REVIEW ARTICLE

Management in Patients with Advanced Cancer Cervix in Low Resource Setting

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Abstract

Subjects with an advanced stage of cervical cancer have bleeding which can be alarming to the family as well as treating staff. Sometimes,life threatening bleeding occurs. Pre-planning is required in all bleeding situations, especially in advanced stage patients and in those with the potential for massive bleeding. Interventions are based on prognosis , effectiveness, patient preferences and past medical history.

In low resource settings we need to modify our treatment plan. Bleeding in patients with advanced cancer can be due to variety of underlying processes and presents clinically in different ways, from chronic, low-volume bleeding to acute episodes of major haemorrhage. Depending on whether the bleeding is originating from capillaries or from larger vessels will affect the treatment plan. Local modalities available to manage bleeding these include topical hemostatic agents and dressings, radiotherapy, endoscopic procedures, and TAE or balloon placement through interventional radiology. There is increase in use of interventional radiology. Patients at risk for major hemorrhages should be identified, and their families and caregivers should be prepared. End-of-life decision making should be based on comfort and the optimization of quality of life.

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Introduction

Bleeding in patients with an advanced stage of cervical cancer can be alarming to the family as well as treating staff.[1] Pre-planning is required in all bleeding situations, especially in advanced stages of cancer. Interventions are based on prognosis , effectiveness, patient preferences and past medical history.

Causes of Bleeding in these Patients

Due to tumour growth through different pathways, bleeding happens from blood vessels.[2] Coagulation abnormalities results from primary and secondary fibrinolysis, disseminated intravascular coagulation (DIC), medications and liver disease due to liver failure or metastatic disease.[3] Besides Cancer malnutrition, warfarin like drugs & zinc, folic acid deficiency can also cause bleeding.

Management

We may be able to control bleeding by local interventions viz. (i) packing (ii) dressing with compression effect, (iii) dressing with topical haemostatics/astringents and (iv) postural changes.

Packing/Tamponade

Packing is often done along with local medication depending upon the site of bleeding. Acetone or formalin soaked roller gauze can be used for genital bleeding[4,5] Formalin (4–5%) causes proteolysis, coagulation and cross linking of proteins and thus helps in stopping the bleeding.[6] Sometimes Monsel's solution may be used. Sucralfate has cytoprotective action and can be mixed with Monsel'ssolution & KY jelly and applied on oozing sites.[7]

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Compressive Dressings

Alginate dressing with compression has good haemostatic effect. Calcium ions in the dressing are replaced by sodium ions emanating from wound fluid. The sodium causes alginate fibre to swell & form a gel that causes compression.The degree of swelling is determined principally by the chemical composition of the alginatewhich depends on its origin.[8]

Hemostatic Agents

Fibrin sealants derived from components of plasma are in use. Since 1970, antifibrinolytic agents like bovine aprotinin & $CaCl_3$ has been used to control bleeding and seal tissues.[9] They are sprayed over the friable tissues, as handling tends to increase bleeding. Risk of re-bleeding increases when factor XIII is not sufficient due to poor clot formation,as factor XIII is very important in clot formation.[9] When fibrinogen and thrombin are mixed, fibrinogen is converted to fibrin monomers with subsequent completion of the coagulation.[9] Some of the tissue sealants used for bleeding surface are, Gelfoam, FloSeal, oxidized cellulose.[10,11] and collagen based haemostatic agents.[12] Formalin can also be used to control bleeding from small vessels by causing chemical cauterization.[13-15] No toxic adverse effects is seen with 4% solution of formalin.[15-17]

Zinc ions released from Mohs' paste works by releasing it when it comes into contact with cancer cells.[18] After contact,it precipitates wound proteins to help stop Bleeding.[19]

For bleeding from cervix, Monsel's solution (ferric subsulphate), a haemostatic agent that can be applied directly.[20-25] Its role is to coagulate proteins,cause tissue necrosis and eschar formation thereby improving thrombosis and haemostasis.

Astringents

(i) Cotton swabs containing silver nitrate & potassium nitrate can be easily applied. Silver nitrate a strong oxidizing agentwhich oxidizes organic matter, coagulates tissue, and destroys bacteria by releasing free radicals.[26] (ii) Alum (either aluminium ammonium sulphate or aluminium potassium sulphate) increase protein precipitation from bleeding areas. This leads to narrowing of intercellular space, vasoconstriction, capillary endothelial sclerosis and reduction in swelling, inflammation and exudates. Alum has been used in the bladder to treat haematuria caused by a tumor or radiation therapy. Cotton swabs soaked in 5% formalin can also be inserted in bladder through endoscope to control bleeding.[27,28]

Other Temporizing Measures

Warm saline irrigation, palliative radiation therapy and palliative chemotherapy.

Systemic Interventions

Vitamin K

In chronic liver disease, low intake of green leafy vegetables, small bowel diseases or resection and intrahepatic and extrahepatic biliary obstruction, vitamin K is an essential factor in the production of clotting factors II, VII, IX. Treatment with Vitamin K, may be helpful. The recommended dose is 2.5 to 10 mg.

Antifibrinolytic Agents

Tranexamic acid (TA) and aminocaproic acid (EACA) block the binding sites of plasminogen, thus inhibit conversion of plasminogen into plasmin by tissue plasminogen activator resulting in decreased lysis of fibrin clots. Tranexamic acid is about 10 times more potent than EACA. Intravenous dose of TA is 10 mg/kg, three to four times a day, administered over 1 hour. EACA is given in doses of 4 to 5 g, 250 mL over the first hour then 1g per hour 50 mL continuously for 8 hours or until bleeding has been controlled. Nausea, vomiting, and diarrhoea are common side effects and are dose dependent. They may also be used as a topical, rectal or intravenous infusion. Thrombo-embolism is rare.

Blood products

Platelet transfusion in advanced cancer should be, aimed to control symptom of bleeding. 4 to 6 units of platelet concentrates are usually required to control bleeding. The short half-life of platelets limit their usefulness in severely thrombocytopenic patients with end-stage disease.

Ethically it is difficult to decide whether to continue or not continue platelet transfusions in thrombocytopenic patients with endstage disease. Patients and families may believe that the stoping of transfusions as withdrawal of life-sustaining therapy. One needs to be sensitive and empathetic while discussing with patients' family, the attending physician and health team and explore their expectations, fears, and concerns before engaging in advanced end-of-life support and commitment to provide optimal comfort care.

End-Of-Life Considerations

In the terminal phases of cancer the goals of care should be comfort. Invasive treatments may be more of a burden than benefit. Comfort without invasive procedures take precedence. Sometimes, it is not clear whether or not a

local or systemic measure will be of benefit. A platelet transfusion or an antifibrinolytic agent will provide benefit and may be warranted in select cases.

When a terminally sick persistent is at chance for a major hemorrhage, family individuals and caregivers ought to be sharpened and educated and arranged, as these occasions can be upsetting. Simple measures are to use dark towels to absorb blood, to apply pressure to the site of haemorrhage, and to place the patient in a lateral position in case of hematemesis or hemoptysis.. A rapid-acting sedative such as Midazolam, 2.5 or 5 mg intravenously or subcutaneously, serves this purpose well and may be repeated after 10 to 15 minutes. Orders for a sedative in case of such an emergency should be entered.The subcutaneous administration of the medicine should be taught to families and caregivers. If there is an emergency, families should be informed who to call. It would be inappropriate to call 108 if the patient indicated a preference for comfort measures.

Conclusion

Bleeding in patients with advanced cancer can be due to variety of underlying processes and presents clinically in different ways, from chronic, low-volume bleeding to acute episodes of major haemorrhage. The treatment plan will be affected, depending on whether the bleeding is caused by a capillary or larger vessel. Topical hemostatic agents and dressings, radiotherapy, endoscopic procedures, TAE or balloon placement through interventional radiology are local procedures available to manage bleeding. The use of interventional radiology has increased. Patients at risk for major hemorrhages should be identified, and their families and caregivers should be prepared. Comfort and the optimisation of quality of life should be taken into account in the choice of endof life. The use of interventional radiology is on the rise. Patients at risk for major hemorrhages should be identified, and their families and caregivers should be prepared. Comfort and optimising the quality of life should be considered when making decisions on endoflife.

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