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Review Article

Platelet rich plasma: a newer modality of cervical erosion treatment

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ABSTRACT

Cervical erosion is a condition in which squamous epithelium of the vaginal aspect of cervix is replaced by columnar epithelium. Some of the common causes of cervical erosion are poor hygiene, trauma, excessive use of chemicals, infection, malnutrition, low immunity, multiple partners and early age of sexual activity. The common clinical symptoms are mucoid discharge per vaginum, post coital bleeding, lower abdominal pain, low backache and deep dyspareunia. Asymptomatic erosions usually heal on their own, but symptomatic erosions need to be treated. Antibiotics and anti-inflammatory agents are used as the first line of treatment. Cryotherapy is a commonly used treatment modality which causes controlled destruction of tissue by freezing. Another method which holds promise is Carbon dioxide Laser. It works by ablation or vaporisation of abnormal cells and has better precision as well as insignificant pain post procedure. Chemical cautery with silver nitrate stick is also an easy and cheap method of treatment. Platelet rich plasma is a newer modality in which platelet derived growth factors help in tissue healing and epithelisation. It does away with the troublesome side effect of watery discharge post treatment, which is known after all other treatment modalities.

Keywords: Cervical erosion, Platelet rich plasma, Squamous epithelium

INTRODUCTION

Cervical erosion is a common condition in which the squamous epithelium of the vaginal aspect of cervix is replaced by columnar epithelium which in turn is continuous with the lining of the endocervix.[1] It is actually not an area of denuded epithelium as the name implies. Small areas of ulceration seen microscopically may be due to secondary infection or local trauma or they can be just artifacts. An ectopy has a bright red appearance with a clearly defined edge, the colour being explained by underlying vasculature showing through thin columnar epithelium. The columnar epithelium may be arranged in a regular pattern, but sometimes it may be proliferative and heaved up to form villous projection-papillary ectopy. Tissue underneath the epithelium often shows round cell infiltration and glandular proliferation. It is assumed that these signs are indicative of chronic infection, which usually precedes and is the cause of ectopy. Superadded inflammatory process, however, is commonly seen as the columnar epithelium is less resistant to infection than the normal stratified epithelium. Cervical erosion / ectopy is a common condition seen in women of all age groups.[2]

The endocervical canal is lined by columnar epithelium containing racemose glands which secrete mucus and Infective organisms usually get lodged deep in these racemose glands, persisting as a septic focus. As the endocervical lining is not shed during menstruation, like the uterine endometrium, infection cannot be treated easily, leading to chronic cervicitis. Chronic cervicitis clinically manifests as an erosion or as a Nabothian follicle. The extension of the columnar epithelium beyond the external cervical os to replace the squamous epithelium covering the portio vaginalis of the cervix usually causes erosion. Nabothian follicles occur when the mouth of an endocervical gland opening gets blocked, it gets distended with inspissated secretion resulting in a cystic bulge (Nabothian follicle). Some of the common causes of cervical erosion are poor hygiene, trauma, excessive use of chemicals, infections (sexually transmitted diseases like

chlamydia, gonorrhoea, trichomonas vaginalis, viral infection like herpes simplex virus and human papilloma virus) malnutrition, low immunity, multiple partners and early age at onset of sexual activity.[3]

CLINICAL EXAMINATION

Cervical erosion is easily diagnosed on speculum examination. Erosion presents as a bright red area around the external os which has an inner margin continuous with the endo-cervical lining and a well-defined outer margin. The erosion may be slightly raised above the level of the squamous epithelium of portio vaginalis of cervix and appears smooth and glistening as it is covered by columnar epithelium. When erosion is associated with chronic cervicitis, the cervix becomes fibrosed and bulky with nabothian follicles around the area of erosion. Mucoid discharge may also be seen coming through os and around the erosion. The erosion bleeds easily if swabbed vigorously during examination

Clinical features

The most common clinical symptom with which patients present is mucoid discharge, which may be mucopurulent if there is superadded infection and sometimes it maybe blood stained. Other common symptoms may be post coital bleeding, low backache, abdominal pain and deep dyspareunia. Erosion occurring during pregnancy are very vascular and bleed easily.

Management of cervical erosion

Asymptomatic erosions usually heal on their own, but symptomatic erosions need to be treated. When a patient presents to the OPD with clinical manifestations suggestive of erosion , a diagnosis of cervical ectopy is easily made on speculum examination. A Paps smear is taken routinely in all patients to rule out any possibility of malignancy. The first line of treatment is usually a course of antibiotics and anti-inflammatory agents for a period of one to two weeks. If the lesion does not heal, procedures like cryotherapy, laser or silver nitrate cautery are done.

Cryotherapy

Cryotherapy is a treatment modality being used since ages.[4] The basic principle of cryotherapy is controlled destruction of tissue by freezing.[5] It is a double freezing technique in which the tissue is frozen for 3 minutes, thawed for 5 minutes and refrozen for 3 minutes.[6] In order to achieve hypothermia, nitrous oxide is forced through a small hole at a pressure of 750-900 pounds per inch.[7] This produces a very low temperature at the surface of the probe due to Joule-Thompson effect. The temperature at the probe tip can range from -65 to -85°C. Cell death occurs due to crystallization of intracellular water at -20 to -30°C.[8] Cryotherapy gives good therapeutic results, but hydrorrhoea or watery discharge per vaginum for two to four weeks following the procedure is a troublesome feature. Uterine cramping may last for twenty four to thirty six hours. Vasomotor reaction in the form of flushing, dizziness or headache can also occur during the procedure. Although not very expensive but the cryotherapy apparatus has to be maintained and gas cylinders have to be refilled from time to time .

Laser therapy

Carbon dioxide laser beam is used to destroy the abnormal cervical epithelium seen on magnification by a colposcope. It is an outpatient procedure, done without any anaesthesia. It works by ablation or vaporization of abnormal cells. It helps to treat the lesion precisely and does not affect the surrounding healthy tissue. A power range of 5-10 Watts and exposure time of 1-2 minutes is used.

The laser beam is directed radially from inner margin of ectopy to its outer margin.[9] The deep glands in the squamocolumnar junction can also be reached and destroyed. Some cramping pain, bleeding and watery discharge is to be expected for 3-4 weeks because of epithelial regeneration but the exudation gradually subsides. The squamous epithelium regenerates in about six month time. Complications like bleeding, infection, narrowing or stenosis of cervix may occur and sometimes lead to infertility. A rare possibility of cervical incompetence is also there. However laser is very expensive and requires a lot of maintenance. Proper precautions to prevent harm to operator (like eye protection) have also to be taken.

Chemical cautery

Silver nitrate comes in the form of a chemical stick, also known as caustic pencil. It contains silver nitrate and potassium nitrate. This is applied to the ectopy for one to two minutes and it cauterises the area.[10] It is not used on large areas and no anaesthesia is required. When applied to the erosion, a thin eschar is formed. Silver nitrate stick delivers free silver ions, in presence of moisture, that bind to tissue proteins, leading to their precipitation. These precipitates obstruct small vessels and cause coagulation necrosis of the erosion.

Silver nitrate cautery is very cheap, has a quick learning curve and is a very fast procedure. However there may be some watery, black discharge for one week due to sloughing of dead tissue. Sexual intercourse has to be avoided as it may cause burns to the partner.

Platelet rich plasma

Platelet rich plasma is a new modality for treatment of cervical erosion. Platelet rich plasma (PRP) is defined as blood plasma, which has been enriched with platelets by using centrifugation. It may also be defined as a portion of the plasma fraction of autologous blood having a platelet concentration above baseline. Normal platelet counts in

blood range between 1,50,000/ ul and 4,00,000/ul with an average count of about 2,00,000/ ul. Plasma with a platelet concentration of 1,000,000 platelets / ul is the accepted value for PRP. PRP is recently being used as a safe, non-surgical, biological therapeutic measure for treatment of osteoarthritis and musculoskeletal healing and in several other orthopaedic and dermatologic conditions.[11]

Platelets are a component of blood cells, that are formed in the bone marrow. They have a life span of 7-10 days. Many intracellular structures containing glycogen, lysosomes and two types of granules (alpha granules and dense granules) are found in platelets. The alpha granules contain the clotting and growth factors. These are released in the healing process. Normally platelets are in the resting state, they require a trigger for activation, then they participate in homeostasis and wound healing.[12] When activated by thrombin, the platelets change into different shapes and develop branches, called pseudo-pods that spread over injured tissue. This process is known as aggregation. Eventually the granules contained within platelets release various growth factors which stimulate the inflammatory cascade and healing.[13]

Role of PRP in cervical erosion comes from the fact that the body's first response to tissue injury is to deliver platelets to the injured area. These platelets promotes healing through growth factors and other cytokine which are released. Platelet rich plasma or PRP is made from an individual's whole blood, which is centrifuged to remove red blood cells. The remaining plasma has a 3-5 fold higher concentration of platelets than the whole blood. These platelets when activated release growth factors (platelet derived growth factors, transforming growth factor beta, fibroblast growth factor, insulin like growth factor 1 and 2, vascular endothelial growth factor, epidermal growth factor) which have been found to promote natural healing. They attract stem cells to the site of injury which help in regeneration of tissue.

Applying autologous PRP to diseased tissue is a simple, natural, low cost and invasive way of ensuring a good local concentration of autologous growth factors and the method holds promise. In recent years, autologous PRP has become more and more popular in the fields of orthopaedics, dentistry, dermatology, ophthalmology and cosmetic surgery.

PRP is a new modality on which research is being done around the world for treatment of cervical ectopy. Only few studies, have been done and all showed encouraging results. Over the past two years, in our hospital, we used PRP in 60 to 70 patients with cervical erosion and found very satisfying results. After a detailed history and examination and having ruled out malignancy by doing a pap smear, patients were explained the procedure and informed consent was taken. Around 15 ml of whole blood was collected from each patient by venepuncture in two preloaded anticoagulant tubes. The sample was checked for platelet count to be within normal range. The sample was processed by density dependent separation in laboratory at 1800 rpm for 12 minutes. The plasma including buffy coat was put into another tube. This sample was put for centrifugation again at 3200 rpm for 6 minutes. Supernatant was removed. The lower part was rich in platelets and 0.2 ml of this sample was checked for count. Usually 2 ml of PRP was made from 15 ml of blood sample.

On OPD basis, patient was put in lithotomy position and cervical erosion was visualized with speculum. Using 1 ml syringe with 20/22 gauge needle, around 0.25 ml of PRP was injected in approximately 1 square cm area, so number of sites was decided according to approximate size of lesion. Around 1.5 ml of PRP was injected in and around the erosion at 4 to 6 sites. 0.5 ml was smeared directly over the area of erosion.

To avoid spillage while injecting, smaller amount of PRP was taken into the syringe at one time. The patient was allowed to rest for half an hour. She was then sent home with instructions to avoid coitus and pessary for 4 weeks Patients were called for follow up at 2, 4 and 12 weeks. As early as at 2 weeks follow up, patients showed dramatic relief in terms of white discharge, burning sensation, lower abdominal pain and backache etc. Patients were very comfortable and felt a general feeling of well-being and relief from their symptoms. Erosions gradually healed in 6 weeks to 12 weeks .

A thorough search of the available literature showed Hua et al compared PRP with laser treatment for cervical ectopy.[14] They concluded PRP application appeared promising as it yielded a shorter tissue healing time and milder adverse effect (watery discharge) than laser treatment. Jain et al in Madhya Pradesh compared antibiotic therapy and PRP for cervical erosions.[15] They injected PRP at 3-4 sites on the cervix. They found better clinical benefits, regeneration and healing of epithelium and an increased perception of recovery in patients in the PRP group without additional medication.

Aitah et al, evaluated the therapeutic effect of applying an autologous PRP in cervical erosion versus chemical cautery with silver nitrate, in Egypt.[16] Patients were followed up for lesion size changes, symptom relief, pain every 2 weeks till 1 month. They found no significant difference.

CONCLUSION

The cervix heals by re-epithelialization , which takes place in majority of patients by 6 weeks and in all patients by 3 months. Cryotherapy works by controlled destruction of tissue by freezing, Laser beam also destroys abnormal cervical tissue, but, in PRP, there is no tissue loss. Platelets are separated from whole blood by centrifugation. The resulting concentrate has a larger concentration of platelets and other cellular plasma components than whole blood.

Platelets when activated release growth factors which encourage re-epithelialization and healing of erosion.

Autologous PRP therapy is an emerging treatment strategy for chronic cervicitis, with promising result for inflamed and damaged cervical tissue, with healing of erosion and better cervical health. Since it is autologous, being generated from patient's own blood, it is biologically safe, easy to obtain, free from development of immunogenic complication and economically viable option for the treatment of cervical erosions and its symptoms. It does away with the troublesome side effect of watery discharge. The relief obtained after a single application PRP was extremely remarkable at 2 weeks follow-up, in view of white discharge, backache, lower abdominal pain and burning sensation. The comfort and relief obtained was very rewarding for the patient.

So, although cryotherapy, laser and chemical cautery are all good procedures, but PRP offers to be a promising modality for treatment of cervical erosions as a simple, non-immunogenic and economic option for providing early relief of symptoms without any major side effects.

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