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### RESEARCH ARTICLE

## EFFECTIVENESS OF AUTOLOGOUS PLATELET RICH PLASMA IN THE TREATMENT OF HIGHT PERIANAL FISTULA.

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#### Manuscript Info

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##### Key words:-

high perianal fistula, platelet rich plasma.

#### Abstract

**Background:** The main issue involves high perianal fistula management, as fistulotomy would represent an unacceptable risk of incontinence in such patients. Platelet rich plasma (PRP) is defined as a portion of patient own plasma with high concentration platelet and growth factor levels as obtained by centrifugation. Platelets have alpha granules that contain several proteins with multiple actions on the various aspects of tissue repair.

**Aim of the study** was to evaluate the use of autologous platelet rich plasma in the treatment of perianal fistula.

**Methods:** A prospective study including patients with high perianal fistula who presented to General Surgery Department of Zagazig University in the period from September 2016 to February 2019.

**Result:** We had 16 patients with a diagnosis of high perianal fistula, 9 males and 7 females. We had a clinical success rate of 75% (12 patients out of 16 were completely healed with no recurrence throughout the follow up period). Two patients (12.5%) developed postoperative abscess formation and another two patients (12.5%) showed persistent external opening.

**Conclusion:** Platelet rich plasma is promising in the treatment of high perianal fistula without affection of fecal continence.

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#### Introduction:-

Anal sepsis is one of the most common benign anorectal diseases managed by surgeons. Of all patients who present with perianal abscess, up to 65% will develop a chronic or recurrent anal fistula.<sup>1</sup> Operative intervention remains the only effective modality to treat this condition. Although the principal goal of treatment is to eradicate the fistula, it is also important to preserve anal continence, minimize postoperative complications, and decrease risk of recurrence.<sup>2,3</sup>

The anatomy of the fistula and degree of anal sphincter muscle involvement can cause a significant challenge to the surgeon. There are several surgical options currently available, including fistulotomy, fistulectomy, endorectal advancement flap, seton drainage, anocutaneous flap, fibrin glue injection, anal fistula plug, and ligation of the intersphincteric fistula tract (LIFT).<sup>4</sup>

PRP is defined as a portion of one's own plasma with high concentration of platelet and growth factor levels obtained with centrifugation. Platelets have alpha granules that contain several proteins and growth factors (PDGF,

FCT- $\beta$ , VEGF, IL-1, FADP, ECGF, osteocalcin, osteonectin, fibronectin, fibrinogen, and thrombospondin) with multiple actions on the various aspects of tissue repair.<sup>5</sup>

The aim of this study is to evaluate the use of autologous platelet rich plasma in the treatment of perianal fistula.

### Patients and methods:-

A prospective study from September 2016 to February 2019, 16 patients with final diagnosis of high perianal fistula were prepared for perianal fistula management using autologous PRP at the Surgery Department in Zagazig University. All patients were appropriately discussed, and their consent was obtained.

Inclusion criteria were: 1) to have diagnosis of recurrent or complex perianal fistula; 2) aged 18-70 years.

Exclusion criteria were: 1) simple fistulas requiring fistulotomy; 2) age < 18, > 70 years; 3) patients unfit for surgery; 4) current pregnancy; 5) patients with thrombocytopenia; 6) patients on steroid therapy; 7) patients with perianal fistula secondary to Crohn's disease; 8) perianal active infection.

All patients were clinically examined by taking history and digital rectal examination, and preoperatively investigated by complete blood count (CBC), PT, PTT, INR, liver and kidney functions, hepatitis B, C viral markers and MRI fistulogram.

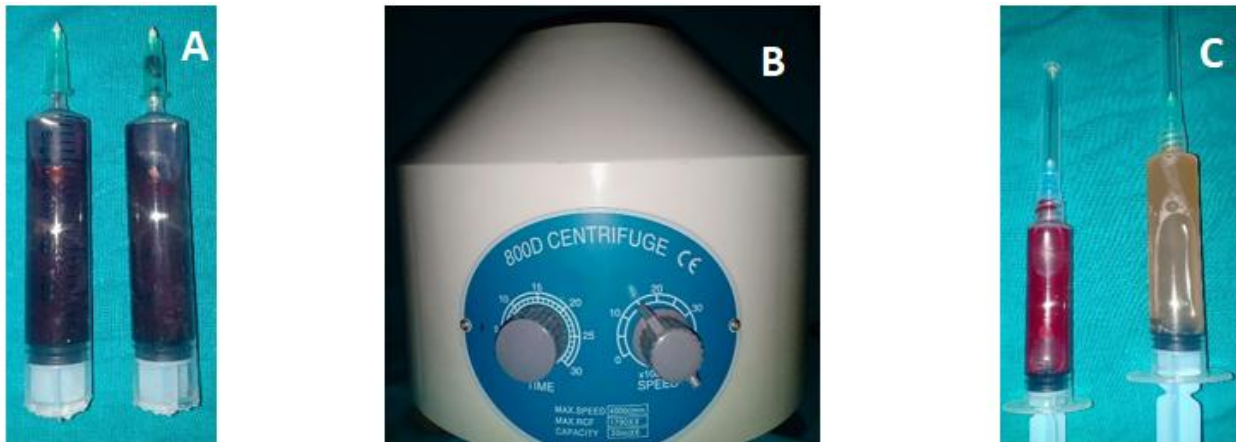
All patients received preoperative oral metronidazole 500 mg tid for 5 days and did single enema in the morning of the day surgery.

### Procedure:

#### Preparation of platelet rich plasma:

Precautions before the procedure: the patient should stop any non-steroidal anti-inflammatory drugs, steroids, anticoagulants and antiplatelets at least 10 days preoperatively as these drugs interfere with platelet functions.

20 ml blood was sampled from the patient into two 10 ml syringes containing anticoagulant, Na citrate. The syringes were prepared to be used in the centrifuge by cutting the plunger and fingers grip (fig. 1A). We adopted double spin technique for PRP preparation using (800D centrifuge<sup>®</sup>) (fig. 1B). The first spin was at speed 1000 rotation per minute (RPM) for 10 mints, and the second one was at speed 3000 RPM for another 10 minutes. The initial centrifugation is to separate red blood cells followed by a second centrifugation to concentrate platelets in the smallest final plasma volume and we discard the superficial platelet poor plasma (fig. 1C). Platelet count was measured in the blood sampled from the patient and in the PRP to confirm the success of the process of the separation of the PRP then activated by adding calcium gluconate 10%; every 9 ml were activated by 1ml calcium gluconate.



**Fig 1:-**Two syringes 10 ml containing whole blood after being prepared to fit into the centrifuge (A). 800D centrifuge<sup>®</sup> (B). Two syringes 5ml syringe on the left aontaing PRP and 10ml syringe on the right containing pallete poor plasma (C).

**The operation:**

The surgical procedure was performed under spinal anesthesia in lithotomy position. A complete anorectal examination was performed to identify the fistula's external opening, tract and internal opening.

Identification of the internal opening was also carried out by irrigating of the fistulous tract using methylene blue through the external opening and noticing the coming out of the dye from the internal opening while an anoscope was inserted.

Probing and curettage of the fistulous tract was done using a piece of gauze between two strings (fig. 2A) and different sizes of curettes, then irrigation of the fistulous tract by saline and hydrogen peroxide to clear the tract from debris and insure hemostasis of the inside of the tract after curettage.

The fistulous tract was filled with activated autologous platelet rich plasma which is delivered by syringe (fig. 2B) and left to form gel, and the tissue around the tract was infiltrated by activated PRP. Finally, the internal opening is closed by simple sutures using polyglactin 3-0.



**Fig 2:-**curettage of the fistula tract using piece of gauze between two strings (A). Injection of the fistulous tract with activated PRP (B).

**follow up:**

the patients were not allowed to receive NSAID, antiplatelets or steroids in the postoperative period. The only allowed analgesics are oral paracetamol and/or pethidine.

Follow up is performed at the outpatient clinic every week for 2 months then monthly for 12 months. During each visit, the patients under went clinical assessment for anal pain, incontinence, discharge and/or infection. The procedure was considered successful if the patient became asymptomatic (no pain with closed external opening). Failure of the surgical procedure was considered when pain, suppuration and/or external opening persisted after 6 months.

**Results:-**

from September 2016 to February 2019, we had 16 patients with a diagnosis of high perianal fistula, 9 males and 7 females (fig. 3) with mean age 32 years (table 1) and follow-up period for 12 months. The most common presentations were pain, discharge, recurrent perianal infection. None of our patients had thrombocytopenia with average platelet count  $234.38 \times 10^3 / \text{mm}^3$ . Platelet count in the PRP was doubled at least with the mean platelet count in prepared PRP about  $608.69 \times 10^3 / \text{mm}^3$ (table 2).

We considered recurrence if the patient had persistent symptoms for 6 months postoperatively (pain, discharge, persistent external fistulous opening or abscess formation). We had 14 patients of complete healing of the external opening of them two patients (12.5%) developed abscesses, one at two months postoperatively and the other at 4 months postoperatively which necessitated surgical drainage. Another two patients (12.5%) had healing failure and persistent external opening for more than six months (table 4).

According to our study the duration of healing was  $24.86 \pm 5.39$  days (table 5) in 14 patients who showed healing while the remaining two patients showed persistent external opening.

We had a clinical success rate of 75% (12 patients out of 16 were completely healed with no recurrence throughout the follow up period). Only 4 patients (25%) had recurrence in the form of persistent external opening or develop an abscess (table 6).

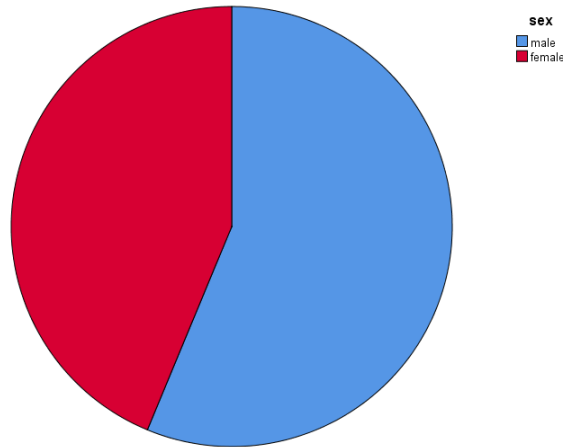


Fig 3:-Pie graph shows sex distribution among patients.

Table 1:-shows age distribution

	N	Minimum	Maximum	Mean	Std. Deviation
age	16	19	52	32.94	9.341

Table 2:-shows platelet counts in the whole blood and in PRP.

	Mean	N	Std. Deviation	Std. Error Mean
plat1	234.38	16	40.779	10.195
plat2	608.69	16	40.442	10.111

Plat1: platelet count in the whole blood

Plat2: platelets count in PRP

Table 3:-shows the correlation between the platelets count in the whole blood and PRP

	N	Correlation	Sig.
plat1 & plat2	16	.598	.014

Table 4:-shows the frequencies of healing of the fistula and the recurrence in the form of suppuration or persistent external opening

	Frequency	Percent	Valid Percent
Healed and no abscess formation	12	75.0	75.0
persistent external opening	2	12.5	12.5
Abscess formation after healing	2	12.5	12.5
Total	16	100.0	100.0

Table 5:-shows the duration of healing in days

	N	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Duration of healing	14	15	36	24.86	1.441	5.390

Table 6:-shows the frequencies of healing and recurrence

	Frequency	Percent	Valid Percent
no recurrence	12	75.0	75.0
recurrent fistula	4	25.0	25.0
Total	16	100.0	100.0

**Discussion:-**

Fistula surgery remains a matter for colorectal surgeons and an exhausting process for patients with impaired quality of life. Simple fistula is treated usually by fistulotomy, that provides healing for about 90% of patients with low risk of incontinence.<sup>6</sup> The main problem lies in the treatment of complex perianal fistula, as fistulotomy represents an unacceptable risk of incontinence in these patients.<sup>7</sup>

Platelet  $\alpha$ -granules contain mitogenic and chemotactic growth factors (GF) and associated healing molecules in an inactive form, important in wound healing, such as platelet-derived growth factor (PDGF), transforming growth factors  $\beta$ 1,  $\beta$ 2,  $\beta$ 3, platelet-derived angiogenesis factor, insulin-like growth factor 1, platelet factor 4 (PF-4), epidermal growth factor, epithelial cell growth factor, vascular endothelial cell growth factor (VEGF), basic fibroblast growth factor and others cytokines. During normal wound healing, trapped platelets become activated and degranulate, resulting in releasing of  $\alpha$ -granule content. The secreted growth factors immediately bind to the external surface of cell membranes in the wound via transmembrane receptors in mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells.<sup>8,9</sup>

This work aimed to evaluate the effect of the use PRP in when it is used as adjunct in the treatment of high perianal fistula

In our study, we had 16 patients in the middle age group with mean age  $32.94 \pm 9.34$ . nine males and 7 females were included

The gold standard technique for the treatment of complex fistula is likely the advancement flap. In most series recurrence rates range from 0% to 33%.<sup>10</sup>

*Sentovich* in 2003, showed that single treatment with fibrin glue achieved 60 percent fistulas closure. Retreatment with fibrin glue brought the successful number of fistula tracts closed to 69 percent. Bowel function and fecal incontinence were not altered by the fibrin-glue treatment. Late recurrences (>6 months) occurred in 6 percent patients<sup>11</sup>.

In our study, we used autologous platelet rich plasma as adjunct in the treatment of high perianal fistula and obtained cure rates of 75%. As regard incontinence, our study we had no case develop fecal incontinence.

**Conclusion:-**

Platelet rich plasma is promising in the treatment of high perianal fistula without affection of fecal continence.

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