ANTI COAGULATION AND BLOCKS

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We now live in a scenario doomed with lot of co-morbidities .One of the important being the cardiovascular and thrombo-embolic problems. The improvement of patient outcomes particularly, the morbidity and mortality have reduced by the attenuation of hyper coagulable response and responsible usage of regional anaesthetic techniques. The anti-coagulation process is usually not by using a single drug, but always a combination of several drugs.

The drugs commonly used are unfractionated Heparin, LMW Heparin, thrombolytic drugs ,drugs which interfere with the platelet mechanism such as Thienopyridines, Gp IIb/IIIa antagonists, drugs which potentiate the anti-coagulation like NSAIDS and Herbal medications ,Thrombin inhibitors, Factor Xa inhibitors and newer oral drugs.

Thus the process of using anti-coagulation and anti- platelet drugs have made us to follow certain principles and guidelines while performing neuraxial blocks, peripheral blocks, deep plexus blocks and catheter insertions, inorder to prevent complications due to anticoagulation. The neurological symptoms such as surgical neuropraxia anterior spinal artery syndrome ,epidural abcess have occurred due to neuraxial blockade. But the main problem of neuraxial blocks being the spinal hematoma, as a risk of hemorraghic complication leading onto neurological dysfunction. This occurs because of bleeding into a non-compressible space , the spinal space epidural space. In a peripheral plexus block the hemorraghic complication usually does not lead to a neurological problem, but serious complications have occurred after neurovascular sheath cannulation for surgical, radiological and cardiac indications. Overall nearly 26 cases of hemorraghic complications have been reported after deep peripheral/ plexus blocks. The major bleeding problems occurred after lumbar symphathetic block, psoas compartment blocks in the presence of anti-coagulants and anti-platelet drugs .These are usually a concealed blood loss leading to massive transfusion and even death. Neurological problems are not common.

The incidence of neurological problems associated with neuraxial blockade as quoted in the literature and is about less than 1 in 150,000 epidurals , less than1 in 220,000 spinals., 87% hemorraghic abnormality or traumatic needle placement being the cause. Already in the last ten years study period in Sweden among 250,000 spinals and 450,000 epidurals, 33 spinal hematomas have been reported, in which 25 occurred in

epidurals, among which 23 were females. Majority of spinal hematomas occurred in epidural space because of epidural venous bleeding. They become symptomatic after several days of needle placement or catheter removal. The volume of blood required being less than, what used for a blood patch.

The main contributing factors are : Age ,Associated abnormalities of spinal cord and vertebral column, Underlying coagulopathy, Difficult needle placement , Traumatic needle placement (blood in needle or cather during placement or removal) , Indwelling catheter during sustained theraupetic anti-coagulation.

Though prompt diagnosis is needed for prevention of a permanent neurological damage its better we practice certain guidelines and protocol in performing neuraxial techniques and nerve blocks in patient who is going to be anticoagualated in the post-operative period ,or has been anticoagulated in the preoperative period prophylactically or theraupetically. The guidelines I will be mentioning here has been put on, and practiced by the leading wizards of regional anaesthesia and anti-coagulation of our world after coming into a consensus in American Society of Regional Anaesthesia and Pain Medicine 2010, consensus based on lots of epidemiological surveys and studies. The guidelines for nueuraxial blockade are applicable for deep plexus and deep peripheral blocks.

Patients on Thrombolytic and fibrinolytic theraphy.

These drugs dissolve the fibrin clots that have been already formed. Plasminogen activators such as thrombokinase and urokinase dissolve thrombus and also affect circulating plasminogen and fibrin. Rt-PA is more selective on fibrin and less effective on plasmin .Fibrin degradation products themselves have an anticoagulant effect by inhibiting platelet aggregation.

The guidelines to be practiced are

1.Avoidance of these drugs for 10 days after puncture of non-compressible vessels.

2.Strong recommendation to avoid spinal, epidural or peripheral block in patients receiving these drugs.

3. The patients who have received neuraxial or peripheral blocks near the time of fibrinolytic or thrombolytic therapy should be monitored neurologically for 24 hrs at an interval less than 2 hrs.

4.For removal of catheter, fibrinogen levels should be monitored, which is the last factor to recover.

Patients on Un-fractionated Heparin

Heparin binds to anti-thrombin and this accelerates the ability to inactivate thrombin(IIA) ,factor XA ,factor IX A. Intravenous Heparin acts immediately whereas the subcutaneous form acts in 1-2 hrs delay. Biological half life is dose dependant. Anti-coagulant activity is monitored by aPTT. Advantage of Heparin is it can be reversed by Protamine,1mg of protamine for every 100 mg of Heparin. Heparin dosage may be of different ways. Intravenous Heparin 5000 to 10,000 U for medical and surgical indications to keep aPTT 1.5 times the normal. Sub-cutaneous Heparin 5000 U every 12 hrs for DVT prophylaxis .Here aPTT never exceeds more than 1.5 times.

Guidelines;-

1.Evaluate the use of concurrent medications such as LMW Heparin, oral anti- coagulants and anti-platelet drugs before deciding a technique.

2. Sub-cutaneous dosing of twice daily is not a contraindication to any technique.

3.Patients who receive more than 10,000 U or thrice daily sub-cutaneous dosage needs close neurological monitoring.

4. If Heparin used for more than 4 days platelet count in mandatory before neuraxial,deep block or catheter removal.

5.Heparin should be delayed for 1 hr after needle placement. Neuraxial catheter should be removed only after 2 to 4 hrs of last Heparin dose and assessing the coagulation status . Re-Heparin only 1 hr after catheter removal.

Patients on LMW Heparin.

Main relevant features of LMW Heparin are lack of a monitoring tool for anti-. coagulation response, prolonged half life and irreversibility with protamine.The elimination half life after subcutaneous injection is 3 to 6 hrs .Anti Xa levels peak after 3-5 hrs, and present upto 12hrs. Its increased in renal failure.The LMW Heparin are used nowadays for DVT prophylaxis, as a bridge therapy in patients anticoagulated with warfarin, including pregnant patients, patients with artificial cardiac valves, AF, pre-existing hyper-coagulable conditions. The reported cases of spinal hematomas with prevalence of neuraxial techniques in patients based on LMW Heparin sales rates to be 1 in 3000 continuous epidurals and 1 in 40,000 spinal anaesthesias.

GUIDELINES;

1. Other concurrent anti-platelet or anti-coagulant medications may increase the risk of spinal hematomas.

2. If blood during needle placement or catheter insertion LMW Heparin should be iniated only after 24 hrs after the procedure.
3. Pre-operative LMW Heparin;
    i. Needle or catheter placement should occur 12 hrs after 1 st dose of LMW Heparin.
    ii. If high dose of the drug such as enoxaparin >1mg/kg or 1.5mg/kg or twice daily dose is used, needle insertion should be done 24 hrs after the last dose.
4. Post-operative LMW Heparin.
    i. If twice dosing regimen planned dose should be administered only after 24 hrs regardless of the anaesthetic technique.
    ii. If twice daily dosing its unsafe to have the catheter inside hence its better to remove it before the first dose. LMW Heparin should be delayed for 2hrs after the catheter removal.
5. Single daily dosing.

i. 1 st dose of LMW Heparin should be administered 6-8 hrs post- operatively. 2nd dose 24 hrs after the 1 st dose.
ii. Catheter removal 10 to 12 hrs after last dose. Subsequent dose 2hrs after the catheter removal.

Patients on oral anti-coagulants.

Oral anti-coagulants including warfarin exert their effect indirectly by interfering with synthesis of vit-K dependant factors ,factorII (thrombin),factor VII,factor IX ,factor X. Their half lives being
Factor VII- 6-8 hrs, factor IX - 24 hrs, factor X 25-60 hrs, factor II 50-80 hrs respectively.. A single dose of Warfarin (3-5mg) will result in prolongation of Prothrombin time in 20% of individuals. The anti-coagulation is monitored by PT and INR. INR is the standardization and comparision of PT values between laboratories, where the patient is anticoagulated for 6 weeks. Hence INR is less reliable in early course of the therapy. Bleeding occurs if any one of the factors is of value 20%-40%. The PT is sensitive to factor VII and X , but insensitive to factor II. If the drug is discontinued the INR drastically reduces indicating that the factor VII is recovering fast. But still factors II and X have not been restored to normal activity ie. >40%. If the factor VII is >40% INR is 1.4, if its > 55% the INR is <1.2. During the first few days of the therapy PT is reliable and reflects only factor VII activity, later in the therapy X and II also contribute to PT. In emergency situations the effect of warfarin can be reversed by Vit-k (iv) or oral and/or transfusion of FFP.

GUIDELINES;

1.Anti-coagulation therapy should be stopped 4 to 5 days before a planned procedure and PT and INR should be normalized before performing a deep plexus block or a neuraxial block.
2.If a patient is with a neuraxial catheter and is receiving low dose warfarin, monitoring of INR is mandatory.
3. If thrombo-prophylaxis with warfarin has been initiated the catheter should be removed when INR is <1.5. (factors > 40%).
4.If the INR is 1.5 to 3 in a patient with a indwelling catheter the neurological status should be assessed before catheter removal.
5. Indwelling catheter patients should not have an INR >3. If so the warfarin should be withheld.

Patients on anti-platelet medications.

The drugs are NSAIDS,Thienopyridines, GpIIb/IIIa antagonists **(abciximab,eptafibatide,tirobifan**),new drug **Prasugrel**. NSAIDS usually potentiate the effects of anti-coagulants .Presence of NSAIDS alone is not a contraindication for a block.
Thienopyridines (Clopidogrel and Ticlopidine);- Inhibit ADP induced platelet aggregation. They also ihibit platelet- fibrinogen binding and platelet-platelet interaction. Their effect is irreversible till the lifetime of platelets .Platelet dysfunction is present for 5-7 days for clopidogrel and 10-14 days after discontinuation of Ticlopidine.
GpIIb/IIIa antagonists (abciximab,eptafibatide,tirofiban);- They inhibit platelet aggregation by interfering with platelet-fibrinogen binding and platelet – vWF complex and crosslinking of platelets. All these drugs are usually given in the combination with aspirin,for acute coronary syndromes and patients intended for coronary stenting .Normal activity of platelets return in 8 hrs after stopping Eptafibatide and Tirobifan and 24 hrs after stopping Abciximab.
Prasugrel ;-This newer thienopyridine acts more rapidly ie; within 2 hrs of administration nearly 50% of platelets are inhibited .Platelets become normal within 7 days of drug stoppage.

GUIDELINES;-

1. Neuraxial blockade and deep plexus/peripheral blocks are withheld for 14 days for ticlopidine , 7 days for clopidogrel and 7 -10 days for prasugrel from the time of their discontinuation. If block indication warrants within 5-7 days then platelet function should be documented.
2. For GpIIb/IIIa antagonists its 8 hrs for eptafibatide and 48 hrs for abciximab.

Patients on Herbal Medications.

There are a wide range of herbal medications such as garlic, ginkgo, ginseng which may cause potential interactions with warfarin.They add the risk of spinal hematomas in patients undergoing spinal or epidural since addition of these drugs will increase the risk of bleeding complications in these patients.

FONDAPARINUX.

It's an injectable synthetic pentasaccharide approved in 2001.It produces anti-thrombotic effect through Factor-Xa inhibition. Plasma half life is 21 hrs.Single daily dosing, with first dose administered 6^{th} hour post-operatively. So far only 1 case of spinal hematoma has been reported all over the world.

GUIDELINES;-

1. Single needle pass, atraumatic needle placement and no catheter insertion during theraphy.
2. Indwelling epidural catheters removed 2 hrs before Fondaparinux administration or 36 hrs after last dose of Fondaparinux. Subsequent dose was delayed for 12 hrs after catheter removal.

THROMBIN INHIBITORS
(Desirudin,Bivalirudin,Lepirudin,Argatroban)

These drugs are indicated in the treatment and prevention of thrombosis in patients with heparin induced thrombocytopenia and adjunct to angioplasty procedures. Desirudin is approved for DVT prevention. The effect of thrombosis prevention are monitored by aPTT and is present 1-3 hrs after IV administration. There is no antidote for these drugs and cannot reversed pharmacologically. No clear guidelines have come for this drug, but strict recommendation is that no neuraxial technique or block for patients under these drugs.

ORAL THROMBIN INHIBITORS.

Dabigatran;- This is a pro-drug,converted to active metabolite in the GIT by esterases. It inhibits free and bound fibrin. Plasma levels peak at 2 hrs after single dose. Half life is 8 hrs after single and 17 hrs after multiple doses. 80% of the drug is excreted unchanged in urine. It prolongs the aPTT, but its effect is not linear but reaches a plateau in higher doses ,however ECT(escarin clotting time) and TT(thrombin time) are sensitive. The only labeled indication is non-valvular atrial fibrillation.

GUIDELINES;-

1. In view of the irreversibility of Dabigatran, it should be discontinued 7 days before neuraxial or deep plexus block.
2. Catheters should be removed 6 hrs before initiation of Dabigatran therapy.
3. If a shorter time is desired of any of these the reversal of anti-coagulation should be documented by ECT and TT documentation.

ORAL FACTOR Xa INHIBITOR.

Rivaroxoban;- It's a potent, selective and reversible factor Xa inhibitor. Its oral bio-availability is 80%. After administration the maximum inhibitory effect occurs in 1-4 hrs, inhibition is maintained for 12 hrs. The antithrombotic effect can be monitored by both PT and aPTT. The terminal elimination half life is 9 hrs, may prolong to 13 hrs in elderly.

GUIDELINES;-

1. According to European guidelines 22-26 hrs should elapse between discontinuation of Rivaroxoban and neuraxial blockade.
2. Indwelling catheters are contra-indicated during Rivaroxoban therapy.
3. 4-6 hrs are recommended between spinal anaesthesia and initiation of Rivaroxoban therapy.

Recognition of risks associated with spinal, epidural, deep plexus/peripheral blocks and anti-coagulation, surveillance and evaluation of the current information and education, are critical in preventing the following catastrophes related to anti-coagulation and regional anaesthesia. The introduction of newer anticoagulants, anti-platelet drugs to treat and prevent thrombo-embolic problems and evolving indications for regional analgesia and anaesthesia compels us to follow an individualistic approach.The timing of the procedure ,putting the catheter into the patient in a status of anticoagulation should be made in an individual basis, weighing the risk and benefit of regional anaesthesia to the specific patient. Practising the guidelines alone will not completely eliminate the complications of spinal hematomas and compartmental bleeds. Vigilance monitoring is mandatory to allow early evaluation of neurological dysfunction and to have a safe Regional anaesthesia.

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