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Need for the Change of Anticoagulants In The Reproductive Age Group Women

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ABSTRACT

Hemorrhagic ovarian cysts usually result from haemorrhage into a corpus luteum or other functional cysts. It is a frequent and potentially life threatening complication in women on chronic anticoagulation therapy. Surgical management has been a traditional approach in managing hemorrhagic ovarian cyst. However conservative management is now dominating the trend in carefully selected patients .For prevention of recurrence of ovulation related bleeding it is mandatory to use a ovulation suppressing agent during the monthly follow up. Here we present two case reports who had been receiving oral anticoagulants – Vit K antagonist for prosthetic heart valves and are treated as a result of ruptured corpus luteal cyst. One was treated surgically other was treated conservatively. They were discharged with advise of DMPA for ovulation suppression in the follow up. Even though VKA'S are cost effective and efficacious in preventing valve thrombus, because of life threatening hemorrhage and periodic INR monitoring necessitate the need for researches to find an safe and effective alternative newer oral anticoagulants for women in reproductive age group.

Keywords: Hemorrhagic ovarian cysts, anticoagulants , hormone therapy

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INTRODUCTION

In developing countries like India, warfarin is still routinely used as an anticoagulant in women after mitral valve replacement. Most of the women with heart disease on oral anticoagulants are in reproductive age group and they ovulate every month and hence they have high probability of rupture of corpus luteum leading to haemorrhagic ovarian cyst. Hemorrhagic ovarian cyst is the most common cause of acute pelvic pain in an afebrile woman receiving anticoagulant therapy. There are newer anticoagulants which have increased efficacy and at the same time with lesser bleeding risk compared to vitamin K antagonists. They act by inhibiting the coagulation factors. Either new oral anticoagulants with lesser haemorrhagic risk has to be used in female cardiac patients or in conditions in which Vit K antagonist is the only optional drug available, there is a role of strict monitoring with I N R and guidelines to patients for adherence to the treatment protocols

CASE 1:

She was a 18 yrs old unmarried girl receiving oral anticoagulant Acitrom 4 mg od for past 20 months following MVR surgery. She presented with acute lower abdominal pain and on evaluation her admission Hb was 6.5 gms, INR – 4.7,USG and MRI confirmed bilateral haemorrhagic ovarian cyst 7X 7cm R > L. Her last period was two weeks ago. She had history of laparotomy for ruptured corpus luteal ovarian cyst 6 months back. This patient was treated conservatively with blood and blood components and as a result she did not require second surgery. Now she is treated with DMPA injection once a month for ovulation suppression. She is under continuous follow up in OG and cardiology departments.

Figure 1: USG shows Rt Haemorrhagic cyst

Figure 2: MRI shows lt ovarian cyst

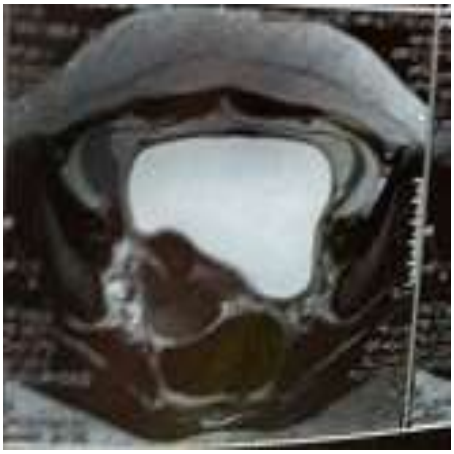

Figure 4: shows free fluid in pelvis

Figure 4: B/l haemorrhagic ovarian cyst

CASE 2:

21 yrs old P2L0 woman on oral, anticoagulant Acitrom 2 mg following MVR surgery 2 years ago, came with acute abdominal pain on evaluation by USG ruptured corpus luteal haemorrhagic

cyst was revealed. Her admission Hb was 6 gms, INR – 4.5,amoun of haemoperitoneum 1 litre. She was surgically managed with right ovarian cystectomy.

Confirmed HPE: Corpus luteal cyst

Patient was started on DMPA injection every month 50 mg IM and reviewed regularly . Planned to continue injection up to 1 year. Later planned for next pregnancy

DISCUSSION:

Mechanical heart valves prosthesis have a high thromboembolic potential, there is therefore no doubt that these patients should receive a lifelong anticoagulants, which unfortunately is associated with a increased risk of hemorrhagic complications.

Ovarian haemorrhage is rarely seen in healthy women and usually have a little clinical importance. However more serious and life threatening bleeding episodes have been described in women treated with anticoagulants.

So cardiologist, haematologist and gynaecologist should together pay attention to these types of treatment related life threatening hemorrhagic complications to find out an appropriate anticoagulants in ovulating women.

The occurrence of the hemorrhagic ovarian cyst are not only treatment related but it is a postovulatory event of a corpus luteal haemorrhage which means there is a high chance of recurrence.

A hemorrhagic or a ruptured ovarian cyst is the most common cause of acute pelvic pain in an aferile premenopausal woman . It typically develops as a result of ovulation. Due to hormonal influence stromal cells surrounding a maturing graffian follicle become more vascular and after ovulation, the graffian follicle develops into a corpus luteum with a highly vascular and fragile granulosa layer which ruptures easily to form a hemorrhagic ovarian cyst.

The accurate diagnosis depends on the clinical presentation, results of the work up and high index of suspicion. Negative pregnancy test is important to exclude ruptured ectopic pregnancy.

Characteristics associated with increased risk of bleeding- history of past bleeding, recent surgery, concomitant medications that potentiate bleeding, hypertension, renal insufficiency (serum creatinine>1.5), severe anaemia (hematocrit <30%)(1).

It also appears that women on anticoagulation tend to suffer more severe haemorrhage. Among them, corpus luteal haemorrhage can be fatal in 3-11% of cases and recur in nearly 25-31% even when INR is still within therapeutic range.

In some cases, conservative management is possible if the diagnosis is accurate and patient remains stable. Close observation , serial hemotological investigations , analgesia and correction of coagulation , replacement of blood and blood products and cardiopulmonary support might be required.

Surgical intervention might be necessary if other causes of acute abdomen are suspected, if patient is unstable or if the bleeding fails to subside with conservative management in a reasonable time. Laparotomy is the standard approach in hemodynamically unstable patients. Women on anticoagulation tend to require oophorectomy . Fortunately its rate has reduced as the conservative surgical approach is dominating the current trend.

Regulation of INR for optimizing Acitrom use INR > target range but < 5.0 , if no bleeding lower or omit next warfarin dose. INR to be evaluated in in 7-14 days. If bleeding suspected medical evaluation should be done.

INR > 5.0 but < 9.0 ,If no bleeding then omit the next dose or two doses of the drug and evaluate the INR in 24- 48 hrs. IF patient has more than or equal characteristic associated with increased risk of bleeding, then omit the next dose warfarin. Vit K 2.5 mg IM given. INR should be evaluated in 24-48 hrs. If bleeding suspected medical evaluation should be done.

INR >9.0, medical evaluation should be done and oral, subcutaneous, or intravenous vit K should be given. hold warfarin therapy until INR <5.0 then resume warfarin dose INR should be evaluated in 3-5 days. After mitral valve replacement with mechanical valve, warfarin is indicated to achieve an INR of 2.5 -3.5 (2)

If INR > 20 and the patient has serious bleeding (or overdose of warfarin), stop warfarin. Vitamin k 10 mg is given by slow iv infusion, fresh frozen plasma transfusion or prothrombin complex concentrate as needed when appropriate; heparin can be given until the patient becomes responsive to warfarin

Prevention of formation of hemorrhagic ovarian cyst(3)

Special considerations for women of reproductive age on anticoagulation –jan 2012 gives guidelines on prevention of hemorrhagic ovarian cyst

1. The progestin only methods which consistently suppress ovulation include the (implants (etonogesrol) and DMPA
2. The levonorgestrol IUD and progestin only pills suppress ovulation for some but not all women
3. Hemorrhagic ovarian cyst occurs more frequently when INR > 4

4. The use of COC(Containing an estrogen and progestin) pills in such patients at increased risk of thromboembolism is controversial(4)

DMPA as effective ovulation suppressing agent :(5)

Progesterone only injectables are in use since 1992. Intramuscular DMPA consistently suppresses ovulation.

The injectable, containing 150mg of DMPA, effectively inhibits ovulation. Intramuscular injections are administered every 3 months. A subcutaneous form consisting of 104mg is also available and dosed every 3 months. This grace period is 2-4 weeks. Return of fertility is 4 months after stoppage of drug.

The most common Sid effects are 1.irregular menstruation2.weight gain,. Amenorrhea after 1 yr of use,. Affects BMD with prolonged use but, after discontinuation of the drug they can regain much of their bone loss..

NOAC's- the alternatives for warfarin

NOAC's are clinically equivalent to warfarin. Practical advantages of NOAC over warfarin are lack of dietary interaction, convenience in usage, frequent laboratory monitoring is not required , few drug – drug interactions , in patients whom warfarin is ineffective. Limitations of NOAC are high cost, no specific lab monitoring tests, no antidote, serious bleeding in renal failure.

Realign study; (dabigatran vs warfarin in patient with prosthetic valve) (6)

Even though realign study is withdrawn because of higher incidence of thrombo embolic complication in NOAC group. Further studies are needed to prove the safety and efficacy of NOAC (dabigatran) compared to VKA(warfarin) group.

CONCLUSION

Although significant ovulation related ovarian bleeding is rare in healthy women , it carries a considerable risk to women on anticoagulation. It should be prevented by inhibition of ovulation in those women on anticoagulation. DMPA seems to be safe and effective to suppress ovulation in those women. However meticulous surveillance should be provide during the follow up , including close monitoring of anticoagulation intensity. Hence monitoring the INR Within the therapeutic range(INR below 4 is to be strictly followed). Though NOAC'S Are available in india, they are extensively studied for use in non valvular Atrail fibrillation only. So still now the only optional drug extensively available for our large population is oral vitamin K antagonist only. more researches to be done for effective alternative new oral anticoagulants, in women after mitral valve replacement. The guidelines for INR monitoring and ovulation suppression

should be known to all obstetricians to avoid such complications. So Cardiologist should refer women with heart valve replacement to the gynaecologist for DMPA IM/SC injection as the contraceptive as well as prevention of CL hemorrghage.

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