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Platelet Rich Plasma: A New Biological Modality in Treatment of Atrophic Rhinitis: Review Article

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ABSTRACT

Background: Atrophic rhinitis is a chronic debilitating nasal disease which may be primary, or secondary to various underlying etiologies. Several methods of treatment have been previously adopted with minimal success rate. In order to achieve effective and long-standing method of treatment for this challenging pathology, this method should work mainly on reversal of the pathologic changes in nasal microanatomy.

Objective: Review article investigating the use of platelet- rich plasma in treatment of atrophic rhinitis.

Methods: We scoured scholarly journals and databases including PubMed, Google Scholar, and Science Direct for reports on Treatment of atrophic rhinitis, Platelet-rich plasma and new biological modality between November 1990 and April 2023. However, only the latest or most comprehensive study was considered. The authors also assessed the usefulness of references drawn from similar books. As a result, non-English documents have been overlooked due to a lack of resources to translate them. It was commonly recognized that scientific research did not include things like unpublished publications, oral presentations, conference abstracts, or dissertations.

Conclusion: Platelet Rich Plasma (PRP) is a plasma fraction with a very high platelet content that also contains phagocytic cells, a significant amount of fibrinogen, a number of chemotactic factors and cytokines that may be used to control tissue inflammatory response, as well as growth factors that can help with tissue healing and regeneration. It is now considered the best treatment for treating atrophic rhinitis as a result.

Keywords: Atrophic rhinitis, Platelet rich plasma (PRP).

INTRODUCTION

The chronic, crippling condition known as atrophic rhinitis damages the nasal mucosa (AR). Beginning in the middle of the 20th century, some authors distinguished between two conditions when describing atrophic rhinitis (primary and secondary). The aetiology determines how the two disease entities are distinguished from one another.

A-Primary atrophic rhinitis (PAR):

Primary atrophic rhinitis, or ozena, is a progressive chronic nasal disease characterized by mucosal atrophy with resorption of the underlying bone, formation of thick crusts, and a distinct fetid odor [(1)]. It has unique epidemiological features and clinical characteristics. For decades, clinicians and researchers have tried to suggest theories for the etiology of primary atrophic rhinitis [(2)].

Incidence: In tropical and subtropical nations like India, Pakistan, Egypt, and Bangladesh, PAR is a frequent ailment. Young and middle-aged adults are often affected, with a female predominance (F: M = 5.6:1) [(3)].

Etiology: As the cause of PAR is still a matter of discussion, many otorhinolaryngologists, microbiologists, and epidemiologists have been interested in this problem for more than a century. The exact etiology of the disease is still unknown, but multiple suggestions have been proposed. It is unknown if atrophic rhinitis is purely an infectious disease or a combination of infectious, hereditary, dietary, and vascular disorders of the paranasal sinuses [(1)].

Clinical features: The clinical manifestations of PAR include a persistent feeling of nasal obstruction, formation of nasal crusts, epistaxis, fetor (the most distressing symptom), olfactory disturbances like hyposmia and anosmia in certain cases. Other symptoms, which may be involved include facial pain, dryness of nasal mucosa, dyspnea, sleep disturbance, headache and occasionally mucopurulent nasal discharge [(4, 5)].

During examinations, nasal endoscopy is utilised to diagnose AR. This method exposes the nasopharynx and choanae, as well as atrophic, occasionally crusty, or ulcerated nasal cavity mucosa. It also denotes the inferior and/or middle turbinates being absent, hypoplastic, or atrophying, and varying degrees of sinonasal wall destruction. It is often secondary atrophic rhinitis when these symptoms are present, but this must be validated by a clinicopathological work-up. These signs may include synechiae, septal perforation, osteochondral erosions, the aftereffects of past sinonasal surgery and Wegener's granulomatosis, or sinonasal sarcoidosis [(6)].

A rhinomanometric analysis will reveal noticeably reduced resistance and very high nasal airflow rates. Acoustic rhinomanometry will show that the nasal cavities are bigger in cross-section than usual [(7)].

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Histopathology: Atrophic rhinitis is a chronic inflammatory illness accompanied by atrophy and fibrosis, according to a histopathologic examination. Not only is the nasal mucosa impacted by the metaplastic transition of the respiratory epithelium from ciliated pseudostratified columnar to squamous epithelium. The flattened squamous epithelium loses its ability to facilitate mucociliary clearance with later secondary crustation [(8)].

Moreover, there is glandular atrophy, which impacts both the serous and mucous components, with the serous ones being more severely damaged. Less moisture is accessible due to the malfunction of the remaining seromucinous glands, which encourages greater crusting. Common observations include the loss of cilia, goblet cells, and compound alveolar glands. Vascular structures are also impacted by the disease process. Dilated subepithelial capillaries and endarteritis obliterans are differentiating changes. Together, these mechanisms result in poor circulation, decreased moisture, and increased crusting [(8)].

Diagnosis:

The primary method of diagnosing PAR is exclusion with an emphasis on evaluating the potential causes of secondary atrophic rhinitis. Clinical diagnosis and endoscopically guided middle meatal cultures are used to confirm the diagnosis.

Nasal biopsy samples may reveal atrophy of the mucus glands as well as the lack of the typical pseudostratified columnar epithelium. When K. ozaenae is identified by a nasal culture, it is strongly suggested that other related organisms should also be diagnosed and isolated. Many bacteria, including as Proteus, Escherichia coli, and Staphylococcus aureus, are regularly grown [(9)].

In order to collect culture material and prevent culture contamination, the endoscope must be used. The most upsetting and psychologically damaging symptom of atrophic rhinitis seems to be the feeling of a bad smell. The diagnostic assessment of atrophic rhinitis typically includes a CT scan due to the high prevalence of concomitant sinusitis. Using computed tomography, **Pace-Balzan *et al.*** [(10)] noted the following distinctive changes in the nose and paranasal sinuses**:** (1) The mucosa of the paranasal sinuses thickens. (2) Lack of osteomeatal complex definition. (3) The maxillary sinuses are hypoplastic. (4) Widening of the nasal cavities along with lateral nasal wall erosion and bowing. (5) Mucosal atrophy and bone resorption of the inferior and middle turbinates. Another observation was the reduced degree of anteromedial and anteorbital pneumatization in the maxillary sinuses.

B-Secondary atrophic rhinitis (SAR):

Chronic rhinosinusitis, persistent granulomatous illness, invasive surgery, nasal trauma, or radiotherapy can all lead to secondary atrophic rhinitis (SAR). The management of AR is significantly influenced by knowledge of the underlying cause [(9)]. Sarcoidosis, mucous membrane pemphigoid, and granulomatosis with polyangiitis are autoimmune disorders that frequently cause atrophic rhinitis. Syphilis and tuberculosis are thought to be the most often reported causes of this kind of rhino-sinusitis among granulomatous infections. SAR is far more frequently detected, yet it is still poorly understood. Common features of both types of atrophic rhinitis include paradoxical nasal congestion, mucosal atrophy, resorption of the turbinates, nasal crusting, and enlarged nasal cavities.

Radiological imaging signs suggestive for SAR:

A computed tomography scan provides enough information to analyse osteochondral structures precisely (the turbinates, septum, sinonasal walls, osteomeatal complex, sinuses and skull base). A CT scan, however, may reveal the underlying cause (such as Wegener's granulomatosis or sinonasal sarcoidosis), even if histology evidence is required [(11)]. In a few rare instances, magnetic resonance imaging may offer a sharper view of the architecture of the sinonasal mucosa and the severity of the disease process. In complicated cases of sarcoidosis with AR, positron emission tomography in conjunction with CT may be utilised to evaluate the diagnosis and track the effectiveness of the treatment [(11)].

Turbinoseptal connections and nodular bruises are two imaging results that may contrast, depending on the underlying reason. For cases of sarcoidosis, terrible nasal osteochondral wounds affecting the turbinates, septum, and sinonasal walls, and rot of the nasal or even nasopharyngeal mucosa occasionally with mucosal thickening (the turbinates, sinusal walls, or sinuses), the average turbinates and septum should be kept in mind. Cervical, external muscle, and brain bruises in the setting of serious illnesses, of which AR is primarily one perspective and sclerosing wounds or bone remodeling in people with Wegener's granulomatosis or after radiation treatment. No matter the primary aetiology, an enlargement of the nasal depressions up to the choanae is the most common imaging brand name [(9)].

Disease mechanism and etiologies of atrophic rhinitis: Nasal physiology can be considerably altered by atrophic changes to the nasal mucosa and osteochondral structures, which can impair the nasal organ's ability to perform its respiratory, secretory, ciliary, and olfactory activities.

Chronic inflammation, impaired nasal secretion drainage, and bacterial colonisation may all be caused by a mix of hereditary and environmental factors that cause these structural changes, which could have a negative influence on the patient's quality of life [(6)]. It might be feasible to distinguish between primary forms of AR with unknown causes and secondary forms, where AR manifests as a result of invasive sino-nasal surgery and craniofacial radiation, or other treatments,

or as a local, locoregional, or systemic disease process. The outcomes of clinical, endoscopic, and imaging examination can be used for this, together with any other investigations (biopsies, microbiological testing, and rhinomanometer) that may be required [12]. Since it has a substantial impact on the diagnosis and treatment of AR, making the distinction between PAR and SAR is important from an academic perspective as well as from a therapeutic and prognostic one. For instance, the therapy of PAR and SAR differs from the care of secondary AR induced by sarcoidosis, TB, or Wegener's granulomatosis, which necessitates a specialised, early treatment approach [9].

Treatment plans for atrophic rhinitis:

The objectives of treatment for AR include eradicating the contributing factors, moisturising the nasal mucosa, removing the nasal crusts, and enhancing the function of the nasal and paranasal sinus mucosa.

Many treatments, including local, systemic (medical), and surgical ones, have been tried. However, conservative methods, such as nasal irrigation, washes, and drops made of glucose-glycerin, menthol-paraffin, antibiotics, and vasodilators, are the most frequently used. Nasal irrigation, which removes crusts and guards against the nasal mucosa's drying up, is the most crucial stage in the treatment of atrophic rhinitis. The irrigation needs to be done numerous times daily to make this treatment effective [6]. Although there are many different rehabilitation techniques, the outcomes are still poor, and the best course of action has not yet been determined. From the patient's perspective, receiving treatment for a long time with only minimal symptom improvement is challenging**.**

The Young's operation and its modifications are just a few of the surgical techniques that have been suggested to close the nasal cavities. Other methods include using teflon, acrylic, silicone, or silastic grafts, human placenta extract, or implants made of autologous bone, cartilage and fat, or muscle. The essential specific treatment should be initiated as soon as is practically possible in cases of AR caused by a systemic illness to decrease the cumulative, permanent damage to sinonasal tissues. The possible treatments for systemic disorders depend on the severity of the sickness and the involvement of certain organs. Corticosteroids, immunosuppressive or cytotoxic drugs such as methotrexate, cyclophosphamide, azathioprine, and infliximab for various connective tissue diseases, as well as antibiotics are examples of approved lines of particular treatment (multi-agent treatment for tuberculosis) [6].

Platelet-rich plasma (PRP) and treatment of atrophic rhinitis:

Definition: PRP is a biological substance with a platelet concentration above background that is a part of the plasma fraction of autologous blood. PRP contains significant amounts of platelets and clotting components. It also contains a large number of growth factors, chemokines, cytokines, and plasma proteins, as well as a significant amount of platelets [13].

Preparation Considerations:

Regarding PRP, a number of factors need to be taken into account, such as platelet concentration above baseline, the presence of leucocytes, and if exogenous activation is necessary. The platelet count is the first factor to be taken into account. Depending on the platelet concentration in the participants' peripheral blood, there is a variance in the absolute platelet count. Lower (2.5–3 times baseline concentration) and higher (5–9 times baseline concentration). PRP devices can typically be classified as such. The ideal concentration of PRP, according to **Graziani *et al.*** [14], was 2.5 times baselines, and anything above that may have an inhibitory impact. However, further research is required on this subject [14].

PRP's biologic activity will change when white blood cells are present, making it different from PRP without them. The whole blood is separated into two sections in systems with lower platelet counts: one retains the cellular components, and the other contains serum in which the platelets are suspended. The three components of whole blood that are separated by higher platelet count techniques are red cells, serum, and buffy coat. Platelets and white blood cells are both present in the latter [15]. Understanding another component, PRP activation before to injection, requires additional research. Via the use of calcium chloride or thrombin, PRP can be exogenously induced. After activation, a fibrin network begins to form, stiffening the plasma and producing a fibrin clot or membrane. If the activation is carried out thus forcefully, a bivalent fibrin network will emerge as a result. Tetra molecular stable networks will arise as a result of increased physiological activation, which improves the enmeshment of cells and growth factors. When injecting PRP into soft tissues, it is not advisable to make it very viscous [16].

When growth factors are activated, they release quickly within 10 minutes, 90% of the premade factors are released. Since many growth factors have brief half-lives, activating them at or soon before injection may produce the most impact. PRP is not typically activated by commercial PRP kits [16].

Release of growth factors encourages an inflammatory response that takes place over the course of three days once activation at the injection site has been accomplished. At the injection site, fibroblasts begin to accumulate, signaling the start of the proliferative phase of healing, which lasts for several weeks. After then, the fibroblasts' deposited collagen matrix undergoes remodeling [17].

Platelet Biology: Between 150,000 and 400,000 platelets per L are physiologically present in the bloodstream. They are made up of lysosomes, dense granules, and alpha granules. 50–80 granules or so make

up each platelet. The majority of platelets are in charge of the aggregation process. The primary purpose is to support equilibrium. Platelets get activated during a vascular lesion, and their granules release substances that encourage coagulation. Before, it was thought that platelets only had hemostatic effects, but modern scientific research and technological developments have helped us comprehend platelets and their functions more thoroughly. Studies have shown that platelets are a rich source of cytokines and growth factors that can affect the migration of stem cells, angiogenesis, inflammation, and cell proliferation [(15)].

Role of PRP in stimulation of wound healing and tissue regeneration:

The alpha-granules degranulate and release growth factors and cytokines as platelet activation takes place in PRP, which changes the pericellular environment. Some of the most important GFs produced by platelets in PRP are vascular endothelial GF, fibroblast GF, platelet-derived GF, TGF-, insulin-like GF-1, GF-2, interleukin-8, and platelet-derived angiogenesis factors are among examples. PRP also contains white blood cells, phagocytic cells, a high native fibrinogen content, and vasoactive and chemotactic compounds in addition to the previously described components [(18)].

***History of Platelet-Rich Plasma:** PRP is also known as platelet-rich fibrin matrix and platelet-rich growth factors. PRP was first utilised to treat patients with thrombocytopenia in the 1970s, when haematologists described it as plasma with a platelet count higher than that of peripheral blood. In open heart surgery in 1987, PRP was used for the first time in a surgical procedure. PRP was first used in maxillofacial surgery ten years later. Fibrin displayed excellent adhesion and homeostatic qualities, whereas PRP's anti-inflammatory effects encouraged cell growth. PRP has since been utilised mostly in the treatment of sports injuries to the musculoskeletal system. It gained significant public attention after being utilised by professional athletes and is now commonly employed in this industry [(19)].
This material has many uses in cardiothoracic surgery, orthopaedic surgery, neurosurgery, plastic surgery, dentistry, paediatric surgery, gynaecology, urology, and oral and maxillofacial surgery due to its value in bio stimulation and its great ability to accelerate wound healing. It is simple to prepare autologous PRP extraction and injection in a matter of minutes using two centrifuge procedures and is not linked to allergic reactions (autologous material). Lately, PRP therapy has been used to help individuals with atrophic rhinitis regenerate their nasal mucosa [(20)].

Preparation of PRP: Traditional PRP preparation employs dual-speed centrifugation. Blood is divided into red blood cells, platelet-poor plasma, and a buffy coat during the initial "soft spin." Platelet-rich plasma and platelet-poor plasma are separated by the second "hard spin" (PPP). Thrombin or calcium chloride are added to the isolated platelet-rich plasma to create a gel-like product that has five to eight times the platelet concentration of whole blood [(21)].

Platelet-rich plasma in rhinology surgery: excerpts from books released in 2016, there were 5 reports on the use of platelet-rich plasma in rhinology that was discovered. **Pomerantz and Dutton** [(22)] assessed the quality of life of 16 patients who had packing with platelet-rich plasma after endoscopic sinus surgery in 2005. Their investigation's findings were contrasted with data later gathered from a second group of 16 control patients who underwent standard packing. Before and after surgery, each group completed two Sino-Nasal Outcome Test 16 questionnaires. Those who received platelet-rich plasma improved more. Yet there wasn't really much of a difference between the groups.

Rice D [(26)] examined the use of platelet-rich plasma as packing material following endoscopic sinus surgery in a novel prospective research. Platelet-rich plasma had little effect on the first 13 patients, and some even got worse after surgery. The study couldn't be concluded because of these troubling findings. For a group of 30 patients who had submucosal diathermy of the inferior turbinate, **Salah El Din and Hussein** [(20)] injected PRP into the inferior turbinates. Patients who had PRP treatment significantly improved in terms of crusting, bleeding, and mucociliary clearance when compared to the saline-treated control group (n=30).

In order to cure AR, **Friji *et al.*** [(23)] in 2014 suggested using autologous fat and PRP transplantation. Five patients had autologous lipoaspirate injected into the septum, floor, and inferior and intermediate turbinates of both nasal cavities. The same regions also received injections of platelet-rich plasma. Each of the five individuals reported an improvement in their symptoms. A clinical examination found that there were no signs of shrinking and that the nasal mucosa was shining. Six months following the procedure, scores on the Sino-Nasal Outcome Test 20 went from an average of 36 to 8. Moreover, the nasal mucociliary clearance time (960 seconds) was much quicker after surgery than it was before (1995 seconds). The writers supported this approach because they discovered that it produced favorable subjective and objective results.

In a research by **Businco *et al.*** [(24)], 46 patients were randomly assigned to one of two groups, with one group getting platelet-rich lipotransfer and the other receiving only standard medical care. The purpose of the study was to evaluate the safety and efficacy of PRL in treating ENS in comparison with medical treatment only. However, the postoperative subjective nasal symptoms and endoscopic nasal objectivity were only statistically (p0.05) improved in those who had PRL. Both procedures showed no adverse effects [(24)].

Similar results were observed by **Mostafa & Ayad** [(25)] in a study to assess the use of PRP as a biogenic stimulator for healing acceleration in PAR. They

recommended PRP as a potential innovative, minimally invasive treatment that may be helpful in treating tissue dystrophy [25].

DECLARATIONS

- **Consent for publication:** I attest that all authors agreed to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
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