

ORIGINAL RESEARCH

Evaluation of utility of autologous PRP in the treatment of anal fistula

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Received: 19 October, 2023

Accepted: 02 November, 2023

ABSTRACT

Aim: To assess the effectiveness of PRP in the treatment of anal fistula

Method and material: Total 100 patients with anal fistula were selected and divided into 2 groups. In patients with Group 1 PRP was administered topically just immediately after fistulous tracts excision (study group) while in group 2 PRP therapy was not given after fistulectomy (control group). Patients were evaluated clinically for anal pain, incontinence, discharge, and/or infection at each visit. If the patient became asymptomatic (no pain with a closed external opening), the procedure was regarded successful. After six months, the surgical procedure was deemed unsuccessful if pain, suppuration, or external opening persisted.

Results: It was observed that after 10 days in group 1 only one (2%) patients had infection while in control group 6 (12%) patients had infection ($p=0.05$); 4 (8%) patients in study groups while in control group 5 (10%) patients had pain ($p=0.72$) (table 1). After 3 months no recurrence was seen in study group while the recurrence rate was 12% after 3 months in control group ($p<0.05$). While after 6 months the recurrence rate was 4% and 2% in study and control group respectively ($p>0.05$). The time taken by study group was significantly less than taken by control group ($p<0.001$).

Conclusion: In present study PRP showed favorable safety and was seen to be effective in the treatment of anal fistula on combining with the fistulectomy.

Keywords: Prp anal fistula and fistulectomy

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INTRODUCTION

Anal fistula is the result of abscess ulceration or incision drainage around the anus and rectum, manifesting as the formation of abnormal channels connecting the anal canal and rectum with the epidermis surrounding the anus. A fistula-in-ano is an epithelial-lined tract that connects the anal canal to the perianal epidermis. Fistula classification is determined in relation to the anal sphincters.¹ It is believed that simple anal fistulas are caused by a glandular obstruction that leads to an anorectal abscess and, ultimately, a fistula. A simple fistula is characterized by a single tract, subcutaneous tract, and involvement of less than 30% of the external sphincter. Simple fistulas are the simplest to treat and have the lowest rates of recurrence

and complications.¹ Complex fistulas include those that involve more than 30 percent of the external sphincter, those with multiple tracts, recurrent fistulas, and those associated with other predisposing factors, such as Crohn disease and radiation therapy.² Due to the extensive involvement of the external sphincter, a conventional fistulotomy is contraindicated due to the risk of postoperative fecal incontinence. To preserve sphincter function, it is preferred to perform a complex repair or repairs in stages.³ The majority of patients with anal fistula are between 30 and 40 years old, and men are more likely to develop this condition than women.⁴ In addition to having a severe impact on the quality of life of patients, anal fistula has a negative effect on the mental health of patients, who frequently exhibit

depressive or anxious symptoms. In most cases, anal fistula cannot be treated without medical intervention. Surgical intervention is the primary treatment for anal fistula. The optimal treatment criterion is the eradication of the infected lesion, the promotion of adequate drainage, and the closure of the fistula while minimizing injury to the anal sphincter⁵. Treatment options for fistula include fistulotomy, fistulectomy (with or without sphincteroplasty), endorectal advancement flap, anocutaneous advancement flap, fistula plug, fibrin adhesive injection, Fistula-tract Laser Closure (FiLaC) and (LIFT)^{6,7}. Methods based on blood derivatives are among the new treatment options in this field. Platelet-Rich Plasma (PRP) is one of the most important blood derivatives of this bioactive substance, containing over 20 growth factors and other protein molecules such as binding molecules and chemokines involved in processes such as proliferation, differentiation, and cell regeneration⁸. PRP's potentials, such as its therapeutic efficacy, are contingent on the quantity of growth factors it contains. With the addition of certain activating agents, such as thrombin and calcium chloride, which induce and stimulate the growth factor release from the granules Alpha's in PRP, the platelets in PRP begin to secrete growth factors⁹. Platelets present in PRP increase the concentration of growth factors in the environment by secreting these factors. In cells such as endothelial cells and fibroblast cells, growth factors function as a mitogen cell division stimulant, initiating angiogenesis processes as well as differentiation and proliferation of fibroblasts¹⁰. Furthermore, growth factors govern collagen synthesis in addition to promoting cell proliferation and differentiation¹¹. During the first few hours following activation, more than 95% of the synthesized growth factors are released explosively. Due to the effects of platelet-enriched plasma on accelerating the healing of soft tissue injuries and the fact that it is autologous (prepared from the patient's own blood), the treatment is less expensive and saves the surgeon and patient time¹². Due to the complexities of therapeutic methods for anal fistula and the paucity of research on alternative therapies utilizing new technologies, the current study investigated the use of autologous PRP in the treatment of anal fistula.

MATERIAL AND METHODS

This was a comparative -prospective study performed on 100 patients with anal fistula in north India for the period of 3 years after approval by the Ethics Committee. The study included patients aged between 18 and 80 years with diagnosis of low intersphincteric fistula and high fistula determined by MRI pelvis. Exclusion criteria were patients with ASA score 4, inflammatory bowel disease, fistula with multiple tracts or active perianal sepsis, lower and middle

intrasphincteric fistula, rectal polyps as well as pregnant and lactating patients. 100 patients were divided into 2 groups. Group 1: PRP was administered topically just immediately after fistulous tracts excision (study group). Group 2: patients who were not given therapy after fistulectomy (control group) All patients were examined clinically with a history and digital rectal examination, and preoperatively with a complete blood count (CBC), PT, PTT, INR, liver and kidney functions, hepatitis B and C viral markers, and an MRI fistulogram. All patients received oral metronidazole 500 mg bid for 5 days prior to surgery and underwent a single enema on the day of surgery.

Preparation of PRP: After obtaining the patient's consent, the first stage was the preparation of PRP. On the day of treatment, 30 cc of the patient's whole blood was drawn for autologous PRP preparation. Blood coagulation and platelet granule secretion were regulated by the addition of an anticoagulant such as dextrose citrate. The blood sample was centrifuged (850G) at a constant speed to separate it into three distinct strata using a two-stage centrifuge or the double spin method. The bottom layer consisted of red blood cells, the middle layer of white blood cells, and the top layer of plasma-soluble platelets. In the second (1200G) round of centrifugation, the upper and intermediate layers were separated and centrifuged. The solution obtained contained platelet pellets. In addition, the pellet was redissolved in plasma to attain a volume of 12 cc, with the final volume dependent on the treatment volume. Prior to the operation, the patient was recommended to use four Bisacodyl suppositories the day before surgery. The surgical procedure was executed in prone position under spinal anesthesia. A thorough anorectal examination was performed to determine the external opening, tract, and internal opening of the fistula. The internal opening was also identified by irrigating the fistulous tract with hydrogen peroxide through the external opening and observing the bubbles coming out of the internal orifice while inserting an anoscope. Probing and excision of the fistulous tract were performed using monopolar cautery followed by irrigation of the fistulous tract with saline and hydrogen peroxide to clear the tract of debris and ensure hemostasis. The internal orifice was closed with 3-0 R B suture made of vicryl. The tract was then injected with PRP, and the tract was subsequently filled with PRP material, incision was closed with nylon 2 -0 CB interrupted sutures.

Follow up: In the postoperative period, patients received topical NSAIDs. At the ambulatory clinic, follow-up is performed weekly for two months, then monthly for 12 months. Patients were evaluated clinically for anal pain, incontinence, discharge, and/or

infection at each visit. If the patient became asymptomatic (no pain with a closed external opening), the procedure was regarded successful. After six months, the surgical procedure was deemed unsuccessful if pain, suppuration, or external opening persisted.

Post operative instructions

- Patients were put on clear liquid for 2 days followed by semisolid diet for 2 days and normal diet after that.
- Post op medications.
- Ambulation of the patients was done one day after post operatively.
- Patient was advices metronidazole suppository for twice a day for 5 days, diclofenac suppository for thrice a day for 5 days
- No sitz bath was given, hot fomentation and cleaning was done with betadine ointment.
- Around 2-to-3-liter liquid was advised.

RESULTS

The study consisted of 100 patients of which 69% were males while 31% of the patients were females. The mean age of the study population was 48.38±8.18 years.

on comparing both groups both the groups were comparable with respect to age and sex of the patients and no significant differences was observed among both the groups.(Table 1)

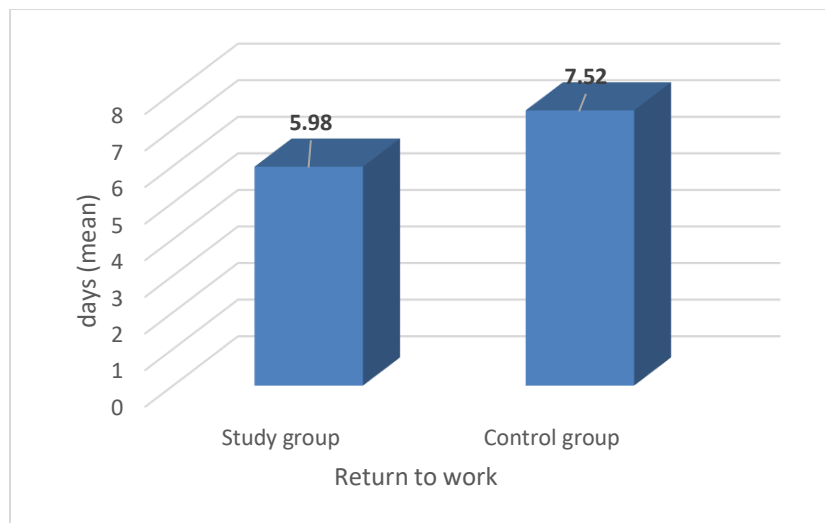
It was observed that after 10 days in patients who were given PRP only 1(2%) patients had infection while in control group 6(12%) patients had infection. This association was statistically significant(p=0.05). (Table 1) After 10 days the pain was present in 4(8%) patients in study groups while in control group 5(10%) patients had pain. This association was not significant.(p=.72)(table 1).It was observed that the after 3 month in study group there was no recurrence while the recurrence rate was 12% after 3 month in control group. This association was statistically significant(p<0.05). While after 6 months the recurrence rate was 4% in study group and 2% in control group. This association was statistically non significant.Figure 1: shows the mean comparison between both groups in relation to time taken to return to normal activity. The time taken to return to work in study group was 5.98±1.05 while for control group it was 7.52±1.23 days. The time taken by study group was significantly less then taken by control group (p<0.001).

Variables		Study group		Control group		total		p-value
		Mean	SD	Mean	SD	Mean	SD	
Age	(mean/SD)	49.88	9.07	46.88	6.968	48.38	8.18	0.06
		n	%	n	%	n	%	
Sex	Male	35	70.00%	34	68.00%	69	69.00%	0.829
	Female	15	30.00%	16	32.00%	31	31.00%	
Infection	Absent	49	98.00%	44	88.00%	93	93.00%	0.05
	Present	1	2.00%	6	12.00%	7	7.00%	
Pain	Absent	46	92.00%	45	90.00%	91	91.00%	0.72
	Present	4	8.00%	5	10.00%	9	9.00%	

Table:1 shows the comparison of various variables assessed between the two groups.

Recurrence		Study group		Control group		total		p-value
		Mean	SD	Mean	SD	Mean	SD	
		n	%	n	%	n	%	
After 3 Months	Absent	50	100.00%	44	88.00%	94	94.00%	0.01
	Present	0	0.00%	6	12.00%	6	6.00%	
After 6 Months	Absent	48	96.0%	49	98.0%	97	97.0%	0.55
	Present	2	4.0%	1	2.0%	3	3.0%	

Table: 2 shows the recurrence rate of the two groups at 3 and 6 months.



DISCUSSION

Platelets play a crucial role in hemostasis, tissue regeneration and host defense. Based on these settings, platelet-rich plasma (PRP) and its derivatives are therapeutically used to promote wound healing in several scenarios.¹³ PRP is an autologous product derived from whole blood and therefore with no risk of transmitting infections, allergies, and rejections. Various cytokines freed from platelets granularities such as PDGF, TGF-B, FGF, VEGF, and IGF are responsible for creating a fibrin clot which works as a scaffolding for granulocytes, endothelial cells, and fibroblasts with following formation of well vascularized fresh granulation tissue, and finally fistula healing. The platelet concentrate was applied into the tissues surrounding fistulous tract due to its fluid consistency, slightly larger than plasma. Hence, mechanical compression of internal orifice as well as fistulous canal by edematous tissues soaked with PRP is one mode of action. On the other hand, it promotes fistula healing due to a high concentration of platelet derived growth factors^{9,14}. A variety of approaches have been proposed for the treatment of complex perianal fistulas, which reflects the fact that no method has yet proven complete satisfactory. Conventional surgery for anal fistula often provokes continence disorders, and so much consideration has been given to new procedures aimed at achieving significant preservation of the sphincter apparatus. In present study we evaluated the use of autologous PRP in the treatment of anal fistula. We found that patients who were given PRP had less infections post surgically and the rate of recurrence was significantly low in patients who were given PRP. Also the patients who were given PRP returned to their routine activity early then who were not given PRP. De La Portilla et al. conducted a randomized, double-blind clinical trial in 2019 to assess the therapeutic effects of employing autologous PRP vs. fibrin glue in the

treatment of cryptoglandular anal fistula. At one week, three, six, and twelve months after surgery, patients had clinical and endoscopic evaluation. The rate of fistula recovery—complete, partial, or no improvement—was the primary goal of this study. Secondary outcomes included fistula recurrence, fecal status, quality of life (QoL), and pain. Out of the 56 individuals participated in the research, 32 received PRP treatments and 24 received fibrin glue treatments. The PRP group showed a 71% overall improvement rate, while the fibrin glue group showed a 58.3% improvement rate. Complete and partial healing rates were 48.4% and 22.6% in the PRP group and 41.7% and 16.7% in the fibrin glue group, respectively. The PRP group had a significantly improved quality of life and a lower incidence of pain. The fecal state showed no negative effects, and all problems were minor¹⁵. Madbouly et al. conducted a prospective experiment in 2021 to investigate PRP's impact on the management of transsphincteric fistula. Patients having a transsphincteric fistula involving more than 50% of the anal sphincter were included in the current investigation. They were divided into two groups, one receiving PRP treatment and the other not, for Ligation of Intersphincteric Fistula Tract (LIFT). There were 49 patients in each group. The primary results of this study were the total closure of the fistula and the amount of time required for recovery. There was a substantial difference between the two groups, with 42 patients in the PRP group and 32 patients in the group without PRP showing full repair of the fistula. The mean postoperative recovery time was significantly reduced in the PRP group (15.7 days) as compared to the control group (21.6 days). Three patients in the group without PRP and four patients in the PRP group showed recurrence after a year. In the PRP group, pain was less severe on days 1 and 7 following surgery, and so did the QoL rate one month later¹⁶. In 2016, Moreno-Serrano et al. looked into how PRP affected the healing

of complex anal fistulas. The research was conducted between 2011 and 2013. Results covered fistula healing, treatment problems, and quality of life. Two patients have been excluded from the study out of the 23 individuals (12 men and 11 women) who were included and followed up for at least 12 months. The remaining 21 patients, 17 of whom had low fistulas. The therapeutic success rate in this study was 62%. After treatment, no patient had incontinence. With the exception of two patients, all patients' QoL improved¹⁷. Orban et al. conducted a study in 2019 to evaluate PRP's effectiveness in treating high anal fistula. From 2016 to 2019, they conducted a prospective research on fistula patients, including nine men and seven women. The recovery rate was 75%, meaning that 12 patients made a full recovery without experiencing a recurrence, while two patients experienced postoperative abscess and two patients had continuous discharge from the surgical site¹⁸.

CONCLUSION

The results of above mentioned study were in accordance to the present study. In present study PRP showed favorable safety and was seen to be effective in the treatment of anal fistula on combining with the fistulectomy. Other than this as this is an autologous product, its use precludes rejection risk and minimizes infection risk. Notwithstanding this, further properly designed, comparative studies (possibly multicenter studies in order to achieve an adequate number of patients) are warranted to obtain solid conclusions.

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