

Autologous Bone Marrow Cell Therapy in Complex Fistula in Ano**Prangya Lochan Chand¹, Biswajeet Pusty², Jyoti Ranjan Behera³, Rupashree Behera⁴**¹Assistant Professor, Department of General Surgery, SCB Medical College and Hospital, Cuttack, Odisha, India, 753001²Assistant Professor, Department of General Surgery, SCB Medical College and Hospital, Cuttack, Odisha, India, 753001³Assistant Professor, Department of Pediatrics, MKCG Medical College and Hospital, Berhampur, Ganjam, Odisha, India, 760004⁴Assistant Professor, Department of Pediatrics, SCB & S.V.P.P.G.I.P, Medical College and Hospital, Cuttack, Odisha, India, 753002

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Abstract:

Introduction: Fistula-in-ano, a highly frequent anorectal problem, is nearly as prevalent as perianal-perirectal suppuration. Because of the disease's private location, which raises morbidity, the shy, timid patient avoids the surgeon. Due to the chronic nature of the illness and its annoying symptoms, which include soiling, itching, and recurrent suppuration, a normally healthy and energetic individual becomes an economic burden, retreats from social engagements, and loses confidence. The majority of patients are shy, and it is difficult to assess the sickness because they refuse to undergo proctologic and rectal tests. Over the previous few decades, a great deal of progress has been made in our understanding of the anatomy of the rectum and anal canal, as well as the mechanics of continence.

Material and Method: The study comprised all patients who were Hospitalised to VIMSAR, Burla's general surgery department between October 2016 and September 2018 and who satisfied the inclusion and exclusion criteria.

Result: Compared to the control group, the research group's post-operative pain was less severe. Patients in the control group did not need an analgesic for wound pain after post-operative day 7, but patients in the study group did not need one after post-operative day 3. Of the 25 patients in the trial, 2 (8%) had post-operative bleeding, while 6 (24%) had control (P value 0.02). Recurrence was seen in 6 (24%) of the 25 patients in the control group, but not in the research group, with a P value (P value 0.004) <0.05.

Conclusion: In order to reduce complications such as bleeding, incontinence, recurrence, and post-operative discomfort at the wound site, as well as to improve traditional wound healing, bone marrow cell treatment is being used for difficult fistula-in-ano. This is demonstrated by the grade of granulation tissue observed following biopsy using an HPE investigation.

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Introduction

A very common anorectal issue is fistula-in-ano, whose prevalence almost exactly matches that of perianal-perirectal suppuration. The disease's unmentionable site increases morbidity, which makes the timid, bashful patient avoid the surgeon.

A person who is generally healthy and active becomes an economic burden, withdraws from social interactions, and lacks confidence due to the chronic nature of the condition and its bothersome symptoms, which include soiling, itching, and recurring suppuration. The majority of patients are shy, and their refusal to undergo rectal and proctologic examinations makes it challenging to evaluate the illness. Understanding the architecture

of the rectum and anal canal, as well as the mechanics of continence, has advanced significantly during the past several decades.

The rectum, allowing the physician to treat the condition drastically without making the patient incontinent. The Latin term for a reed, pipe, or flute is fistula-in-ano. It is a persistent granulating track that joins two epithelial-lined surfaces: the internal hole in the altered skin or mucosa of the rectum, anal canal, or above, and the external opening in the skin of the perianal area. There are instances when this course is more difficult and has several exterior entrances. The track wall is made up of a thick layer of fibrous tissue, which is a fibrous tube

with a layer of granulation tissue lined on the inside. The lower risk of recurrence, shorter period of uneventful convalescence, and decreased morbidity have not been attributed to better surgical technique or treatment. There has been a notable overall decrease in near and remote problems and sequelae as a result of primary closure and/or primary grafting combined with adjuvant antibiotic sterilisation of the stomach. It is widely acknowledged that surgery is the only option for treating ano fistula. Anal continence impairment and subsequent recurrence are such severe consequences that the operations for them have a terrible reputation. These details are crucial to highlight the fact that surgical management of anal fistulas is frequently complicated and requires both bravery and care.

On the other hand, a complicated perianal fistula is a fistula that has several tracts, a horseshoe-shaped tract, suprasphincteric extension, or a recurring fistula. It can also be connected to other conditions including TB, ulcerative colitis, and Crohn's disease. If a thorough surgical debridement is carried out, there is a significant chance of faecal incontinence and a high chance of recurrence with surgical therapy of this kind of fistula.

One innovative way to treat complicated fistula in ano following fistulectomy and avoid its recurrence is the use of autologous bone marrow cell treatment. Through the actions of growth factors, cytokines, immunomodulators, and anti-inflammatory, the cell promotes healing. They cause the production of high-quality granulation tissue by activating fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), granulocyte macrophage colony stimulating factors (GM-CSF), and epidermal growth factor (EGF).

Materials and Methods

All patients who met the inclusion and exclusion criteria and were admitted to the general surgery department of VIMSAR, Burla between October 2016 and September 2018 were included in the research.

Inclusion criteria

- A case of complicated fistula in an individual with several tracts, such as the horseshoe tract with suprasphincteric extension or recurrent fistula, and fistula linked to ulcerative colitis, Crohn's disease, etc.
- Ages 20 to 60 encompass both genders.

Exclusion criteria

A straightforward fistula in an individual with co-morbid conditions such as diabetes mellitus and cardiovascular disease, subcutaneous tract or submucous fistula, chemotherapy-treated patient refusing surgery, etc.

The study was conducted prior to patient informed consent and permission from the institutional ethics committee.

At VIMSAR, Burla, Odisha, India, 50 patients with complicated fistula-in-ano underwent fistulectomy from October 2016 to September 2018. Of them, 25 patients were retained in the study group and the remaining 25 in the control group. All patients underwent a fistulectomy. In the experimental group, bone marrow cells were infiltrated to the ulcer floor and then removed via fistulectomy; however, this did not occur in the control group. Following surgery, the patients underwent the following observations. The results were examined, showing both early and late complications. Pain measured on a 10-point metric. On days 1, 3, 5, and 7, there was a severe purulent discharge from the incision. Which group's postoperative analgesic was needed up to which day?

A biopsy was collected from the ulcer's floor on day five, and it was sent to HPE to examine the granulation tissue quality, including neovascularization, macrophages, fibroblasts, and necrosis, according to HPF. Patients who experience delayed complications, such as recurrences, are urged to follow up monthly for the first year, every three months for the second year, and every sixth month for the third.

Clinical observations will be made of the patient at the wound site, perianal location, and DRE. Compared to the control group, the research group's post-operative pain was less severe. Patients in the control group did not need an analgesic for wound pain after post-operative day 7, but patients in the study group did not need one after post-operative day 3. Of the 25 patients in the trial, 2 (8%) had post-operative bleeding, while 6 (24%) had control (P value 0.02). Recurrence was seen in 6 (24%) of the 25 patients in the control group, but not in the research group, with a P value (P value 0.004) <0.05.

Of the twenty-five patients in the control group, nine (36%) have post-operative seropurulent discharge, and two (8%) in the study group. Incontinence was not seen in either group. In the study group, the average number of fibroblasts per HPF was 10.96, whereas in the control group, it was 3.04. Similarly, the study group had 13.08 macrophase per HPF, while the control group had 5.49; similarly, both study groups had 17.04 and 0.40 necrosis and neovascularization, respectively, while the control group had 5.16 and 6.4. These findings were based on a biopsy taken from the wound floor on post-operative day 5.

Result

Table 1: Post-Operative Bleeding In Both Study & Control Group

	Post-Operative Bleeding	
	Yes	No.
Case	2/25	23/25
Control	6/25	19/25

Table 2: Post-Operative Seropurulent Discharge From Both Study & Control Group.

	Post-Operative Seropurulent Discharge	
	Yes	No.
Case	2/25	23/25
Control	9/25	16/25

Table 3: Recurrences after Surgery in Both Study & Control Group

	Post-Operative Recurrence	
	Yes	No.
Case	0/25	25/25
Control	6/25	19/25

Table 4: Average Number of Fibroblast / HPF in Both Study & Control

	Fibroblast Per HPF
Case	10.96
Control	3.04

P value 0.003 (<0.05)

Table 5: Average Number of Macrophage per HPF in Both Group

	Macrophage Per HPF
Case	13.08
Control	5.44

P value 0.008 (<0.05)

Table 6: Average Number of Neovascularisation per HPF in Both Study & Control Group

	Neovascularization Per HPF
Case	17.04
Control	5.16

P value 0.002 (<0.05)

Table 7: Number of Necrosis per HPF in Both Group

	Necrosis Per HPF
Case	0.40
Control	6.40

P value 0.003 (<0.05)

Table 8: Number of Patient Who Require Analgesic in Respective Post-Operative Day in Both Study and Control Group

	Require Analgesic in Respective Post-Operative Day
Case	2.88
Control	6.52

Discussion: There is certain danger involved in the surgical treatment of this kind of fistula. If a thorough surgical debridement is carried out, there is a significant chance of faecal incontinence and recurrence in complicated perianal fistulas. Research has demonstrated that mesenchymal stem cells (MSCs) derived from bone marrow or fat can

express LEC markers (Prox-1, VEGF-C, VEGF-A). Additionally, these cells can significantly increase fibrosis in vivo when stimulated in cultured media with recombinant VEGF-C, even for short periods of time in vitro. Adult mesenchymal stem cells may therefore play a significant part in healing. Substance-P, neurokinine, and cytokines are

released as a result of inflammation, which reduces pain after surgery. Participants in the control group did not need analgesics for wound pain after surgical day 7, but study group participants did not need analgesics after postoperative day 3. Because they inhibit dendritic cell (DC) maturation [40], B and T cell proliferation and differentiation, attenuate natural killer (NK) cell killing, and support suppressive T regulatory cells, the patients may have experienced significantly less pain than the control group. Additionally, MSCs enhance the quantity of the anti-inflammatory IL-4 generated by T cells and reduce the amount of IL-10 and TNF- α released by DC cells.

Basic FGF and VEGF-A, which are potent mitogens that encourage the proliferation, migration, and differentiation of microvascular endothelial cells, are produced by MSCs. In order to support vascular stability and vasoprotection, MSC also express paracrine factors, such as adrenomedullin. Because of their potential perivascular origin, it has been suggested that MSCs have special capabilities. These functions allow MSCs to reestablish their perivascular niche after the process of vasculature remodelling is complete. Increased vascular development using MSCs generated from bone marrow.

Been proven in vitro to promote the perivascular progenitor cell growth of the long-standing vasculature. Neovascularization may thus have been aided by autologous bone marrow treatment. Histopathological analysis from the wound bed at the time of the operation demonstrated this. Day 5: The neovascularization process Mesenchymal stem cells may have a function in neovascularization; the research group's high power field is 17, whereas the control groups are 5.16. The P value of 0.003 (0.05) indicates that the relationship is extremely significant.

When an adult cutaneous wound heals, pro-inflammatory mediators including interleukin - 6 (IL-6), macrophage inflammatory protein-1 beta (MIP-1 β), monocyte chemotactic protein 1 (MCP-1), and interleukin - 1 beta (IL-1 β) are produced by the wound-recruiting inflammatory cells. These mediators have the ability to promote fibrosis and excessive extracellular matrix (ECM) deposition in addition to causing new inflammation. Additionally, inflammatory cells have the ability to create growth factors including platelet-derived growth factor (PDGF) and transforming growth factor-beta 1 (TGF- β 1), which promote fibroblast proliferation and myofibroblasts.

Conclusion

In order to reduce complications such as bleeding, incontinence, recurrence, and post-operative discomfort at the wound site, as well as to improve traditional wound healing, bone marrow cell

treatment is being used for difficult fistula-in-ano. This is demonstrated by the grade of granulation tissue observed following biopsy using an HPE investigation.

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