

Fibrin glue treatment associated or not with diathermy for recurrent tracheoesophageal fistula: our results after more than 20 years' experience

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ABSTRACT

Introduction. Recurrent tracheoesophageal fistula (RTEF) is a frequent complication (5-10%) in patients with esophageal atresia (EA). Open RTEF surgery has a high morbidity and mortality, so the endoscopic approach represents a promising alternative. We present the long-term results of fibrin glue (FG) bronchoscopic application in patients with RTEF secondary to EA, which was first used by our team in 1994.

Materials and methods. A retrospective review of all patients diagnosed with RTEF following EA repair and treated with FG bronchoscopic application from 1993 to 2019 was carried out. In most cases, diathermy was applied prior to FG sealing. The maximum number of endoscopic sessions was 5. In case of persistent RTEF following the fifth session, open surgery was performed.

Results. 14 RTEF patients were treated with FG. In all but the first 3 cases (11 patients, 78.6%), diathermy was applied concomitantly. Mean first treatment day was day 85 of life (range: 14-770). Patients received a mean of 2.1 (1-5) endoscopic sessions. Mean follow-up was 12.1 (10-20) years. Overall success rate was 71.4%, without significant differences according to whether diathermy was concomitantly applied or not (72.7% vs. 66.6%).

Conclusions. Fibrin glue bronchoscopic application associated or not associated with diathermy is an excellent option for RTEF treatment in EA patients. The endoscopic approach should be considered as the first-choice treatment for RTEF.

KEY WORDS: Tracheoesophageal fistula; Fibrin glue; Esophageal atresia.

TRATAMIENTO CON ADHESIVO DE FIBRINA ASOCIADO O NO A DIATERMIA PARA LAS FÍSTULAS TRAQUEOESOFÁGICAS RECURRENTES: RESULTADOS TRAS MÁS DE 20 AÑOS DE EXPERIENCIA

RESUMEN

Introducción. La fístula traqueoesofágica recurrente (FTER) representa una complicación frecuente (5-10%) en los pacientes con atresia de esófago (AE). La cirugía abierta de FTER implica una alta morbimortalidad, por lo que los abordajes endoscópicos suponen una alternativa prometedora. Presentamos los resultados a largo plazo de la aplicación broncoscópica de adhesivo de fibrina (AF) en pacientes con FTER secundaria a AE, técnica utilizada por primera vez en 1994 por nuestro equipo.

Métodos. Revisión retrospectiva de 1993 a 2019, incluyendo a todos los pacientes diagnosticados de FTER tras la reparación de AE, y tratados con aplicación broncoscópica de AF. En la mayoría de los casos se aplicó diatermia previamente al sellado con AF. El número máximo de sesiones endoscópicas se estableció en cinco; en caso de persistir FTER tras la quinta sesión, se procedió a cirugía abierta.

Resultados. 14 pacientes con FTER fueron tratados con AF; en todos salvo los primeros 3 casos (11 pacientes, 78,6%) se aplicó diatermia concomitante. El día promedio del primer tratamiento fue el día 85 de vida (14 a 770). Los pacientes recibieron una media de 2,1 (1-5) sesiones endoscópicas. El seguimiento medio fue de 12,1 (10-20) años. El éxito global fue del 71,4%, sin apenas variar con la aplicación o no de diatermia concomitante (72,7% vs. 66,6%).

Conclusiones. La aplicación broncoscópica de adhesivo de fibrina asociado o no a diatermia representa una excelente opción para el tratamiento de FTER en pacientes con AE. El abordaje endoscópico debe considerarse como tratamiento de primera elección para FTER.

PALABRAS CLAVE: Fístula traqueoesofágica; Adhesivo de fibrina; Atresia de esófago.

INTRODUCTION

Esophageal atresia (EA) is one of the pathologies most frequently requiring surgical repair in newborns, with an estimated incidence of 1 in 3,000 newborns. There are five types of EA, type III (or type C according to Gross

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classification) being the most frequent one (accounting for approximately 85% of cases), with a fistula communicating the distal pouch with the trachea^(1,2).

Since the first successful EA repair was carried out (reported by Leven and Ladd separately in 1939), diagnostic and treatment advances have led to an overall survival rate of more than 90% in many healthcare facilities. However, complication rate remains a significant problem^(2,3).

One of these complications is recurrent tracheoesophageal fistula (RTEF), which occurs in 5-10% of cases. Open RTEF repair is a highly complex surgery which often involves interpositioning the muscle flaps, the pericardium, the costal cartilage, and even the pleura and the omentum in order to achieve definitive fistula closure^(4,5).

In this context, a tendency towards developing minimally invasive surgical techniques has been observed in the last decade, since they allow for fistula closure with less morbidity and mortality than the open approach^(6,7).

Our team started to use fibrin glue (Tissucol®) in RTEF patients in 1993⁽⁸⁾. Fibrin glue is a fibrinogen-based glue which has been approved as a hemostatic or sealing agent. Owing to its re-epithelialization and fibroblast proliferation activation properties, it seems to provide with the optimal conditions to allow for fistula closure⁽⁹⁾.

Therefore, the objective of this study was to present our long-term results with fibrin glue in RTEF patients, after more than 20 years' experience with this technique.

MATERIALS AND METHODS

Inclusion criteria

A retrospective review of patients developing RTEF following EA surgical repair and treated with fibrin glue sealing in our healthcare facility from 1993 to 2019 was carried out.

Suspected RTEF diagnosis was established based on the presence of respiratory symptoms in patients undergoing EA surgery, while confirmed diagnosis was established following fistula endoscopic visualization.

EA initial repair, FG RTEF closure, and subsequent follow-up were carried out by the same surgical team.

Fibrin glue application technique

Patients were placed under general anesthesia. The procedure was carried out using a rigid pediatric bronchoscope (3.5 x 20 cm, Storz). Following the initial examination of the airway to identify the exact fistula location, a small caliber catheter (Cavafix 255, 0.8 x 1.4 millimeters, B. Braun, Germany) was introduced through the rigid bronchoscope, and FG was instilled through the catheter towards the inside of the fistula. Following instillation, the catheter was removed, the absence of FG extravasation was checked for, and the rigid bronchoscope was removed once adequate patient ventilation had been confirmed.

In most cases (all but the first three), diathermy was applied just before FG instillation. Power was applied using a metallic guide (from the Optisoft 3F, Ref. 3001-0030 (OptiMed) pediatric urethral stent set) to cauterize the mucosa of the fistula and promote re-epithelialization.

Patients were discharged once clinical normality had been confirmed. They were scheduled for an external consultation visit to analyze the results of a control superior gastrointestinal transit test (SGTT) carried out 2 weeks following endoscopy. In order to avoid unnecessary explorations, new endoscopies (and a potential new treatment) were reserved for patients with recurrent RTEF compatible symptoms and for patients with SGTT pathological result. RTEF closure success was established based on either of these two criteria: absence of fistula (or obliterated fistula) at control endoscopic exploration, or completely asymptomatic patient at follow-up with a normal result at the control SGTT.

Endoscopic treatment repetition was initially scheduled for a maximum of 3 sessions, but given the technique's efficacy and the absence of complications associated with the procedure, it was extended to 5 sessions. After a first failed procedure, the next endoscopic sessions were scheduled in case of pathological SGTT or reoccurrence of compatible clinical symptoms. In case of persistent fistula following the fifth session, open surgery repair (cervicotomy or thoracotomy according to fistula level) was carried out.

Statistics

Quantitative variables were represented with mean and range, while qualitative variables were represented with absolute frequency and percentage.

RESULTS

14 patients were included in the study. Mean first treatment day was day 85 of life (range: 14-770). There was one case of RTEF occurrence during follow-up 2 years after EA initial surgery.

Except for the first 3 patients, who received FG treatment only, the remaining 11 patients received a combination of diathermy and FG.

Figure 1 features the flow diagram of our patients. The first endoscopic attempt was successful for RTEF closure purposes in 6 patients (42.9%), whereas subsequent attempts were successful in 4 other patients, with an overall success rate of 71.7%. The remaining 4 patients required open surgery repair, carried out after 5 unsuccessful endoscopic attempts (except for one of the first cases, where open surgery was indicated after the third attempt). Overall technique results are featured in table 1.

No intraoperative or postoperative complications were noted. All patients were subject to clinical and radiological follow-up (postoperative superior gastrointestinal transit

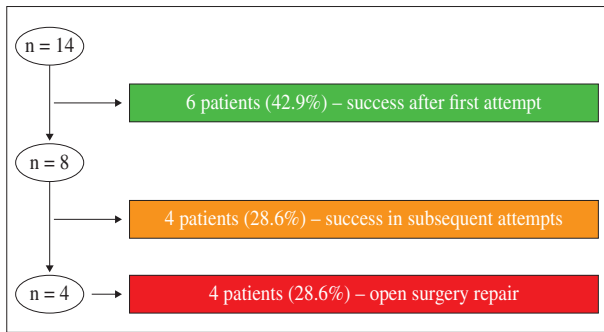


Figure 1. Flow diagram of study patients.

test) to confirm treatment success. Mean follow-up was 12.1 years (range: 10-20). Owing to symptom recurrence or persistence, 8 out of 14 patients (57.1%) required endoscopic assessment during follow-up.

DISCUSSION

Recurrent tracheoesophageal fistula (RTEF) is one of the main complications that may occur following esophageal atresia (EA) initial repair, with an estimated incidence of 5-10% of cases. Open surgery repair is technically demanding and associated with significant morbidity and mortality^(1-5,10).

Therefore, RTEF is being increasingly treated using endoscopic techniques, which represent an encouraging treatment alternative as they are cheaper, less aggressive, and suitable for treatment repetition^(6,7,10,11).

Since Gdaniez and Krause published their experience with cyanoacrylate for tracheoesophageal fistula sealing⁽¹²⁾, various fistula closure methodologies using endoscopic techniques (mainly bronchoscopy, as it allows for improved fistula visualization), with several methods such as laser^(13,14) and most recently trichloroacetic acid^(15,16), have been developed.

Our team started to use fibrin glue (Tissucol®) in 1994, as it had already been approved as a hemostatic and sealing agent to protect high-risk anastomoses⁽⁸⁻⁹⁾. Fibroblast proliferation activation capacity made fibrin glue an excellent

sealing alternative for various types of fistulas⁽¹⁷⁾, and it had recently been used to close a tracheoesophageal fistula secondary to intubation in an adult patient⁽¹⁸⁾. In 2006, we published the first results from our series (made up of 7 patients back then)⁽¹⁹⁾, and in the last years, other teams have published positive experiences with fibrin glue for RTEF treatment^(20,21).

Given that other publications in the literature discuss diathermy's efficacy in RTEF closure⁽⁶⁾, we decided to combine both treatments from the fourth patient on, in an attempt to improve success rate, and considering that a "damaged" mucosa could re-epithelialize better.

A 42.9% success rate following the first endoscopic attempt is an excellent result, superior to that reported in Aworanti et al.'s systematic review⁽¹⁰⁾, which assessed 57 different endoscopic treatments with a mean success rate of 37% following the first attempt. Similarly, a 71.7% overall success rate is a very good result, superior to that of diathermy and fibrin glue when applied separately. Indeed, according to Meier et al.'s review⁽²²⁾, the overall success rates of diathermy and fibrin glue were 50 and 55%, respectively, which made the authors recommend fibrin glue over other agents. Laser is another endoscopic treatment with an excellent success rate of 67-100% for this pathology. However, these results are based on studies with very few patients^(7,23). Finally, Lelong et al. published their experience with trichloroacetic acid in 14 tracheoesophageal fistula patients in 2015, with a 100% success rate after a mean of 1.8 endoscopic sessions per patient. Even though mean follow-up was shorter than that of other studies (41 months), these are extraordinary results⁽¹⁶⁾.

This study was a retrospective review of an infrequent pathology. However, in spite of the long period of time covered by the study, the sample was still small. Therefore, prospective studies with an adequate number of patients comparing various materials (fibrin glue, laser, trichloroacetic acid, etc.) are required to identify the most effective agent for RTEF closure purposes. Nevertheless, this will be highly complicated given how rare this pathology is and how difficult this type of studies are to carry out. What does seem clear is that endoscopy should be considered as the first-choice treatment for this pathology, since it is easy to apply, it allows for treatment repetition, and it involves virtually no complications.

Table 1. Overall technique results and results according to the use or non-use of diathermy concomitantly.

	Total of patients (n = 14)	FG (n = 3)	FG + diathermy (n = 11)
Number of endoscopic sessions	2.1 (1-5)	2 (1-3)	2,1 (1-5)
Success rate after first attempt	6 (42.9%)	1 (33.3%)	5 (45.5%)
Overall success rate	10 (71.7%)	2 (66.6%)	8 (72.7%)

FG: fibrin glue.

CONCLUSIONS

The endoscopic approach should be considered as the first-choice treatment for patients with recurrent tracheoesophageal fistula following esophageal atresia initial repair. Bronchoscopic application of fibrin glue combined with diathermy represents an excellent treatment option.

REFERENCES

1. Richardson JV, Heint SE, Rossi NP, et al. Esophageal atresia and tracheoesophageal fistula. *Ann Thorac Surg.* 1980; 29: 364-8.
2. Hicks LM, Mansfield PB. Esophageal atresia and tracheoesophageal fistula: review of thirteen years of experience. *J Thorac Cardiovasc Surg.* 1981; 81: 358-63.
3. Gutiérrez C, Vila JJ, Segarra V, et al. Long-term nutritional evaluation of patients operated on for esophageal atresia. *Pediatr Surg Int.* 1988; 3: 123-7.
4. Briganti V, Mangia G, Ialongo P, Calisti A. Usefulness of large pleural flap for the treatment of children with recurrent tracheoesophageal fistula. *Pediatr Surg Int.* 2009; 25: 587-9.
5. Bonnard A, Paye-Jaouen A, Aizenfisz S, El Ghoneimi A. Laparoscopically harvested omental flap for recurrent tracheoesophageal fistula in a newborn baby. *J Thorac Cardiovasc Surg.* 2007; 134: 1592-3.
6. Rangelcroft L, Bush GH, Lister J, et al. Endoscopic diathermy of recurrent tracheoesophageal fistulae. *J Pediatr Surg.* 1984; 19: 41-3.
7. Schmittenebecher PP, Mantel K, Hofmann U, et al. Treatment of congenital tracheoesophageal fistula by endoscopic laser coagulation: preliminary report of three cases. *J Pediatr Surg.* 1992; 27: 26-8.
8. Gutiérrez C, Barrios JE, Lluna J. Tratamiento de la fistula traqueo-esofágica recidivada con adhesivo de fibrina. Comunicación oral al XLVI Congreso Nacional de Cirugía Pediátrica, 1993.
9. Schlag G, Thurnher M, Redls H. Fibrin sealing in surgical and nonsurgical fields Springer-Verlag. 1994; 1: 25-36.
10. Aworanti O, Awadalla S. Management of recurrent tracheoesophageal fistulas: a systematic review. *Eur J Pediatr Surg.* 2014; 24: 365-75.
11. Lal DR, Oldham KT. Recurrent tracheoesophageal fistula. *Eur J Pediatr Surg.* 2013; 23: 214-8.
12. Gdanietz K, Krause I. Plastic adhesives for closing esophago-tracheal fistulae in children. *Z Kinderchir.* 1975; 17 (Suppl): 137-8.
13. Schmittenebecher PP, Mantel K, Hofmann U, et al. Treatment of congenital tracheoesophageal fistula by endoscopic laser coagulation: preliminary report of three cases. *J Pediatr Surg.* 1992; 27: 26-8.
14. Rakoczy G, Brown B, Barman D, Howell T, Shabani A, Khalil B, Sheehan Z. KTP laser: an important tool in refractory recurrent tracheo-esophageal fistula in children. *Int J Pediatr Otorhinolaryngol.* 2010; 74: 326-7.
15. Sung MW, Chang H, Hah JH, Kim KH. Endoscopic management of recurrent tracheoesophageal fistula with trichloroacetic acid chemocauterization: a preliminary report. *J Pediatr Surg.* 2008; 43: 2124-7.
16. Lelonge Y, Varlet F, Varela P, Saitúa F, Fourcade L, Gutiérrez R, Vermesch S, Prades JM, López M. Chemocauterization with trichloroacetic acid in congenital and recurrent tracheoesophageal fistula: a minimally invasive treatment. *Surg Endosc.* 2016; 30 (4): 1662-6.
17. Rabago LR, Ventosa N, Castro JL, et al. Endoscopic treatment of postoperative fistulas resistant to conservative management using biological fibrin glue. *Endoscopy.* 2002; 8: 632-8.
18. Antonelli M, Cicconetti F, Vivino G, Gasparetto A. Closure of a tracheoesophageal fistula by bronchoscopic application of fibrin glue and decontamination of the oral cavity. *Chest.* 1991; 100: 578-9.
19. San Román CG, Barrios JE, Lluna J, Ibáñez V, Hernández E, Ayuso L, García-Sala C. Long-term assessment of the treatment of recurrent tracheoesophageal fistula with fibrin glue associated with diathermy. *J Pediatr Surg.* 2006; 41: 1870-3.
20. Benko I, Molnar TF, Horvath OP. A case of fibrin sealant application for closing benign tracheo-esophageal fistula (TEF). *Acta Chir Hung.* 1997; 36: 25-6.
21. Richter GT, Ryckman F, Brown RL, Rutter MJ. Endoscopic management of recurrent tracheoesophageal fistula. *J Pediatr Surg.* 2008; 43: 238-45.
22. Meier JD, Sulman CG, Almond PS, Holinger LD. Endoscopic management of recurrent congenital tracheoesophageal fistula: a review of techniques and results. *Int J Pediatr Otorhinolaryngol.* 2007; 71: 691-7.
23. Bhatnagar V, Lal R, Srinivas M, Agarwala S, Mitra DK. Endoscopic treatment of tracheoesophageal fistula using electrocautery and the Nd:YAG laser. *J Pediatr Surg.* 1999; 34: 464-7.