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Menorrhagia, Mechanical Heart Valves and Management Issues.

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Objective – To propose a protocol for managing menorrhagia in patients with mechanical valves. **Methods** – Analysis of four cases treated by us and meta analysis of reports in the literature was undertaken. **Results and Conclusion** – Bleeding should be tackled rapidly. Surgery if needed can be undertaken safely in most of the patients with short interruption of oral anticoagulant alone. Heparin preferably intravenous, should be used only in selected cases with high thrombotic risk.

Key words : menorrhagia, mechanical heart valve, oral anticoagulant, perioperative anticoagulation.

Introduction

Patients with mechanical heart valves used to have short life span due to anticoagulant related complications [1]. Refinement in prothrombin time (PT) monitoring and anticoagulant therapy have led to an increasing number of such patients living longer and women reaching menopause. Menorrhagia, a common menopausal problem is difficult to manage in those on permanent anticoagulation.

In our hospital, 110 patients with mechanical heart valves are currently on regular follow- up in the Cardiology Department. In the last 20 years none of them had any major surgery. However in the year 2000 alone eight of them underwent surgical procedures like hernia repair, cholecystectomy, Cesarian section, dilation and curettage (D and C) and abdominal hysterectomy. The issue that emerged in patients with menorrhagia were analyzed to evolve guidelines for future.

Materials and Methods

Case 1 – Mrs. Q (para 6+1), aged 42 years was admitted on 16th June 2000 with bleeding for 15 days. She had menorrhagia for six months, not responding to mefenamic acid. On vaginal examination the uterus was anteverted, parous size, mobile and fornices were free. She was posted for D and C.

She had Starr–Edwards prostheses implanted in aortic and mitral positions in 1990 and was taking nicoumalone 4 mg/day. D and C was done after stopping the oral anticoagulant (OAC) for three days. Prothrombin time on the day of surgery was INR (International Normalized Ratio) 1.8. Normal looking endometrial tissue was curetted and nicoumalone 2 mg was started on the evening of surgery. Slight vaginal bleeding responded to norethindrone acetate 5 mg bds. Ampicillin and gentamycin were given for infective endocarditis prophylaxis and she was discharged after five days. Histopathology examination (HPE) showed bits of endometrial tissue comprising of some non-secretory and several normal endocervical glands. After two normal menstrual cycles she attained menopause.

Case 2 – Mrs. BV (para 4+0), aged 42 years was admitted on 10th Feb 2000 with continuous vaginal bleeding for six days and menorrhagia for six months. Vaginal examination showed retroverted uterus of parous size and free fornices.

She had aortic valve replacement with Starr-Edwards prosthesis in 1989 and was taking nicoumalone 1 mg/day. She was in sinus rhythm and heart size was normal. On admission INR was 7.4 (PT ratio 3) and hemoglobin was 8.5 gm/dl. Anticoagulant was omitted, two units of blood transfused and norethindrone acetate 5 mg 8 hourly was started. D and C done elsewhere on 30.10.1999 showed non-secretory endometrium and acute endometritis. Total abdominal hysterectomy was planned. Intravenous heparin was infused at 750 – 1000 units per hour, guided by partial thromboplastin time (PTTK) and continued for four days. After stopping the infusion for six hours the surgery was performed. Blood loss was less than average. Heparin infusion along with OAC was given from the second post-operative day. Ampicilin, gentamycin and metronidazole were given for five days and she was discharged after 18 days of hospital stay. HPE: Chronic cervicitis, early secretory endometrium, normal myometrium, normal tubes and ovaries.

Case 3 – Mrs. US (para 3+1), aged 44 years had menorrhagia with clots for six months. Per vaginal

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examination showed a fibroid in the left fornix and ultrasound confirmed multiple fibroids.

She had aortic valve replacement with St. Jude prosthesis in 1996 and was taking nicoumalone 2 mg/day. She was in sinus rhythm and heart size was normal.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done on 21st July 2000 after stopping the anticoagulant for four days. On the day of surgery her hemoglobin was 11 gm/dl and INR 1.5. Intra-operative bleeding was more than average; one unit blood was given and hemostasis achieved. Nicoumalone was restarted on the first post-operative day. She did not receive heparin. Cephotaxime and metronidazole were given for five days. Her total hospital stay was 12 days. HPE: multiple leiomyoma and non-secretory endometrium with few cystically dilated glands, minimal inflammatory changes in cervix and a hemorrhagic corpus luteal cyst in left ovary.

Case 4 – Mrs. BD (para 1+0), aged 42 years complained of menorrhagia for six months not responding to norethindrone acetate. D and C done six months earlier showed cystoglandular hyperplasia and she was scheduled for abdominal hysterectomy.

In 1994 she had undergone mitral valve replacement with Medtronic-Hall valve, and was taking warfarin, furosemide and digoxin. She had aneurismal left atrium, atrial fibrillation and normal ejection fraction. In 1998 she had prosthetic valve thrombus, treated with streptokinase.

The OAC was stopped for four days and she was hospitalized one day preoperative. INR on the day of surgery was 2.0. Total abdominal hysterectomy and

Table I : Profile of Perioperative Anticoagulation in Four Patients with Mechanical Heart Valves

Parameter	Case 1	Case 2	Case 3	Case 4
Age in years	42	42	44	42
Type, site and year of valve replacement	Starr-Edward aortic and mitral, 1990	Starr-Edward aortic, 1989	St.Jude, aortic, 1996	Medtronic-Hall, mitral, 1996
Pre-op OAC[a]	Stopped 3 days pre-surgery	Stopped 7 days pre-surgery	Stopped 4 days pre-surgery	Stopped 4 days pre-surgery
Post-op OAC[a]	Started in evening of surgery	Started on 2nd post-op day	Started in evening of surgery	Started on 2nd post-op day
Pre-op Heparin	Not used	IV for 4 days before surgery	Not used	Not used
Post-op Heparin	Not used	IV from 2nd post-op day for 48 hours	Not used	IV from 2nd post-op day for 48 hours.
Bleeding due to anticoagulant therapy	Nil	In pre-op period, treated with vitamin K and blood	Nil	In post-op period treated with vit. K and vaginal pack
Thrombotic complication	Nil	Nil	Nil	Nil
Surgery Histopathology	D and C Non-secretory endometrium	TAH with BSO[b] Early secretory endometrium	TAH with BSO[b] Multiple leiomyoma	TAH with BSO[b] Non-secretory endometrium
Hospital stay	5 days	18 days	12 days	7 days

[a] - Oral anticoagulant [b] - Total abdominal hysterectomy with bilateral salpingo-oophorectomy

ilateral salpingo-oophorectomy was done and emostasis achieved. On the second post-operative ay heparin infusion with OAC was started and ontinued for 48 hours. Cephotaxime and netronidazole were given for five days. She was ischarged on the seventh post-operative day with arfarin 5 mg OD but re-admitted after three days or vaginal bleeding. It responded to IV vitamin K menadione acetate) 5 mg and vaginal pack. However er INR was 3.5. She was discharged after two days ith warfarin 5 mg and 2.5 mg on alternate days. HPE: on-secretory endometrium, normal myometrium, ormal cervix, normal tubes and normal left ovary; ght ovary showed a follicular cyst.

Discussion

atients with mechanical heart valves are prone for hrombosis and need to be on permanent nticoagulation. The conventional practice is aimed PT ratio of 1.5 to 2 but slight deviations would cause otting or bleeding. The introduction of INR format 1983 improved the standardization of PT results ermitting a wider range of anticoagulation tensities. In 1998 a task force for British Committee or Standards in Hematology laid down guidelines for nticoagulation based on INR. The recommended rget INR for patients with mechanical heart valves 3.5; complications are the least at this level (< 2 per 00 patient years). But many laboratories have not dopted INR format hence the guidelines are not tilized for monitoring and management of high-risk tuations.

n our Hospital, the survival of patients with nechanical heart valves has improved after the ntroduction of INR to guide the anticoagulant therapy nd we gained insight on various issues [1,2].

ffect of anticoagulant therapy on menorrhagia – Bleeding ue to anticoagulant excess occurs when the INR xceeds 5[3]. Therapeutic level of anticoagulation can xaggerate bleeding from pathological tissues[4]. Case had anticoagulant excess (INR 7.4) at the time of dmission and case 4 had secondary hemorrhage with NR in the therapeutic range.

nteraction between oral anticoagulants and the agents sed for dysfunctional uterine bleeding – Mefenamic acid sed in dysfunctional uterine bleeding is one of the umerous drugs that can alter the effect of OAC. etronidazole often used in post-operative period can xaggerate anticoagulation. If any such drug is rescribed for more than five days PT must be checked nd adjustment in the dose of OAC made [3].

Safe protocol for perioperative anticoagulation – The fear of thrombosis if OAC is interrupted in the perioperative period and bleeding if it is continued leads to avoiding surgery in patients on long term anticoagulation [4,5]. As the number of patients with mechanical heart valves is growing, this issue needs to be addressed. Suboptimal or interrupted anticoagulation predispose to thrombosis in the following circumstances: (1) mechanical valve in mitral and multiple sites, (2) older generation prosthesis like cloth-lined Starr-Edwards, (3) early years after mechanical valve implantation, (4) atrial fibrillation, (5) dilated cardiac chambers, (6) heart failure and (7) thrombosis or embolism within one month[6-8]. Safe protocol in them would be to stop the OAC four days before surgery (range 3-5 days) and infuse heparin 500 – 1000 units per hour, guided by PTTK at 6, 12 and 24-hour intervals, one day pre and postoperatively. The infusion can be stopped six hours before surgery and resumed when the surgical team feels it is safe, usually after 6 – 12 hours [3,8].

Patients with mechanical prosthesis in aortic position, sinus rhythm and normal LV function carry a low risk for thrombosis from a short interruption of anticoagulation. In such patients a cost-effective protocol with short hospital stay will be safe. The OAC can be stopped four days (range: 3 to 5 days) before surgery and resumed as soon after the surgery when the operating team feels it is safe. If the INR on the operating day is 1.8 surgery can be undertaken. If the INR is > 2.0 a small dose of vitamin K (1 mg) can be given subcutaneously. This approach is devoid of heparin-related bleeding [3,8].

Two of our patients (Cases 1 and 4) had greater predisposition to thrombosis due to their prosthesis type, site, atrial fibrillation and left atrial enlargement. In the first case OAC had to be stopped for menorrhagia and D and C was done. Case 4 received heparin in the post-operative period only but neither of them developed thrombus. Cases 2 and 3 carried low risk for thrombosis from their aortic prostheses and could have been managed with short interruption of oral anticoagulant alone.

Large scale case controlled studies have not been conducted to test the efficacy and safety of different regimens for perioperative anticoagulation. After analyzing 46 studies involving 13,088 patients Cannegieter et al[3] calculated the thrombotic risk for one day from a short interruption of anticoagulation to be as low as 0.016% (1.6 in 10,000). Routine perioperative heparin in all the patients with mechanical heart valves for every surgical procedure

will increase the cost through longer hospital stay, frequent blood tests and expose the patient to bleeding complications [9].

Patients with mechanical heart valves need optimum consistent anticoagulation. Therefore menorrhagia and any other source of bleeding must be tackled rapidly. If surgery is indicated it can be undertaken safely in most of the patients with a short interruption of oral anticoagulant alone. The use of heparin should be limited to selected cases with high thrombotic risk and intravenous route is preferred.

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