiously by industry keen to tap into a large aging population with valvular heart disease, many of whom do not qualify when risk stratified for open surgical repair or replacement. As technology, technique and experience develop it is foreseeable that some of these commercial systems will find a wider application in patients for who open intervention would currently be recommended. Two leading systems for each of the aortic and mitral valves are presented for interest. With respect to aortic valve surgery, we will look at both Transcatheter AVR, and Aortic Valve Bypass Grafting.

Transcatheter aortic valve replacement or TAVI is a novel endoluminal style AV replacement currently reserved for high risk patients with aortic stenotic disease. There are two main industry players – Edwards and Core Valve and two main approaches to device placement – retrograde via femoral or subclavian artery, and anterograde via the LV apex through a minithoracotomy. In the retrograde approach, a wire is passed across the valve, a balloon is passed over the wire, the balloon is inflated crushing the valve and converting severe AS to severe AR, the replacement valve is then deployed across the native valve annulus. When arterial anatomy is unfavourable, the LV apex is approached directly via a mini thoracotomy. In order to facilitate accurate positioning, circulatory standstill is achieved by rapid ventricular pacing. Early reports found successful implantation rates of upwards of 75%, with valve areas maintained at least in the medium term. Naturally there are a variety of problems from ongoing paravalvular aortic regurgitation to death by tamponade and stroke. Valve migration down the aorta or back into the left ventricle, has also proved to be a dramatic complication. Despite these teething troubles, it will be increasingly likely that the very elderly with severe AS will be salvaged to survive to present for other surgical interventions as increased longevity allows.

Aortic valve bypass grafting or apico-aortic conduit has some theoretical advantages over TAVI insofar as it may be more applicable in bicuspid anatomy and that access to the coronary arteries is preserved post procedure. Cardious provide a tooled system that obviates the need for cardiac standstill or cardiopulmonary bypass. Via an incision in the 5th interspace, the aortic graft is anastomosed to the descending aorta and the apical graft to the LV apex. A bioprosthetic valve is then seated between the grafts completing the apex to aorta conduit. The native aortic valve is left intact. Does it work? – we just don't know yet. While aortic valve bypass grafting as a technique is nearly 100 years old, this particular system designed for off pump use is still very much in the trial phase.

With respect to the mitral valve, two approaches of interest are percutaneous annuloplasty via the coronary sinus and percutaneous Alfieri stitch. Basic anatomy describes the greater part of myocardial venous drainage occurring via the coronary sinus, which in part encircles the anterior, lateral and posterior aspects of the mitral annulus. Although an oversimplification, mitral annular dilation is a major component of much mitral regurgitation in the community. Percutaneous annuloplasty exploits this arrangement by passing a transvenous wire into the RA, selectively cannulating the coronary sinus, and subsequently feeding an anchored circlage device. Tightening the circlage effectively creates a cinch or belt around the mitral valve and drags the AP diameter back towards normal dimension. Reported results are favourable to a degree with procedural success rates towards 90%, with reductions in effective regurgitant orifice, mitral regurgitation jet length, and overall severity grading of MR in about 2/3rds of patients. There are at least 10 device systems in development and at least three undergoing clinical trials at present. Complications and problems are inevitable, and a relook at anatomy suggests a number of predictable issues. Cinching the device must inevitably put some strain on the circumflex coronary artery. The coronary sinus is a thin walled structure designed to carry blood at low pressure – perforation with or without

tamponade will occur on occasion. Further, we already use the coronary sinus as a free conduit for the LV lead of biventricular pacing devices – presumably there is only so much "stuff" you can safely stow inside one coronary sinus.

The edge to edge clipping technique is a fundamentally different approach and emulates the open repair technique pioneered by Professor Alfierri. In essence a double barrelled mitral valve orifice is created by pinning the anterior and posterior valve leaflets together. The typical device is advanced transvenous to the right atrium and then transeptal across the interatrial septum to approach the mitral valve anterograde. Then, under echo guidance the free edges of the mitral valve are crimped together. Does it work? – possibly. Cardiac surgeons have generally been disappointed with the results of open Alfierri – a third or more patients have recrudescence of moderately severe MR by some 18 months. With percutaneous approaches acute procedural success rates (the device was successfully deployed) approach 80% with about 2/3rds achieving some meaningful reduction in MR. The results of Everest 2 seen this year pitted the Mitraclip (Abbott) device against conventional repair or replacement and whilst this single trial is a presentation on its own, broadly the findings favoured clipping for safety in the short term and open repair for most effective reduction in MR. What remains to be seen is how the clip systems will stand the test of time, and what if any impact clipping will have on the ability to perform a direct surgical repair.

So, as a general statement, there is much change and development on the horizon. What will stand the test of time and what will drift by the wayside remains to be seen. Sometimes one could be forgiven for wondering whether medicine is the art of finding better and more expensive solutions to problems ever more obscure and inconsequential. Regardless, there will likely always be a role for both healthy and perhaps unhealthy scepticism.

References

1. Llau, Juan V; Ferrandis, Raquel : New Anticoagulants and Regional Anaesthesia Current Opinion in Anaesthesiology: October 2009 – Volume 22 – Issue 5 – 661-666
2. Annemien E van den Bosch, Anton HJ Koning, Folkert J Meijboom, Jackie S McGhie, Maarten L Simoons, Peter J van der Spek and Ad JJC Bogers. Dynamic 3D Echocardiography in Virtual Reality, Cardiovascular Ultrasound 2005, 3:37
3. Transcatheter Aortic Valve Implantation (TAVI). A position statement of the British Cardiovascular Intervention Society (BCIS) and the Society for Cardiothoracic Surgery (SCTS)
4. Peter L. Gross, Jeffrey I. Weitz. New Anticoagulants for Treatment of Venous Thromboembolism Arterioscler Thromb Vasc Biol 2008; 28; 380-386
5. Henri Bounameaux. The novel anticoagulants: entering a new era. Swiss Med Wkly 20 09; 139(5–6): 60–64H
6. Jenny Kwaka, Michael Andrawesb, Sean Garvinc and Michael N. D'Ambra. 3D transesophageal echocardiography: a review of recent literature 2007–2009. Current Opinion in Anaesthesiology 2010, 23: 80–88
7. Goris Bol Raap, Anton HJ Koning, Thierry V Scohy, A Derk-Jan Harkel, Folkert J Meijboom, A Pieter Kappetein, Peter J van der Spek and Ad JJC Bogers. Virtual reality 3D echocardiography in the assessment of tricuspid valve function after surgical closure of ventricular septal defect. Cardiovascular Ultrasound 2007, 5: 8
8. Valle-Fernandez Raquel del, Ruiz, Carlos. Transcatheter Aortic Valve Implantation – TAVI: so much done yet so far to go. EuroInterv 2008, 4: 169-72
9. Mitraclip – mitral valve repair system. www.evalveinc.com/europe/press/press_release_38.html