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History and progress of trachea transplantation in Mexico

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Abstract

Central airway obstruction and particularly tracheal stenosis is a clinical problem where definite resolution is a tracheal resection, evaluating the magnitude, length, and ventilatory compromise of patient. The resectable fragment is limited to 30% of the total length in children, or 6 cm in adults with terminal end anastomosis. The replacement of longer sections through allogeneic transplantation has been disappointing due to the unfeasibility of the organ, rejection of the graft, and the highly complicated surgical procedure. Tissue bioengineering has designed the replacement of functional organs generated in vitro in the short term, with the absence of immunological responses to the graft. This is based on a non-biological matrix where epithelial and mesenchymal cells are planted in such a matrix. In this document, we review the history and development of trachea transplantation in Mexico as well as the application of these new technologies in the context of its world development, which is a reality in other countries as a new alternative in obstructive illness of the airway. (Gac Med Mex. 2015;151:517-9)

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Introduction

Tracheal stenosis is s common condition that is produced after direct trauma or can be secondary to scarring due to prolonged inubation in patients on assisted ventilation[1]. Other causes are of infectious or inflammatory origin due to tuberculosis, sarcoidosis, fungal infections, etc.

It can also be caused by toxic substances' inhalation, intrinsic and extrinsic neoplasms, accidental or therapeutic exposure to ionising radiation, gastroesophagic reflux or idiopatic[2]. The treatment consists in tracheal resection with termino-terminal anastomosis. When the stenosis encompasses a larger longitude, hindering this surgery, a tracheostomy is performed as a palliative measure, which has a high degree of morbidity and mortality. Definite treatment is replacement of the affected segment or tracheal transplantation, which has not been successful because repeatedly this procedure has been carried out conventionally as if it was a single organ, avascular transplantation, which has inevitably led to necrosis of the transplanted tissue[3], even with the use of growth and vascularization promoters. Tracheal transplantation should be considered as a composed tissue transplantation, a modality that involves blood irrigation and the use of immunosuppressants[3-7]. Even considering this, revascularization of the trachea enveloped in vascularized tissue is not possible due to permanent mobility of the organ and direct exposure of the airway to the environment[8-10]. Delaere demonstrated in the year 2010 that the only way to achieve revascularization of the trachea was by placing it immersed in immobilized vascularized tissue from an adequately immunosuppressed host. This involves taking a trachea from an allogeneic donor, implanting it in the forearm of the previously immunosuppressed receiver, periodically implanting tongue cells in the mucosa of the implanted

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trachea portion, and four months later moving the graft to the cervical region. The procedure described by Delaere is very complicated and involves a long period of time with consequences in the prognosis. Recently, trachael transplantation has been achieved by means of tissue engineering, using decellularized donor's trachea and stem cells from the receptor[2,11]. This procedure has revolutionized existing concepts, thus providing a viable option in the treatment of airway stenosis. These novel technologies have not been implemented in Mexico, but experimental studies have been conducted.

Historical review

In Mexico, tracheal surgery was initiated in the Distrito Federal in the second half of the 20th century with the development of replcement and reconstructive surgical techniques, until arriving to its current phase. Tracheal surgery starts in Mexico at the Hospital General between 1944 and 1946, thanks to the renowned pneumologists Julián González Méndez and Alejandro Celis[12].

In the decade of the 50's, Carlos Pacheco initiated experimental works with suture and reconstruction of the cervical trachea, and observed that the traction of the ends was an important factor in the production of stenosis and infection relapse. Together with Octavio Rivero, in 1954, under the direction of Celis, he experimentally performed tracheal transplantations in animals[12]. In the same decade, at the *Instituto Mexicano del Seguro Social*, patients with mediastinal tumors, aneurism of the aorta and tracheal tumors that exerted endothoracic tracheal compression were treated testing a new anesthetic technique known as transthoracic tracheostomy, a work by León Green. In 1959, the clinical experience of Alfonso Serrano Rebeil at the Hospital General, with problems of larynx and cervical trachea loss, was reported, and in 1960, his experience with 12 patients with loss of cervical trachea was reported. He published, together with Pablo Ortiz Monasterio, a case of larynx and trachea trauma lesion repaired with costal cartilage; in addition, he worked experimentally in this area with dogs, reporting their incision and double V suture. He also described the suture with tracheal torsion and the resection of 14 to 16 tracheal cartilages without restenosis with head fixation in forced flexion[13,14]. In 1967, Díaz and Pacheco reported on their experience with 10 surgeries of the airways with resection and reconstruction of the tracheal bifurcation[15-17]. That same year, Cosío used extracorporeal circulation in a tracheal repair. Díaz initiated the experimental works on tracheal transplantation in 1971[18]. In 1974, the *Instituto Mexicano del Seguro Social* and the Hospital General communicated on the importance of bronchoscopy[19] as a diagnostic method for respiratory diseases[21]. In 1977, Radillo published the performance of an endothoracic tracheoplasty using extracorporeal circulation[21]. In 1980, Yarza published on his surgical experience with cicatricial tracheal stenosis[22]. On that decade[23] treatment of tracheal stenosis was successful in 90% of cases by resection and anastomosis in reference centers of the Distrito Federal, such as the *Centro Médico Nacional Siglo XXI*[24]. Between 1992 and 1997, José Gallardo, at the *Hospital Central Militar*, endoscopically managed tracheal stenoses, grafts and tracheoplasties with 85.7% of success[25]. In 1984, at the *Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas*, the Trachea Clinic was created due to the increased incidence of tracheal disease. In 1994, the first six-year experience was published with the treatment of 97 patients with benign tracheal stenosis, out of which 13 required tracheostomy and use of T-tubes; the remaining patients were performed a resection with anastomosis by José Morales Gómez and José Luis Téllez Becerra[26].

In 2003, Álvarez reported on a prospective study on subglottic stenoses surgically treated with laryngotracheoplasty or cricotracheal resection at the *Hospital Infantil de México*[27].

In 2001, García, of the Hospital General, shared his experience with tracheoplasties and endoscopy[28]. In the *La Raza Hospital,* 30 patients were treated with tracheoplasty over the course of 8 years with good results. Santiago Romo[29,30], reported the cases of 11 patients treated between 2000 and 2003; two of them had restenosis as complication[31]. In the rest of the Mexican Republic, experiences on tracheoplasty have been reported at the *Centro Médico Nacional de Occidente, in Guadalajara*, where 16 patients were treated in the 2002-2004 period[32].

The *Hospital Regional de Especialidades Cardiovasculares y del Tórax No. 34* and the *Centro Médico Nacional de Monterrey,* from the year 2000 until 2003, treated 30 tracheal stenosis-diagnosed patients with resection and anastomosis[33,34]. In the annual congress of the *Sociedad Española del Respiratorio* celebrated in Barcelona (Spain), we reported in 2013 our experience in tracheal surgery since 1998 with the treatment of 17 patients with the same diagnosis and treatment[35].

Current situation

Currently, in the *Instituto Nacional de Ciencias Médicas y de Nutrición Salvador Zubirán*, Jaime Villalba and Patricio Santillán Doherty, together with the investigators Rogelio Jasso Victoria, J. Raúl Olmos Zúñiga[36], J. Alfredo Santibáñez Salgado, Avelina Sotres Vega[37], Miguel

Gaxiola Gaxiola and Matilde Baltazar, have created a team and have made contributions to the promotion of wound healing with the use of wound healing modulators and graft preservation in tracheal transplantation[38,39]. Rodríguez Revilla, et al.[40] asessed macroscopic and microscopic changes in tracheoplasty and autologous transplantation tracheal wound healing after topical application of vascular endothelial growth factor in rats. In these moments, in Mexico, different hospital centers are capable of very successfully treating tracheal stenosis with resection and anastomosis but, nevertheless, the population extension and density require for this condition to be attended to in other regions of the country.

Discussion

Despite the development on different hospitals of the country, there are only reports on allogeneic transplantations with different modifications and no evidences have been found on new tissue engineering technologies implementation to generate viable tracheal grafts to be used for transplantation in respiratory tract conditions. Probably this silence is owing to the development of experimental studies in the area, lo later proceed to their clinical application.

Tracheal transplantation using tissue engineering is a reality in other countries. This procedure offers a very innovative alternative for a health condition that has not been solved, probably due to the complexity of the process both *in vitro* and surgically, which mandatorily requires highly specialized training[41]. At this moment there is the technology and human capital available to initiate these procedures in our country.

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