The Role of Systemic Steroids in Postintubation Tracheal Stenosis: A Randomized Clinical Trial

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Background. **Most patients with postintubation tracheal stenosis are not ideal candidates for airway resection at presentation and their airways must be temporarily kept open by repeated bronchoscopic dilation (RBD). Meanwhile, some sufficiently recover by RBD without further airway resection requirement. We hypothesized whether systemic corticosteroids could lengthen RBD intervals, decrease the number of patients who eventually need airway resection, and shorten the required length of airway resection.**

Methods. **Between February 2009 and November 2012, a randomized double-blind clinical trial with a 1:1 ratio (corticosteroids group [group C], prednisolone 15 mg/day; placebo group [group P]) was conducted on 120 patients without tracheostomy or T tube and in no ideal situation for airway resection at presentation, whose precipitating injury had occurred recently. All underwent RBD until they became asymptomatic or prepared for airway resection. Asymptomatic patients received the capsules (prednisolone or placebo) for 6 months; others discontinued them before surgery. Those requiring RBD at short intervals underwent tracheostomy or T tube placement and were then excluded. Follow-up terminated 6 months after airway resection or capsule discontinuation.**

Results. **There were 105 patients (72 male; 50 in group C), aged 15 to 64 years, who completed their follow-up. There was no significant difference between the two groups in age, sex, history of tracheostomy, intubation cause and duration, time interval between intubation and initial bronchoscopy, length of stenosis, and subglottic involvement. Our study showed a trend for RBD with longer intervals (22 days), and fewer operations, 17% (28 of 50 versus 40 of 55) in group C, although statistically insignificant. Furthermore, the required airway resection length became significantly shorter (5.3 mm) in group C.**

Conclusions. **Early low-dose systemic corticosteroids can be beneficial in postintubation tracheal stenosis management.**

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The most common cause of tracheal stenosis is an acquired disease resulting from the direct trauma of endotracheal tubes in patients with prolonged intubation, a condition known as postintubation tracheal stenosis (PITS) [1, 2]. The majority of these patients are multiple trauma victims who had several days of intubation for mechanical ventilation [1–3]. During this period, direct pressure of the cuff or the tip of the tube on the mucosa and the subsequent ischemia seems to launch an inflammatory process that leads to mucosal edema, granulation tissue formation, fibrosis, and finally, cartilage destruction; all end with tracheal stenosis after extubation. Another etiologic mechanism could be a direct trauma to the tracheal mucosa due to a forceful intubation, especially in severely injured patients by less experienced medical staff.

These patients usually return to hospitals a couple of weeks after extubation for progressive dyspnea and stridor. Unfortunately, many of them are treated as asthma or respiratory infections for a while and eventually referred with severe dyspnea to the specialized centers. More unluckily, some of them also undergo tracheostomy before a correct diagnosis is made by less experienced surgical staff and in an emergent situation, which almost always makes the scenario more complicated for a later definitive airway resection.

On arrival and if the patient's respiratory status allows, fiberoptic laryngoscopy under local anesthesia and intravenous sedation is performed for evaluation of the supraglottic and laryngeal anatomy, and more important, for the function of the vocal cords. Then rigid bronchoscopy under general anesthesia is carried out for both diagnosis and treatment [1]. These procedures should be performed by a surgeon expert in the field of airway surgery for a precise evaluation of the characteristics and length of the stenosis, aspiration of secretions, core-out of granulation tissues, and dilation of the stenotic segments

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as required. This procedure is transiently helpful for most of these patients. It may also be curative in some patients; however, for the majority, especially patients who already have established fibrosis and cartilage destruction, one or even several times of dilation would not be effective, and airway resection and reconstruction would finally be required, if feasible.

Even if airway resection is indicated at the time of the first presentation, many of these patients are not in an ideal situation for surgical resection, because of the concomitant laryngeal injuries, laryngotracheal edema, infection, granulation tissue formation, and mucositis, as well as associated other organs injury or comorbid diseases [4]. In this very usual situation, the airway of patients should be temporarily kept open by repeated bronchoscopic dilation (RBD), while the coexisting problems are fixed or appropriately managed. During 20 years of concentrated work with these patients, we learned that whereas most of them pass the required interval to be prepared for a definitive airway resection, eventually, some of them sufficiently recover by RBD, antibiotics, airway toilet, and humidification.

These RBD require frequent hospital admissions and general anesthesia, which is a significant physical, psychological, and economic burden for these patients and the health system. To find a way to decrease this stress, a question came to our mind that, based on our best knowledge, has never been answered in the literature. The question was whether systemic corticosteroid administration (because of the inflammatory nature of PITS) could be beneficial for this group of patients in this period, in one or some of these ways: (1) increase the interval between the required bronchoscopic procedures; (2) decrease the number of patients who would eventually need airway resection; and (3) shorten the length of trachea needing resection. To answer these hypotheses, a randomized double-blind clinical trial was designed in our hospital.

Patients and Methods

This patients and surgeons blinded parallel study was a single-center trial carried out at our center. The study was approved by the Institutional Research and Ethics Committees (C-87-778 December 2008) and registered at the Iranian Registry of Clinical Trial website (www.irct.ir, IRCT2014103019760N1).

Patient Selection, Randomization, and Blinding

From February 2009 until November 2012, 522 patients with PITS were admitted to our thoracic surgery ward, and their data were prospectively entered in our original database for all tracheal diseases (Alborz Database). Of them, 402 met one or some of the exclusion criteria (Table 1) or had at least one corticosteroid consumption contraindication (Table 2). The remaining 120 eligible patients were enrolled in this study and randomized to either the study group (corticosteroids [group C]) or the control group (placebo group [group P]). After the first bronchoscopy by us, and if indicated, the randomization was performed by our ward general practitioner physician, who had no role in the diagnosis and management of the patients. The surgeons and the patients were unaware of the groups.

Table 1. Exclusion Criteria

Patients who presented with tracheostomy or T tube
Patients for whom, at presentation, more than 6 months had been passed since intubation
Patients fit for airway resection at presentation (pure malatic stenosis or stenosis with matured fibrosis without edema, infection, or granulation tissue), who were also medically stable with no other anticipated surgical procedure
Patients with recurrent stenosis after airway resection
Patients younger than 15 years
No patient consent
No corticosteroid compliance or corticosteroid contraindications (Table 2)
Any patient receiving corticosteroid treatment at the beginning of study for other reasons, such as myasthenia gravis

At bronchoscopy, the data, including length and diameter of stenosis, nature of stenosis, its distance from vocal cords and carina, presence of granulation tissue, edema and infection, as well as anatomy and function of the vocal cords and supraglottic larynx, were precisely evaluated and documented. Then, therapeutic aspiration of secretions, core-out of granulation tissues, and dilation of the stenosis with increasingly larger sized rigid bronchoscopes were performed.

After a full recovery, all potential hazards of corticosteroids (even if the dosage is low) were explained to the patients along with its possible benefits. After taking the patients' informed consent (those under age 18 years also required consent by their parents), they were assigned one by one to each group alternatively: odd numbered arrivals were assigned to group C, and even numbered arrivals to group P.

Intervention

Based on our hospital (as a referral center) protocol for management of patients with PITS, all patients underwent RBD, airway toilet, humidification, and antibiotics administration (if indicated and based on the result of culture), until their respiratory status stabilized or they were prepared for airway resection and anastomosis (Table 3). After randomization, group C patients were

Table 2. Corticosteroid Treatment Contraindications

Severe cardiovascular diseases (such as congestive heart failure)
Severe/uncontrolled hypertension
Severe/uncontrolled diabetes mellitus
Morbid obesity
History of tuberculosis
Active acid-peptic disease
History of psychosis
Glaucoma