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Development of a Bioresorbable Implant for Nasal Valve Collapse

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ABSTRACT

The aim of the present study is to report outcomes after treatment of nasal valve collapse with a bioabsorbable nasal implant. Nasal obstruction is a main occurrence of breathing difficulties, with lateral wall insufficiency (LWI) playing a crucial role. A bioabsorbable nasal implant was recently introduced to treat nasal blockage and rectify lateral wall insufficiency. In this study, a systematic review and meta-analysis were conducted to investigate bioabsorbable nasal implant efficacy in treating nasal obstruction following reconstructive or rehabilitation surgery. A bioresorbable nasal implant is "Y" shaped implant which has inserted into the lateral wall of nose to provide support for unobstructed air-flow. As implant is absorbed by the body, collagen and fresh tissue will give strength after degradation of implant. The implant can be coated with any therapeutic agent to prevent post-implantation consequences i.e. inflammation or infection.

KEYWORDS: Bioresorbable, Nasal collapse, and "Y" shaped blunt implant

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INTRODUCTION

Nasal valve collapse (NVC), also known as nasal valve stenosis, is one of the most common causes of nasal obstruction [15-17]. The nasal valve is the narrow part of the nasal airway. Nasal valve collapse is caused by any muscular/cartilage/lateral wall weakness and narrowing of the nasal valve cause difficulty in breathing [7,11]. To overcome the nasal valve collapse, one of the convenient options is nasal valve dilator, rhinoplasty or strip [2-3].

The currently available device having issue of inflammation after implantation is observed [10]. Present research relates to non-invasive method to support the nasal cartilage, improve breathing and reduces swelling, inflammation and ulcer [1, 18]. The implant is made up of bioresorbable, Poly (L-lactide-co-D–L-lactide) 1-copolymer, material which treats the lateral wall collapse by providing support to keep patency of the nasal valve [21-23]. The implant will degrade over period of 18 to 24 months due to its bioresorbable property. In present research "Y" shaped arm has blunt/un-pointed distal ends which reduce the risk of inflammation [19,24].

Furthermore, the device has coating of therapeutic agent such as anti-bacterial or anti-inflammatory and biocompatible (hydrophilic, hydrophobic or combination) polymer to reduce post operative consequences and scar tissue formation, respectively [12]. Nasal valve collapse is a condition that occurs when the nasal valve is weakened or narrowed which results in congestion, snoring, improper breathing, nasal obstruction as well as sinusitis [6,20]. The sign of valve collapse include nasal congestion and pronounced difficulty in breathing. The nasal valve is a narrow area and any alteration in the structure of nose which affects this area can result in increased resistance or even blockage of airflow [8-9].

The present research is related to non invasive technology to support the nasal cartilage, improve breathing and quality of life [4-5]. In previous research, the issue of inflammation is observed due to pointed distal end of "Y" shaped implant. To overcome this problem, the present research on implant has blunt end which results in reduction of pain, redness and swelling [13-14].

MATERIAL AND METHODS

The nasal anatomy is complex as it is made up of several structures including bone, skin, upper and lower cartilage as shown in fig. 1. The cartilage provides structure and support to the nose. Nasal has small cartilage which link to the nostril and lateral nasal cartilages. Lateral nasal cartilage is a triangular structure, located below the nasal bone. Cartilage of the septum connects the nasal bones and the lateral

cartilages. It provide support to upper as well as lower lateral nasal cartilage.

The implant can be made up of any bioresorbable materials such as Poly (lactide), poly (glycolide), poly (lactide-co-glycolide, poly (lactic acid), poly (glycolic acid), poly (lactic acid-co-glycolic acid), co polymer of polyethylene glycol, poly acetal, poly-L-lactic acid (PLLA), poly-D-lactic acid (PDLA), poly (L-lactide-co-D-lactide) which comprises desired characteristics like adequate strength and flexural rigidity. Poly (L-lactide-co-DL-lactide) has different ratio of L-lactide and DL-lactide i.e., 90:100, 80:20, 70:30, 60:40, and 50:50 with an inherent viscosity ranges from 3.0 to 4.0 dl/g (table 1). The implant primarily has ribbed cylindrical structure with "Y" shaped forked at distal end. The implant geometry at distal forked end is flexible and contract to fit within 15 to 16 gauge cannula of the delivery system.

Table 1: Specifications of the Poly (L-lactide-co-D, L-lactide)

Sr. No.	Test	Method	Specifications
1	L-lactide content	Polarimetry	67-73 mol %
2	DL-lactide content	Polarimetry	33 - 27 mol %
3	Inherent Viscosity	$CHCl_3$,25˚C,0.1 g/dl	3.3 - 4.3 dl/g
4	Residual monomer	GC	Max. 0.1 wt. %

The PDLLA granules are preheated to 70 to 120 ºC for 3 to 4 hours. Preheating granules prior to charging the mold results in a material will reach molding temperature sooner reducing time and heated material is more fluid than cold powder. Preheating also allows moisture and gas to disperse before material is placed into the mold. During the injection phase, plastic material usually in the form of granules is loaded into a hopper on top of the injection unit. The preheated granules are feed into a cylinder where they are heated until they reach their molten form. Within heating cylinder, there is a motorized screw or ram that mixes the molten granules.

Once enough material has accumulated in front of the screw, the injection process begins and screw pushes the melted granules towards the nozzle of the cylinder. The molten granule is then poured into the mold through a spure. Pressure and speed is controlled by the screw which is essential for achieving desired characteristics of implant. Mold is made up of stainless steel with micro finish single cavity, in which the molten granules poured and the shape of the implant is achieved. Mold comprises runner which indicates that mold is filled with molten granules which helps to achieve the implant final shape in presence of chilled water. The chilled water applied on mold externally. The chilling process will helps to set the molten granules with the shape as per required design. There is a draft angle of 0.5 º to 1.0 º range, provided into the mold for easy removal of the implant from mold after chilling process. There are chances of excessive material seen at parting line on implant which need to be removed to get good surface finish of the implant.

The process parameters for the implant manufacturing are listed in below table 2

.

Table 2: Process parameters for injection molding

Injection Temp. (ºC)	Phase	1-.5
	Setting	180 - 230
	Actual	180 - 230
Position Speed	10 -40	
Packing Pressure	Speed	8 -12
	Time (Sec)	0.1 - 0.5
	Pressure (kg f/c)	10 - 180
Cooling Time (Sec)	4-0	
Injecting Time (Sec)	1 -5	
Middle Time (Sec)	0.08 - 0.15	
Injection Max. Pressure (kg f/c)	50 - 80	

In annealing process, the material is heated to specific temperature and cooled down to achieve desired prosperities in implant. The annealing can be performed in a vacuum oven at temperature ranges from 90 to 250 ºC for 3 to 4 hrs. The micro injection molded part which comprises different portions, where distal end comprises "Y" arms. The implant also comprises ribs and ball at proximal end. The "Y" shape distal end also called self expandable "Y" shape member of the implant is designed in such a way that it will create lower profile by contracting both the arms. The "Y" shape distal end has two arms which are separated at the central axis of the implant.

The implant has to travel into the delivery system about 50-70 mm in longitudinal direction from implant port to the cannula end. The implant distal end is designed in such a way that it will help to withstand the pressure applied by delivery system pusher for during deployment of implant. Coating can be applied on the implant. Material of coating include Poly (ortho esters), poly anhydrides, poly (amino acids), poly phosphophazenes, poly alkyl cyanoacrylates, poly (ester-ether), poly (propylene fumarate),poly(vinylalcohol),poly-L-lactide,poly-DL-lactide-co-glycolide,poly-D-lactide,poly-DL-lactic,poly-L-co-e-caprolactone, poly (meth acrylic acid) or their combinations. The thickness of coating applied on the implant outer surface ranges from 5.0 to 50 µm.

For study the visual inspection of samples, *In vitro* accelerated degradation study was conducted. All the samples were visually inspected for any defects before the study (at 0 time interval). A glass jar was filled with 20 ml phosphate buffer saline (PBS) of pH 7.4 ± 0.2. All samples were immersed in individual glass jar containing PBS solution. All jars were incubated at 70 ± 2 °C in oven. Samples were visually observed at frequency of 24 hours for 40 days to check any changes in the polymeric blend implant.

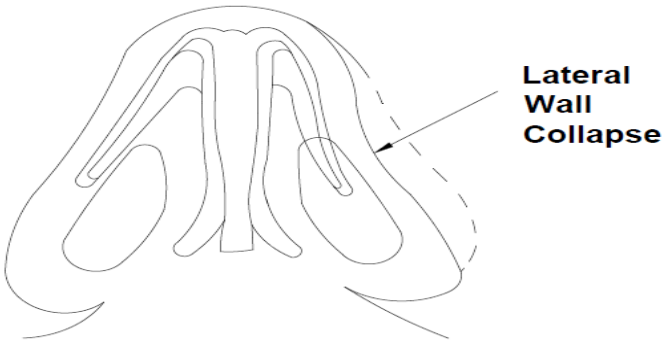

Fig. 1 depicts Collapse Lateral Wall

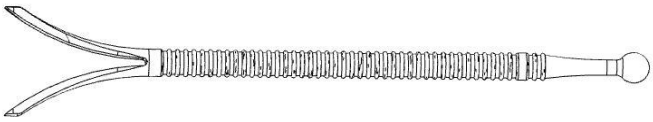

Fig. 2 Micro injection molded implant

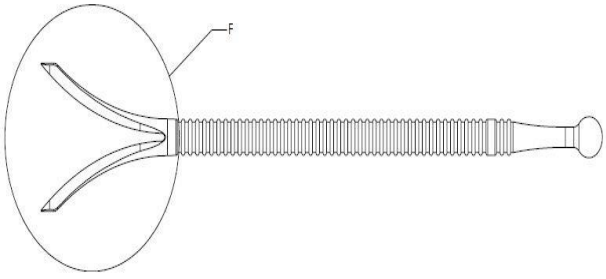

Fig. 3 Micro injection molding implant with detailed view

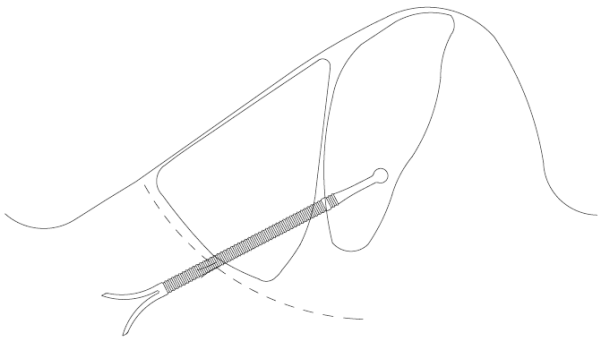

Fig. 4 Implant supporting the upper and lower cartilage

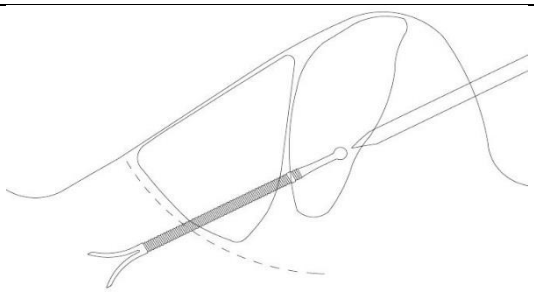

Fig. 5 Implant fully deployed at the treatment site

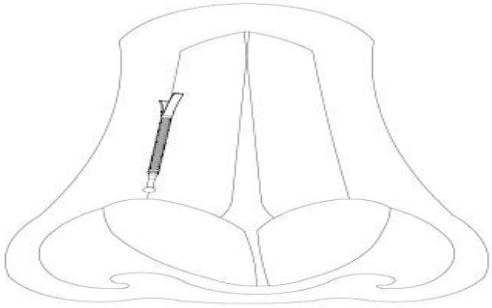

Fig. 6 Implant top view after implantation at treatment site

RESULT AND DISCUSSION

In Vitro Degradation Study

At physiological temperature (37 °C), the complete degradation of bioresorbable polymeric devices takes a long period. As a result, rapid deterioration would allow time and research expenditures to be saved. The results of accelerated deterioration might be used to anticipate how the devices would behave at body temperature. The degradation process might be speed up by employing the specimen's monolayer, the pH, and/or the temperature of the degradation media. Polymer biodegradation is a process in which the polymer structure changes as a result of changes in polymer characteristics caused by the transformational activity of microbial enzymes, such as molecular weight decrease and changes in mechanical strength and surface qualities. The purpose of the mesh accelerated degradation study was to determine the mesh alien's burst strength and overall degradation time.

Accelerated deterioration tests (ADT) are commonly used to evaluate the reliability of long-lasting items. The accelerated *In vitro* degradation study of polymeric blend implant was study in samples with serial no. 2 and 6 (annealed) were inspected visually for any change in implant at the interval of every 24 hours. At initial day of accelerated *In vitro* degradation study visual inspection observed that the surface of the polymeric implant was clear without any crack or holes. At 15 days, there was surface degradation observed and implant was slightly opaque and small amount of surface degradation was seen in the middle region in annealed surface. At 25 days, Implant was changing into white color /opaque and surface degradation was seen in annealed sample. At 30 days, there was white patches was seen on the implant and surface degradation was seen. Implant was brittle, opaque and surface degradation was seen in annealed sample. At the day of 38 and 45, the bulk degradation in sample 2 and also small pieces of implant was seen in sample 2 and 06. At the day of 55, there was a small pieces of implant was observed in both samples.

The accelerated *In vitro* degradation study report of PLLA/PDLA blend polymeric implant:

Sr. No.	Accelerated IVD Days	Sample Serial No.	Visual Inspection
1	Initial	All	The surface of the Polymeric Implant was clear without any crack or holes.
2	03 days	2	Implant was slightly opaque and small amount of surface degradation was seen.
		6	Implant was slightly opaque in the middle region.
3	05 days	2	Implant was opaque and surface has become rough due to surface degradation.
		6	Implant was slightly opaque in the middle region.
4	07 days	2	Implant was opaque and surface has become rough due to surface degradation.
		6	Implant was slightly opaque in the middle region and small amount of surface degradation was seen.
5	11 days	2	Implant was opaque and surface degradation was seen.
		6	Implant was slightly opaque and small amount of surface degradation was seen in the middle region.
6	15 days	2	Surface degradation was seen.
		6	Implant was slightly opaque and small amount of surface degradation was seen in the middle region.
7	20 days	2	Surface degradation was seen.
		6	Implant was opaque and small amount of surface degradation was seen.
8	25 days	2	Implant was changing into white color and surface degradation was seen.
		6	Implant was opaque and surface degradation was seen.
9	30 days	2	White patches was seen on the implant and surface degradation was seen, Implant was brittle.
		6	Implant was opaque and surface degradation was seen.
10	38 & 45 days	2	Bulk degradation and small pieces of implant was observed.
		6	Small pieces of implant was observed.
11	55 days	2 & 6	Small pieces of implant was observed.

The fig. 7 shows the tensile strength of nasal implant for the bond strength. This test method is used to determine yield strength, ultimate tensile strength, ductility, strain hardening characteristics. The tensile strength of the implant is used to find out how strong a material is and also how much it can be stretched before it breaks. It is the ability of a material to resist tearing due to tension.

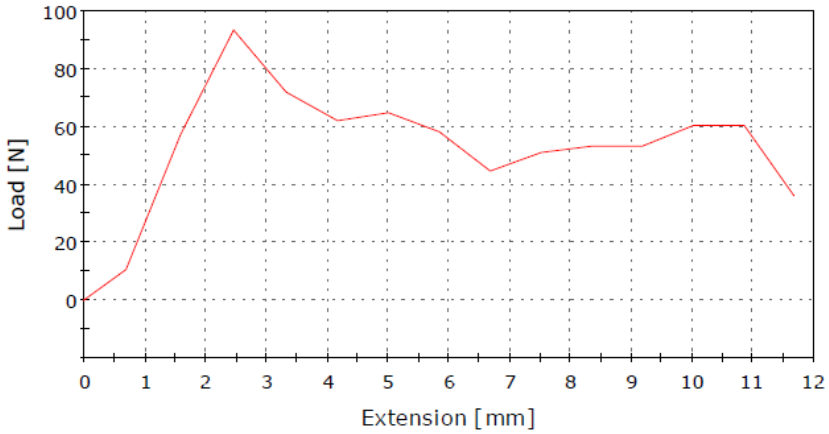

Fig. no. 7 Tensile Strength of Nasal Implant

DISCUSSION

Implant of present research is an absorbable which useful for the treatment of lateral wall weakness to keep patency of the nasal valve. The bioresorbable nasal implant is used to support lower and upper lateral cartilage of nose. Blunt/un-pointed distal ends of implant resulting in low risk of inflammation, swelling and ulcers. The implant prevent the collapse of cartilage tissue/lateral wall and obstruction of nasal airflow [17,24]. Coating can be performed to improve the strength and flexural rigidity of implant. Coating helps in control of implant from pressure and force generated during loading, deployment process and post implantation. Coating of therapeutic agent can be performed to prevent post operative consequences [4].

The non invasive technology to support the nasal cartilage, improve breathing and quality of life. It provides support to upper as well as lowers lateral nasal cartilage. The blunt end causes swelling, redness, and agony to lessen. The good surface finish of the implant observed due to removal of excessive material seen at parting line on implant. Annealing process carried out at specific temperature and cooled down for reduce brittleness, deformation etc. Heat treatment reduces hardness, increase ductility and help to eliminate internal stress. The "Y" shape blunt edge at distal end of the implant reduces inflammation, swelling and inching to the patient. The implant has ribs which help for gripping purpose. The coating provide the flexural and strength. The biocompatible and frictionless coating reduces the possibility for formation of scar tissue. The fig. 8 has continuous ribs at equal distance between each other. It has a conical shape ribs having upside down pattern and having self expandable property just like "Y" shape of the implant. During loading of the implant into the cannula the "Y" shape collapse at distally while the conical upside down ribs are collapse proximally. This pattern and self expandable property of the ribs will help in easiness to deployment of the implant and prevents the implant by anchoring the conical shape ribs with the internal cavity of nasal. This conical anchors help to prevent migration/malfunction of the implant after deployment or during removal of the cannula. The fig. 9 has conical ribs at gradually increasing distance between each other. This shape of the ribs also acts as an anchor, but in particular gradually increasing distance pattern with each other. This shape of the ribs also acts as an anchor, but in particular gradually increasing distance pattern with each other. This ribs are designed in such a way that it anchors with the inside periphery of the nasal cavity. These ribs are self expandable and provide necessary supports to the nasal collapse cartilage. This gradually increase the distance between ribs which prevents migration/malfunction of the implant from its position during removal of the cannula after deployment. The improved design of nasal implant that was easy to handle also with minimum injury. The both implant minimize the injury to the nasal part and have better strength so they easily get fixed in the nose. This, in turn, provides complete flexibility for the implant without migration/deviation.

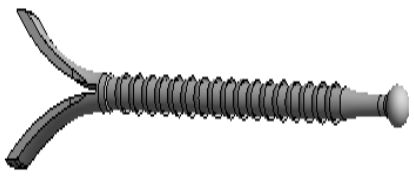

Fig. 8 Nasal implant with Continuos ribs

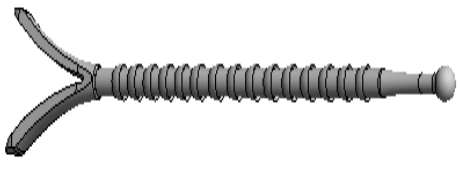

Fig. 9 Nasal Implant with Gradually increase ribs

CONCLUSION

As a result of this research, it was concluded that development of an implant with a "Y"- shape blunt edge end would reduce pain, swelling and redness in the nasal cavity, thus overcoming the issue of inflammation in earliest studies due to the distal end of the "Y"- shaped implant. It is a non-invasive method for supporting nasal cartilage, improving breathing and quality of life. In cases of lateral wall weakness, absorbable nasal implants are beneficial for preserving nasal valve patency. It also provides support to upper as well as lowers lateral nasal cartilage. For patients with the right criteria, the minimum invasiveness of this treatment technique may assist minimize expense, discomfort, and post operative recovery time. The continuous (equal distance) ribs and gradually (step by step) increase ribs prevents migration/malfunction of the implant from its position during removal of the cannula after deployment.

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