

How Safe is Progesterone? Acute Pulmonary Embolisms (APE) Alleged to Progesterone.

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Dear Editor,

Progesterone in the treatment of DUB is popular in our practice. However its safety in prolonged user is a question described herewith in consequence of nearly fatal case of acute pulmonary embolisms (APE) in an obese anemic smoker having sedentary life style.

A 41 P2 was treated for cyclical heavy vaginal bleeding for 4-5 years. She had menarche at the age at 14 and during both the caesarean birth at both the occasions received blood transfusion per operatively.

From the age of 36, history of acquired dysmenorrhea was present worsened by flooding during menstrual cycles that lasted for 6-8 days, confining her to bed refraining her from household activity. There were few records of episodes of severe vaginal bleeding with the drop in hemoglobin to 6gm% when she used to take iron capsule to alleviate weakness off and on.

In the beginning she feared surgery because of blood transfusion and post caesareans pain associated with divarication of rectus.

Later, surgery was deferred on the pretext of poor risk for surgery on the grounds of anemia, two previous caesarean, abdominal wall hernias and obesity.

On many occasions primolut N (norethisterone) 30 mg /day was given for a week and was substituted by tab medroxyprogesterone (devery) 10 mg twice daily non stop.

However when USG showed uterine enlargement of 9x12cm decision for hysterectomy taken on improvement on hemoglobin status.

During the interval period, she almost collapsed from heavy vaginal bleeding and therefore admitted and investigated. Complete blood count showed features of pancytopenia (low hemoglobin estimation reported as 5 gm%, low WBC, RBC and also platelets). For this she was transfused with 3 units of packed cell. In oral hormone therapy, medroxy progesterone acetate was substituted by norethisterone acetate and as usual, was sent home with a decision to operate later once there was subsidence of body edema and return in the tissue perfusion. This was also because on the unavailability of attending doctor.

Unfortunately, on the second evening of discharge, she developed acute shortness of breath, audible wheezes and frothing from mouth and was rushed to Patan Hospital. Examination at that point recorded pulse rate of 170/min and the diastolic blood pressure of 110 mm Hg. ECG showed sinus tachycardia and there was no ventricular arrhythmia. X ray features did not show signs of pulmonary edema.

Because of preexisting anemia and recent history of blood transfusion was managed in the line of left ventricular failure, with oxygen inhalation and i/v lasix. After 6 hours, there was slight improvement as the dyspnoea changed to tachypnea. A diagnosis of pulmonary embolism was made and progesterone was withdrawn. Heparinization was started with sub-

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cutaneous low molecular weight heparin in doses of 7500 twice daily and prothrombin time was monitored. FDP(fibrin degradation product), antinuclear antibody (ANA), double stranded DNA, LE cell, anticardiolipin antibody all were within normal limits that formally excluded SLE.

She was again transfused with 2 units of fresh blood. On the background of adequate platelet, normal bleeding time and clotting time, emergency hysterectomy was permitted by medical team on 7th day of SOB episode because of the passage of clots per vaginum as TVS showed thinning of endometrium to 6mm.

Morning dose of heparin was withheld. At surgery entry to peritoneal cavity was difficult due to dense pelvic and peritoneal adhesion. A subtotal hysterectomy was accomplished with minimal per operative bleeding. Cut section showed empty endometrial cavity devoid of any polyp but there was small 4x5 cms intramural myoma near the fundus of the uterus.

She was started on anticoagulation after 12 hours of surgery and was continued on low molecular weight heparin (fragmin) until the stitches were removed on the 10th day when the wound was found to be healthy. Warfarin (5 mg) was overlapped with heparin till anticoagulation was adequate maintaining PT twice than the control value and international normalizing ration (INR) within normal range of anticoagulation. Finally was discharged on day 18th of admission on warfarin 7 mg.

It is rather remorse retrospectively to admit even the use of progesterone alone could be responsible for APE when shored up risk factors like smoking in addition to anemia is a reason for lesser mobility in a woman with sedentary habit ¹⁻³.

There are reported cases of APE caused by combined oral contraceptive pills, monthly injection of depot medroxy progesterone acetate though estrogen is known to cause VTE susceptible for APE ¹⁻³.

We could incorporate SOB as APE as tachypnea alone as been integrated as APE.

In the management of APE, preference of low-molecular-weight heparin over unfractionated heparin for short-term have proven benefit in reference to emergency surgery, that could be undertaken without any per operative hemorrhagic complications in this case congruous other findings.

In conclusion progesterone must be given cautiously in women having risk factors for pulmonary embolism to avoid life threatening condition that may arise from its erratic use.

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