# New regenerative approach to atrophic rhinitis using autologous lipoaspirate transfer and platelet-rich plasma in five patients: Our Experience

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*Accepted for publication 3 June 2014*

Dear Editor,

Atrophic rhinitis (AR) is a debilitating chronic nasal mucosal disease of unknown aetiology. The condition is characterised by progressive nasal mucosal atrophy, atrophy of the underlying bone of the turbinate, abnormal widening of the nasal cavities with paradoxical nasal obstruction and formation of viscid secretions and dried crusts leading to a characteristic fetor (ozaena).[1]

Atrophic Rhinitis was first described by Fraenkel in 1876, but the aetiology of the disease is still a matter of dispute. Various methods of treatment, both medical and surgical, have been tried without much success. However, clinical features of the disease can be attributed to the destruction of the normal respiratory epithelium and metaplasia to a non-ciliated squamous epithelium and loss of mucociliary clearance. Thus the curative treatment of AR should address the reversal of this basic pathologic alteration in its microanatomy. Promotion of regeneration of normal nasal mucosa must be the aim of any treatment for long-lasting success. The aim of this article is to present a new regenerative approach to reverse atrophy of nasal mucosa by grafting autologous of lipoaspirate.

## Methods

Following appropriate institutional review committee approval, a study was conducted to assess the efficacy of autologous lipoaspirate on tissue regeneration in patients with atrophic rhinitis. First five patients, who received autologous lipoaspirate, were included in this review. The rationale and aim of the procedure was clearly explained, and all patients gave their informed consent. Three were females, and two were males and age ranged from 25 to 36 years. All patients had undergone nasal endoscopy and biopsy to confirm the diagnosis of primary atrophic rhinitis. Subjective scoring was performed using the Sino-Nasal Outcome Test (SNOT-20) questionnaire and mucociliary clearance by saccharine transit time to assess ciliary function.

### *Surgical technique*

The areas eligible to be adipose tissue donor site are the medial area of the knee, the abdominal region and the trochanteric region. The selected region was infiltrated with a cold saline solution with addition of 1 mL of adrenaline and 25 mL of 2% lignocaine per 500 mL. Adipose tissue was removed using 2-mm-diameter cannula and a 2 mL syringe. The lipoaspirate purification was obtained by centrifuging the syringes at 1530 ***g*** for 3 min to separate the tissue from its water content and from the oil produced by the destruction of damaged adipocytes. The layer of oil and the residual liquid was discarded. The remaining tissue containing adipocytes and mesenchymal stem cells were used for injection. The purified lipoaspirate was loaded in 2 mL syringe and injected to inferior turbinate, middle turbinate, floor and septal area of the both nostrils with 18-gauge needle. An average of 3 mL was injected in each nostril. For activation of stem cells, platelet-rich plasma was injected in to the same area after degranulating the platelet by adding 0.5 mL of calcium chloride. Platelet-rich plasma was prepared by drawing 10 mL of blood sample from the patient. The blood was centrifuged at 1530 ***g*** for 10 min to obtain platelet-poor plasma. This was again centrifuged at 2720 ***g*** for 10 min to get platelet-rich plasma. Approximately 1 mL of platelet-rich plasma was obtained from 10 mL blood. Patients were discharged from the hospital next day with oral antibiotics and anti-inflammatory agents for 1 week.

## Results

All patients felt improvement in symptoms within 3 weeks of autologous lipoaspirate transfer. Six months after surgery, all patients felt total disappearance of nasal crusting and appearance of nasal mucosa was normal glistening without

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**Table 1.** Summary of patient assessment before and after treatment

| | | | SNOT-20 Score | | MCT | | Mucosa appearance | | Histopathology |
|---|---|---|---|---|---|---|---|---|---|
| Patient | Age | Sex M/F | Initial | 6 months | Initial | 6 months | Initial | 6 months | Initial |
| 1 | 35 | F | 35 | 8 | 1620 | 900 | Atrophy + Crust + | Glistening Mucosa No crust | Complete squamous metaplasia with keratinization |
| 2 | 25 | M | 42 | 8 | 1755 | 870 | Atrophy + Crust + | Glistening Mucosa No crust | Complete squamous metaplasia |
| 3 | 36 | F | 30 | 6 | 2070 | 840 | Atrophy + Crust + | Glistening Mucosa No crust | Partial squamous metaplasia |
| 4 | 32 | F | 44 | 12 | 2385 | 1170 | Atrophy + Crust + | Glistening Mucosa No crust | Complete squamous metaplasia with keratinization |
| 5 | 32 | M | 29 | 6 | 2145 | 1020 | Atrophy + Crust + | Glistening Mucosa No crust | Partial squamous metaplasia |

SNOT-20, 20 item Sino-Nasal Outcome Test; MCT, Mucociliary clearance Time.

any signs of atrophy. No adverse event was reported in any of the patients. SNOT-20 scores were averaged 36 preoperatively with improvement to 8 at 6 months postoperatively. Nasal mucociliary clearance time was significantly reduced postoperatively (960 s) in comparison with the preoperative value (1995s). (Table 1) Follow-up ranged from 6 months to 18 months. (Fig. 1).

## Discussion

Filatov was one of the pioneers of tissue therapy.[2] He introduced human placental extract and called it a *biogenic stimulator* which acted non-specifically on patients irrespective of the type of the disease. The *biogenic stimulator* action of the placental hypothesis had been applied to implantation of dermofat and pieces of cancellous bone graft in treatment of atrophic rhinitis.[3] Chatterji[3] treated 12 cases of AR with autologous medullary bone graft with gratifying results and found that not only does the graft remain viable and survive permanently, but it stimulates or evokes such a tissue response that the atrophic condition of the nasal cavities is rejuvenated and restored to normal or near normal. He found medullary bone graft better than composite bone graft, dermofat grafts or placental grafts for the purpose of biological stimulation, and the results are substantiated by histopathological examination. He noted improvement in nasal mucosa to continue up to 2 years.

In the light of present day knowledge of stem cells in bone marrow and adipocytes and the growth factors in placenta, the claim of regeneration of mucosa by biogenic stimulator seems to be true, thus paving way for new regenerative approach that repairs tissue dystrophy.

Bone marrow was the first source reported to contain mesenchymal stem cells; however, using it may be detrimental due to the highly invasive aspiration procedures. More recently, adipose tissue, attainable by a less invasive method, has been introduced as an alternative source of mesenchymal stem cells.[4] It is well accepted that

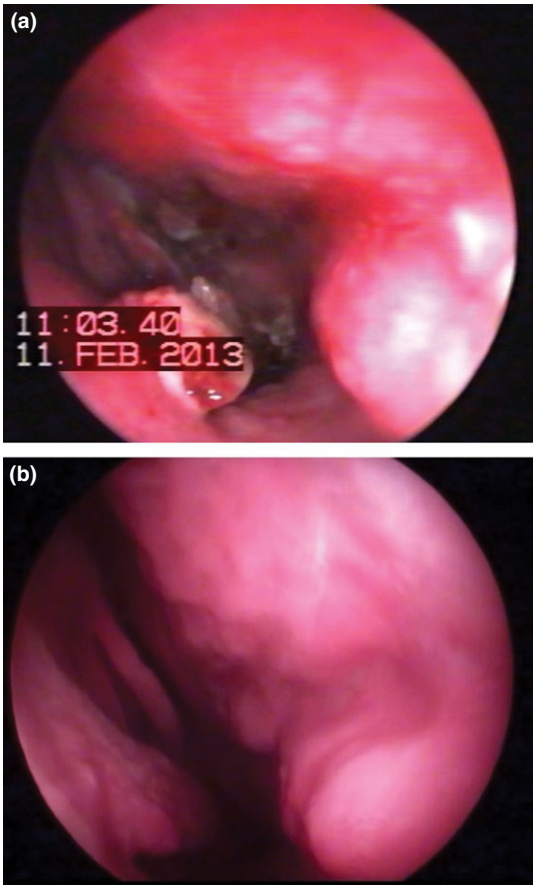


**Fig. 1.** (a) Pre operative view of the nasal cavity in a 25 year old male patient with atrophic rhinitis, showing crusting in the nasal cavity. (b) Post operative appearance of nasal mucosa after one treatment. Lack of crusting and normal appearance of the nasal mucosa is evident.

adipose tissue contains large number of multipotent mesenchymal stem cells. Their regenerative effect, resulting from their capacity to transform into various connective tissue cells, has been reported by Coleman.[5] It was reported that adipocyte-derived stem cells not only enhance angiogenesis[6] but also minimise inflammatory response.[7]

Mojallal.A. *et al.* used autologous fat transfer for volume correction and noticed the dynamic phenomena of tissue regeneration at the recipient site. He has demonstrated improvement in skin quality after fat grafting by clinical observation and animal study.[8] Examples of skin regeneration after radiotherapy damage by lipofilling have been reported.[9] Rigotti *et al.*[9] treated important post-radiotherapy sequelae successfully by using fat tissue grafting. Garcia-Olmo *et al.*[10] reported efficient treatment of chronic ulcerations by fat grafting.

Fat graft and dermofat graft were used for treating atrophic rhinitis as early as 1952.[3,5] This was used primarily for reducing the size of roomy nasal cavity referred as 'recalibration' of the nasal fossae.[2] Sinha *et al.*[5] has found shrinkage and absorption of the fat graft as a major factor for the failure of treatment. We have used an innovative approach to stimulate fat survival and to reduce the graft absorption by adding platelet-rich plasma to the fat graft. Our initial results were encouraging, and we have demonstrated mucosal regeneration by mucociliary clearance time improvement (evidence of ciliary regeneration), improvement in mucosal appearance from atrophied mucosa with crusting to normal glistening mucosa during nasal endoscopy and improvement in patient symptom by SNOT score. We attribute this effect to the stimulation of mesenchymal stem cells within the fat graft. Our results are not due to volume reduction in the nasal cavity. However, we cannot rule out other non-mesenchymal mechanism for this regenerative effect. Further study with isolated stem cells will be needed to conclusively state that these results are due to mesenchymal stem cell effect.

Current medical and surgical management are ineffective for cure of atrophic rhinitis; hence, an innovative regenerative approach is described with the aim of repairing tissue dystrophy. This procedure can be considered effective as therapy for atrophic rhinitis.

### *Strength of the study*

The present study aims to present a new regenerative approach for management of atrophic rhinitis by using autologous lipoaspirate and platelet-rich plasma, possibly by manipulating the stem cells and thereby reversing the basic pathology for long-lasting success.

### *Synopsis*

Atrophic rhinitis is a chronic nasal mucosal disease characterised by the destruction of the normal respiratory epithelium and loss of mucociliary clearance due to metaplasia to a non-ciliated squamous epithelium. A new regenerative approach to reverse atrophy of nasal mucosa by grafting autologous of lipoaspirate and platelet-rich plasma has been proposed.

### *Clinical application of the study*

Current management of atrophic rhinitis fails to give any long-lasting success due to persistence of the basic pathological anatomy. Reversal of basic pathology is a real possibility. The use of autologous lipoaspirate with platelet-rich plasma offers a simple and efficient way to treat this disease by a new regenerative approach.

### Keypoints

- Atrophic rhinitis is a chronic nasal mucosal disease characterised by the destruction of the normal respiratory epithelium and loss of mucociliary clearance due to metaplasia to a non-ciliated squamous epithelium.
- Various methods of treatment, both medical and surgical, have been tried for management of atrophic rhinitis without much success.
- The curative treatment of AR should address the reversal of this basic pathologic alteration in its microanatomy.
- Adipose tissue contains large number of multipotent mesenchymal stem cells and thus offers source of regeneration of nasal mucosa.
- Autologous lipoaspirate transfer and platelet-rich plasma is an effective method to treat atrophic rhinitis by inducing tissue regeneration.

## Conflict of interest

None to declare.

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# Head and neck cancer recurrence: a prospective analysis of 401 follow-up visits to an Australian cancer centre

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*Accepted for publication 3 June 2014*

Dear Editor,

Recurrent disease following curative treatment for head and neck cancer has potentially devastating consequences. Post-treatment follow-up is extremely important, but guidelines vary regarding optimum strategies.[1–3] Up to 90% of recurrences occur within the first 2 years.[1] Most regimens describe frequent clinical review in the first 3 years with less frequent appointments up to 5 years post-treatment. After 5 years most patients may be discharged but should maintain access to the multidisciplinary team. Follow-up strategies vary according to the type, site and stage of the original tumour. For certain tumours and where high-risk behaviour continues, lifelong follow-up is recommended.[4]

It is well known that patient education is essential for effective follow-up. Adequate capacity and rapid access to diagnostic clinics is crucial to ensure timely review of patients with new symptoms.

Previous studies in European populations have demonstrated that patients complaining of a new symptom have a higher rate of recurrence and those seeking an early appointment have higher likelihood of physician suspected recurrence.[5–7]

We performed an analysis of head and neck cancer follow-up appointments at Monash Medical Centre (Melbourne, Australia). The department sees ≈300 new head and neck cancers per annum. A full range of surgical services are provided in addition to state of the art oncology services via The Peter MacCallum Cancer Centre.

We aimed to assess how cases of recurrent disease presented in patients attending as routine follow-up *versus* those who requested an early appointment due to a new symptom.

## Methods

We designed a prospective data collection questionnaire for use in head and neck follow-up clinics (see Appendix 1). All clinics were run as part of a multidisciplinary team follow-up strategy. Patients who had completed definitive treatment with curative intent were included. During treatment, all patients were given contact details of the head and neck clinical nurse specialist and were requested to make contact should they notice any new symptoms. General advice was provided, but no formal educational programme currently exists to describe those symptoms that should be a cause for concern.

Each clinic was triaged by the principal author, and questionnaires were only distributed to those patients meeting the inclusion criteria. During their clinic visit, patients were asked to complete fields regarding the reason for attendance (routine *versus* requested), the presence or absence of new symptoms and a single question related to their satisfaction with the frequency of follow-up. The assessing doctor completed fields regarding any new findings and suspicion for recurrent disease. The time since definitive treatment, site and stage of the primary tumour was also

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