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ORIGINAL ARTICLE

Role of Combination of Autologous Platelet Rich Plasma and Other Modalities of Adjuvant Therapy in Wound Bed Preparation in Diabetic Foot Ulcer

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ABSTRACT

Diabetic foot ulcer is one of the common conditions faced by surgeons. A multidisciplinary team approach is mandatory for successful treatment of the condition. Its complexity is mainly due to involvement of multiple organs and systems. Hence the condition is often found to be difficult to manage. General concept is that appropriate and timely healing of wound can prevent various wound related complications like gangrene, auto amputations, septicemia, multiorgan failure, disfigurement, deformities etc. Adjuvant therapy not only increases the wound healing but also can reduce the requirement of graft/flap by reducing the size of the defect and prevent the incidence of various complications like gangrene, amputation. Through this article we present use of Autologous Platelet Rich Plasma (APRP) therapy combined with other modalities of therapy like external tissue expansion and wound closure (ETEWC) technique using hooks and rubber bands as an effective tool to enhance healing in wound bed preparation of diabetic foot.

KEYWORDS

• Autologous Platelet rich plasma • Wound bed preparation • Diabetic foot ulcer

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INTRODUCTION

Diabetes mellitus continues to be a major global health challenge, with its incidence and prevalence increasing rapidly due to urbanization, unhealthy dietary habits, obesity, and sedentary lifestyles. Current estimates from the International Diabetes Federation (IDF) indicate that India remains cohort of diabetes worldwide. According to recent guidelines from the American diabetes association and the International diabetes federation , early diagnosis, lifestyle modification, and multidisciplinary management are essential to reduce long-term complications and improve quality of life.

Diabetes is associated with several chronic complications affecting multiple organ systems. Among these complications, diabetic foot disease remains a significant cause of hospitalization and lower-limb amputation. ADA Standards of Care emphasize regular foot screening and preventive care to reduce ulcer formation and disability.

Furthermore, diabetes is recognized as a leading cause of Charcot neuroarthropathy, peripheral neuropathy, chronic kidney disease, retinopathy, and cardiovascular disease. Recent guidelines recommend aggressive management of glycemic control, blood pressure, lipid abnormalities, and obesity to minimize both microvascular and macrovascular complications.

Burden of Diabetes-Related Complications

Diabetes and its associated complications contribute substantially to global morbidity, mortality, and healthcare expenditure. These complications are broadly categorized into microvascular complications, such as neuropathy, nephropathy, and retinopathy, and macrovascular complications, including coronary artery disease (CAD), stroke, and peripheral arterial disease (PAD).

Peripheral arterial disease and diabetic neuropathy are also common among diabetic patients and are major contributors to diabetic foot ulcers and amputations. Current guidelines emphasize annual foot examination, early vascular assessment, patient education, and appropriate footwear as important preventive strategies.

Etiology of Diabetic Foot Ulcer

DFU can be classified as Neuropathic, Ischemic, or Neuroischemic depending on the involvement of nervous system, vascular system or both, respectively.[13]

Concept of Adjuvant Therapy

Involvement of multiple systems, complexity of the disease, less awareness towards symptoms of foot at risk and delayed presentation contributes to the severity of the disease and hence management becomes a challenging task. Patients who present late are usually associated with co morbidities and are often unfit for major surgery and requires systematic approach towards both patient and wound . Adjuvant therapy plays an important role in such patients as an adjunct for wound bed preparation (WBP). While the patient is undergoing work up and primary pathology is being normalized, adjuvant therapy improves wound healing, prevents progression or wound complications and makes the wound fit for surgical procedure. Adjuvant therapy should be easy to implicate so that it can be used by both medical and surgical staff to enhance the healing process by the time patient is being prepared for anesthesia and surgery.

In our Institute we used Autologous Platelet Rich Plasma (APRP) as an adjuvant therapy for preparing the wound bed and other modalities like external tissue expansion and wound closure (ETEWC) technique using hooks and rubber bands. Through this article we present a series of 12 patients of diabetic foot, for whom APRP was used for wound bed preparation and all wounds showed satisfactory outcome in a significantly short duration without major complications.

METHODOLOGY

This study was conducted in the Department of Plastic Surgery, JIPMER, Pondicherry, India. This is a retrospective study done during the period of March 2024 to march 2026. Twelve cases of diabetic foot were analyzed in whom APRP was used as adjunct for management of diabetic foot ulcer (Table 1). All patients and wounds were examined systematically; associated co morbidities were detected and managed according to standard

protocol. Ulcer was categorized (neuropathic / ischemic / neuroischemic), and wound was graded according to Wagner's grading system. Thorough limb examination was performed.[14]

Documentation of ulcer was done according to Bates-Jensen Wound Assessment Tool and digital planimetry software at the time of presentation and was repeated weekly to assess the condition of the wound[15] (Figure 1).

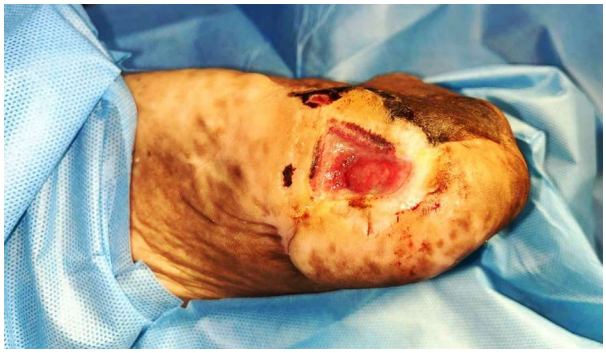

Figure 1: Wound at presentation

After thorough initial workup and documentation, wound bed preparation was started along with other treatments related to primary pathology. The TIME concept was used for systematic and stepwise wound bed preparation.[16]

Wound Bed Preparation (WBP) by "TIME" Concept

- T – Tissue management
- I – Infection and inflammation control
- M – Moisture balance
- E – Epithelial advancement

Surgical and nonsurgical debridement was done for all wounds. Debridement was done for obvious and visible necrotic dead tissue. While in absence of obvious dead tissue, the wound's bioburden and microdebris were reduced using Hydrojet technology with silver solution[17] (Figure)

Figure 2: Hydrojet debridement

To control the infection, systemic antibiotics were used according to the wound culture sensitivity and Nano Crystalline Silver (NCS) was used locally to control wound infection (figure 3).[18] Collagen sheet and granules were used as biological dressing to cover wound bed (figure 4 & 5)

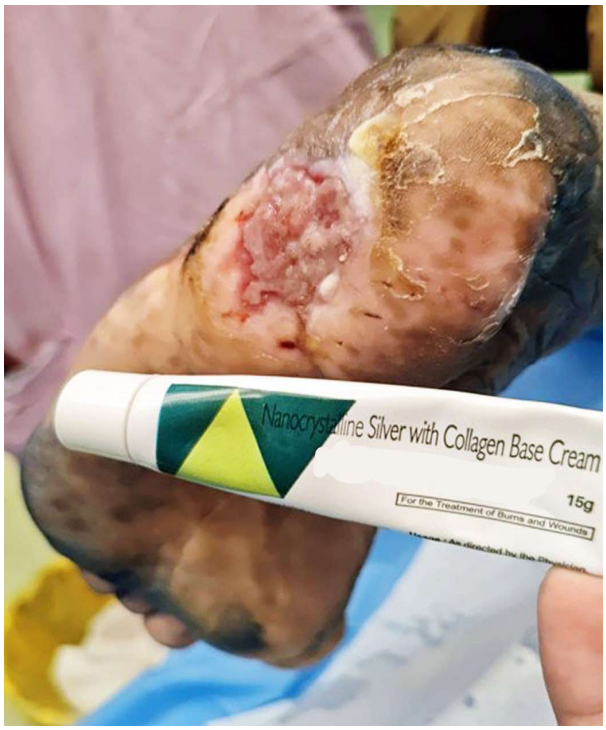

Figure 3: Nanocrystalline Silver application

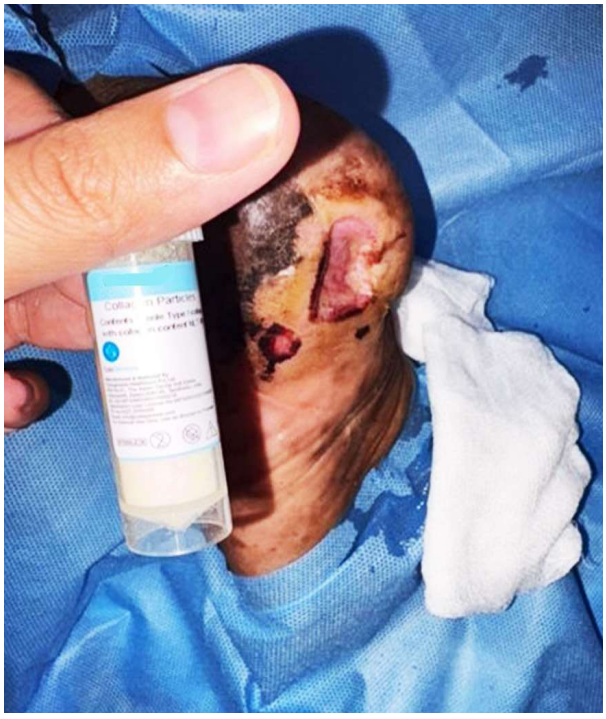

Figure 4: Collagen Granule application

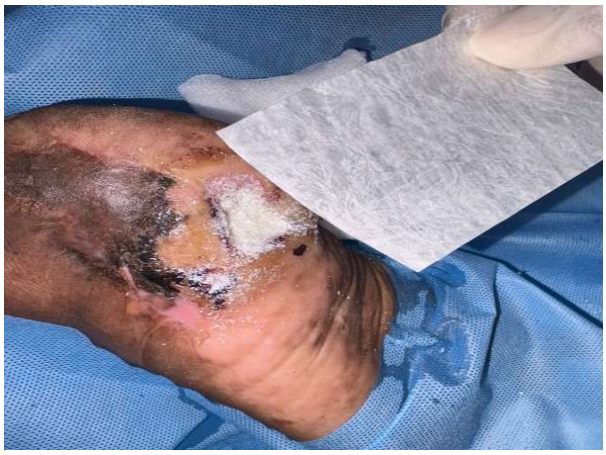

Fig 5. Collagen sheet application

Preparation of APRP

APRP was prepared using standard and validated technique described by Li W. et al[21,22] as follows:

- *Step 1:* Informed consent is taken.
- *Step 2:* Under aseptic precaution, 4.5 ml of whole blood is taken from peripheral vein (Figure 9a).
- *Step 3:* 0.5 ml of 3.2% Sodium Citrate is added in the 4.5 ml of whole blood (blood: anticoagulant = 9:1).
- *Step 4:* Two plastic tubes, one containing mixture of 4.5 ml whole blood with 0.5 ml of Sodium citrate and other containing 5 ml of normal saline (control) are taken and placed in centrifugation apparatus.
- *Step 5:* The centrifugation is done at 3000 rpm for 10 minutes (Figure 9b).
- *Step 6:* After centrifugation 3 portions are seen (Figure 9c).
- Upper portion containing plasma and platelets
- Middle portion containing White Blood Cells (WBCs) with some platelets (Buffy coat)
- Lower portion containing Red Blood Cells (RBCs)
- Middle and lower portions are discarded.
- Step 7: Upper portion is taken in a new tube for re-centrifugation.
- Step 8: Re centrifugation is done at 4000 rpm for 10 minutes.
- *Step 9:* After re-centrifugation two portions are seen.
- Upper 2/3rd portion containing platelet poor plasma
- Lower 1/3rd portion containing platelet rich plasma & erythrocyte with platelet clump (Figure 9d).
- *Step 10:* Upper 2/3rd portion is removed by syringe & discarded. Remaining lower 1/3rd portion without clump is used for APRP therapy. Usually from 4.5 ml of blood, 1 to 2 ml of APRP is obtained.

Figure 6: showing centrifuge of blood after first spin

Figure 7: Showing centrifuge after second spin

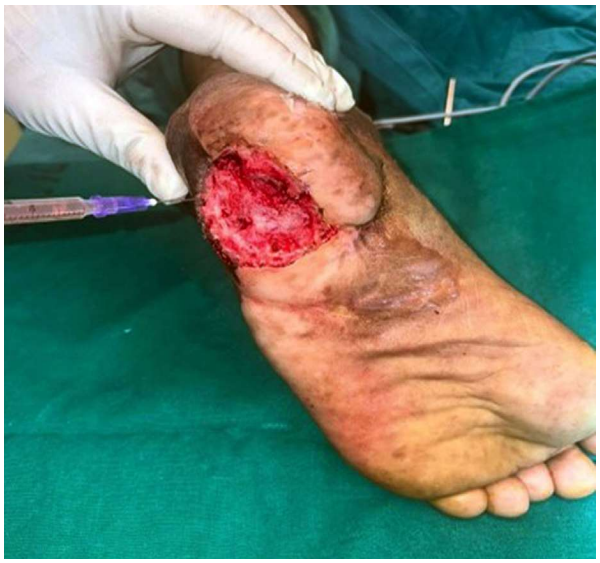

Figure 8: Application of PRP

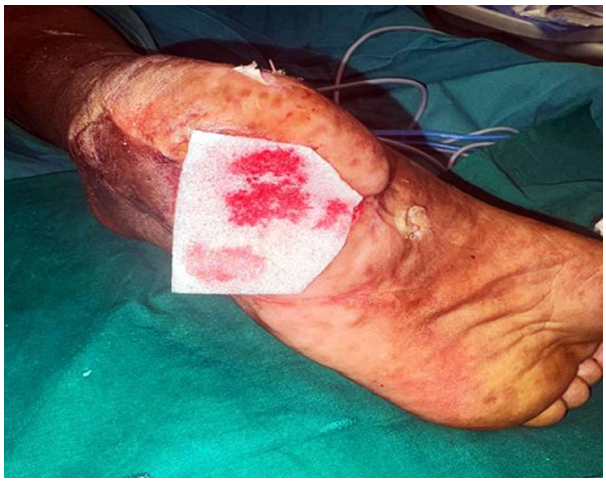

Figure 9: Biodegradable Temporizing Matrix

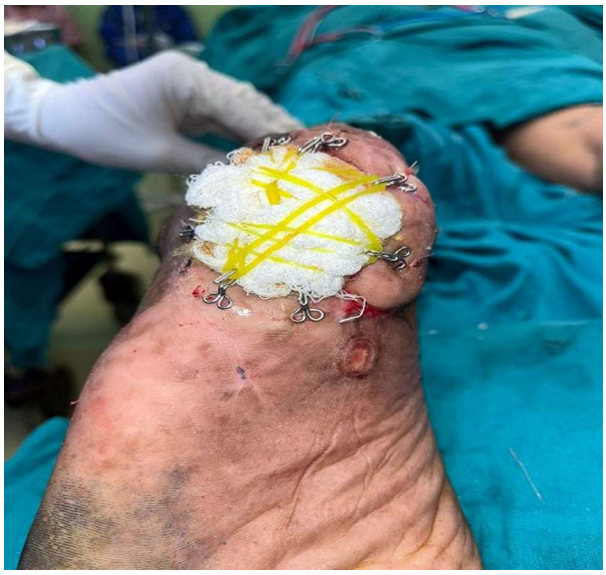

Figure 10: Showing External Tissue Expansion Wound Closure (ETEWC)

APRP was injected in the wound margins and wound was covered by biological dressings. The procedure was repeated weekly till wound healed or became fit for reconstruction. Once the wound bed preparation was completed, various clinical decisions related to repair and reconstruction were taken according to ladder of reconstruction (Figure 10).[23] Low level laser therapy was used in 2 patients and External Tissue Expansion Wound Closure (ETEWC) using rubber bands and hooks were used in 1 patients. Rehabilitative measures were continued post operatively. All the patients were followed up for 6months and no complications were noted.

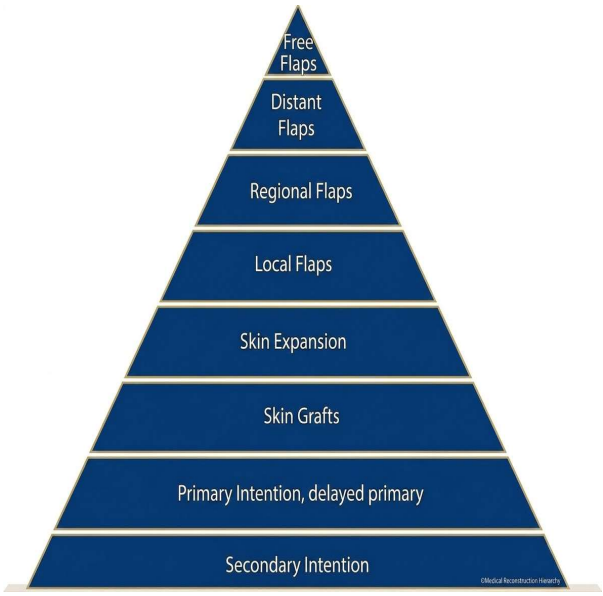

Figure 11: Reconstruction Ladder

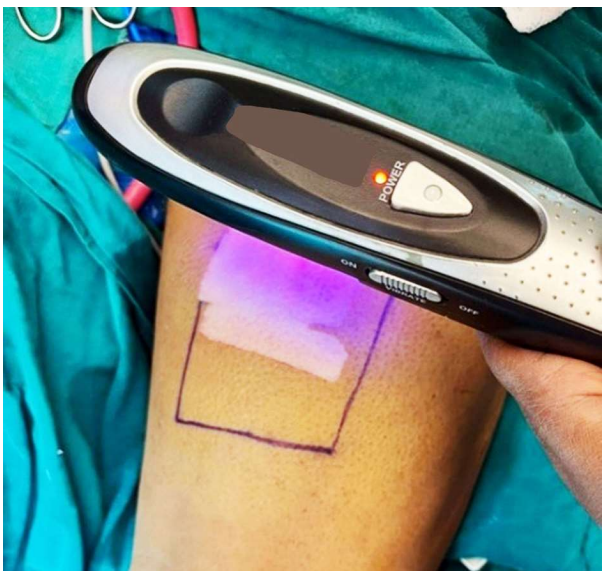

Figure 12: Low Level Laser Therapy

RESULTS

Twelve patients were included in this study. The mean age was 49.16 years with male to female ratio of 6:1. In 7 patients (58.33%) blood sugar was uncontrolled. The most common co-morbidity was anemia, in 8 patients (66.66%), followed by hypertension in 5 patients (41.6%) and 3 patients (25%) were found to have associated renal diseases. Osteomyelitis was present in 6 patients (16.6%). The most common etiology was approximately, in 7 patients (58.33%) and next most common etiology was trivial trauma, in 4 patients (33.3%). Most common site of wound was distal third of foot. Mean duration of wound was 11.75 weeks. 9 patients (75.7%) were on injectable insulin and 3 patients (25%) were on oral hypoglycemic drugs. 1 patient (8.33%) presented with associated cellulitic changes. The maximum size of wound was 20×8 cm. Mean Bates Jensen Wound Assessment Score was 28.

The most common organism grown in tissue culture was pseudomonas, in 4 cultures (33.33%). Methicillin Resistant Staphylococcus Aureus (MRSA) was recovered in 1 case (8.33%). The average duration of systemic antibiotic was 10 days to 3 weeks. The mean duration of wound bed preparation (WBP) was 3.83 weeks.

Autologous Platelet Rich Plasma (APRP) was given in all the 12 cases (100%). Autologous Lipoaspirate Therapy (ALAT) was used in 2 patients (16.66%), low level laser therapy (LLLT) was used in 2 patients (16.66%) and External Tissue Expansion Wound Closure (ETEWC) using rubber bands and hooks were used in 1 patient (8.33%). In one patient wounds was reconstructed with Split thickness Skin Graft (SSG). While in 8 patients wound was managed without any surgery by using APRP as an adjunct. Average duration of wound healing was 10 weeks. No complications were noted in 6 months follow up period (Table 1)

DISCUSSION

Wound bed preparation is an important and crucial step of management of any wound. In chronic and non healing wounds which affect multiple systems, normal process of wound healing is failed and wound either requires cover or various internal and external stimulus to heal faster. If patient, wound or both are not fit for surgery, while making the patient and wound fit some adjuvant therapy is needed for wound bed preparation. Adjuvant therapy not only enhances wound healing but also prevent progression of complications and provide suitable wound bed for reconstruction and rehabilitation.

Platelet rich plasma (PRP) is blood plasma which contains platelets in higher concentrations as compared with normal plasma. PRP is also enriched with several growth factors and cytokines that can stimulate wound healing.

The growth factors and other cytokines present in PRP include:

- Platelet derived growth factors (PDGF)
- Fibroblast growth factor
- Insulin-like growth factor 1
- Insulin-like growth factor 2
- Transforming growth factor beta (TGF ß)
- Epidermal growth factor
- Vascular endothelial growth factor
- Keratinocyte growth factor
- Interleukin 8

APRP is being used in many clinical conditions like nerve injury, androgenic alopecia, osteoarthritis, bone surgeries, oral surgeries, sports injuries etc.[24–27]

Through this article we highlight the use of APRP in diabetic foot management, which contains high burden and is associated with high morbidity and mortality.

APRP Versus other Adjuvants

Other adjuvants which can be used for wound bed preparation are lipoaspirate therapy,[28] bone marrow aspirate therapy,[29] external tissue expansion[30] etc. APRP may be considered as superior to other adjuvant. We found following advantages of APRP:

1. Relatively simple technique.
2. Less time consuming.
3. Non invasive.
4. No need for anesthesia.
5. No associated complications.
6. Useful for all wound care providers (doctors, nurses, general practitioners).

All the patients had successful wound healing without complications in follow up of 6 months. This study has limitations of small sample size, no comparative data and no statistical analysis done. A large randomized controlled study is required to give more significant result for application of APRP in diabetic foot management.

Table 1: Patient Demographic & Procedure Details

S. No.	Age / Gender	Site of Ulcer	Duration of Wound	BMI	Wound Size	Organism Isolated	Comorbidities	Osteomyelitis	WBP Duration	Antibiotic Duration	NPWT Duration	APRP	ALAT/ LLLT/ ETEWC
1	40 / M	Distal third of foot	8 weeks	30	6 × 4 cm	E. coli, S. aureus	Anemia, HTN	No	5 weeks	5 weeks	5 weeks	Yes	Nil
2	35 / M	Distal third of foot	6 weeks	36	4.5 × 7 cm	Sterile	Nil	No	4 weeks	3 weeks	4 weeks	Yes	LLLT
3	45 / M	Distal third of foot	12 weeks	24	3 × 3 cm	Pseudomonas	Anemia	No	5 weeks	4 weeks	5 weeks	Yes	LLLT
4	45 / F	Heel	16 weeks	28	2.5 × 5 cm	Sterile	Anemia	No	3 weeks	3 weeks	3 weeks	Yes	Nil
5	56 / M	Distal third of foot	21 weeks	26	3.5 × 3.5 cm	Pseudomonas	Anemia, HTN	Yes	4 weeks	12 weeks	4 weeks	Yes	ALAT
6	50 / M	Proximal and mid third of foot	18 weeks	30	18 × 8 cm	E. coli	Anemia, Hypoproteinemia	Yes	4 weeks	10 weeks	4 weeks	Yes	ALAT
7	48 / F	Distal third of foot	20 weeks	29	5 × 5 cm	MRSA	Anemia, HTN, MRD	Yes	5 weeks	10 weeks	5 weeks	Yes	No
8	55 / M	Distal third of foot	6 weeks	25	4.5 × 4 cm	S. aureus	Nil	No	3 weeks	2 weeks	3 weeks	Yes	Nil
9	56 / M	Distal third of foot	4 weeks	27	4 × 4 cm	Sterile	HTN, MRD	No	2 weeks	4 weeks	2 weeks	Yes	Nil
10	48 / M	Distal third of foot	10 weeks	25	3.5 × 3.5 cm	Pseudomonas	Anemia	No	4 weeks	3 weeks	4 weeks	Yes	Nil
11	60 / M	Heel	8 weeks	28	4 × 4 cm	Pseudomonas	Anemia, HTN, MRD	No	3 weeks	4 weeks	3 weeks	Yes	Nil
12	52 / M	Heel	12 weeks	28	4.5 × 5 cm	E. coli	Nil	No	4 weeks	3 weeks	4 weeks	Yes	ETEWC

CONCLUSION

APRP is a simple, easy and effective technique to enhance wound healing and to prevent serious complications related to delayed healing. Other various methods of adjuvant therapy are found to be effective although serial studies are required to establish their effectiveness, but are advised as disease like Diabetic foot ulcer needs a multidisciplinary approach of treatment.

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