

Role of Fibrin Glue as a Sealant to Esophageal Anastomosis in Cases of Congenital Esophageal Atresia with Tracheoesophageal Fistula

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Abstract

Objective The aim of this study was to characterize a successful approach for the management of infants with long-gap esophageal atresia (EA) with tracheoesophageal fistula (TEF). The goal was to preserve the native esophagus and minimize the incidence of esophageal anastomotic leaks using fibrin glue as a sealant over the esophageal anastomosis.

Method A total of 52 patients were evaluated in this study. Only patients in whom, gap between the two ends of the esophagus was ≥ 2 cm were selected during January 2005 to January 2007. Patients were divided in two groups on the basis of block randomization. Group A comprised the patients in whom fibrin sealant was used as reinforcement on a primary end-to-end esophageal anastomosis; in group B, fibrin glue was not used. The two groups were compared in terms of esophageal anastomotic leak (EL), postoperative esophageal stricture (ES), and mortality. The statistical analysis was done using Fisher's exact test and the chi-squared test.

Result The number of anastomotic leaks in group A (glue group) was about one-fifth that in group B (no glue group). The incidence of ES was almost twice as high in group B as in group A. The mortality rate was almost threefold higher in group B (no-glue group). The higher incidence of EL

and ES in group B compared to group A was statistically significant.

Conclusion Thus, fibrin glue when used as an adjunct to esophageal anastomosis for primary repair of long-gap EA with TEF appears safe in the clinical setting and may lower the chances of esophageal leak and anastomosis-site strictures. Hence, it can diminish the mortality and morbidity of these patients.

Esophageal atresia, with or without tracheoesophageal fistula, is the most important congenital malformation of the esophagus. Esophageal atresia and tracheoesophageal fistula (EA/TEF), with an overall incidence of approximately 1 in 3000 to 4500 live births [1], is one of the most challenging congenital anomalies for the pediatric surgeon because of its high morbidity and mortality. The ideal treatment consists of division and closure of the fistula with primary repair of the atresia in healthy neonates, although a staged repair is frequently necessary in patients with low birth weight, severe respiratory distress, a long gap between the proximal and distal esophagus, and severe accompanying anomalies [2].

The survival of infants born with EA, TEF, or both has improved dramatically since Cameron Haight's first successful repair in 1941 [3]. Improvements in the survival rate are largely attributable to refinements in neonatal intensive care, anesthetic management, ventilatory support, and surgical techniques. One of the major complications that affect morbidity and mortality in these patients is esophageal anastomotic leakage. In this study, we focused on the factors that cause anastomotic leaks and evaluated a method to reduce its incidence using fibrin glue as a sealant to reinforce the anastomotic site.

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Method

The study was carried out in the Department of Pediatric Surgery S.S. Hospital, BHU, Varanasi from January 2005 to January 2007. It was passed by the ethical committee of our institution. A total of 52 consecutive patients with EA/TEF having a gap length of ≥ 2 cm between two esophageal pouches (before division of the fistula) were selected for the study. Patients were randomized on the basis of a random number table using Strata-9 software (52 random numbers from 1 to 52 without replacement were randomized into two groups, or blocks, on the basis of the random number table); seven patients (four in group A, three in group B) who had an associated cardiac anomaly were excluded from the study, leaving 22 patients in group A and 23 patients in group B. In group A patients, a fibrin sealant (fibrin glue, Tisseel; Baxter, Deerfield, IL, USA) was used as reinforcement on a primary end-to-end esophageal anastomosis, whereas no sealant was used in the group B patients.

All patients were subjected to standard right thoracotomy on days 3 to 5 of life depending on their presentation at our hospital. The gap between two esophageal pouches was meticulously measured by vernier calipers before ligating the TEF. A primary single-layer end-to-end esophageal anastomosis was performed by a single surgeon using Vicryl 5-0 sutures. The esophageal anastomosis was reinforced by fibrin glue in group A, whereas no sealant was used in group B. The patients with no evidence of esophageal leak in the chest tube were subjected to barium swallow examination on postoperative days 7 to 9 for documentation of minor leaks and esophageal strictures. The patients who had a leak, as evident by saliva in the chest tube, were evaluated for esophageal stricture by barium swallow after the third postoperative week. The two groups were assessed for esophageal leak (saliva in the chest tube, barium swallow examination), mortality, and esophageal stricture (clinical and radiologic evidence) by the senior residents and nurses in our department. The two groups were also compared for other parameters, such as birth weight, age of presentation, pneumonitis, gap length, and other associated congenital abnormalities.

Results

A total of 45 patients with EA/TEF were evaluated. Patients with pure esophageal atresia and those with an associated major congenital cardiac anomaly were excluded from the study. The two groups were comparable regarding birth weight, age of presentation, pneumonitis, gap between the two esophageal pouches, and other associated congenital anomalies (Tables 1, 2). The incidence of anastomotic leaks was 26.6% (Table 3). Anastomotic leak was almost five

Table 1 Age, sex, and weight of babies

| Parameter | Group A: glue + (<i>n</i> = 22) | Group B: glue- (<i>n</i> = 23) |
|--------------------------|-------------------------------------|------------------------------------|
| Age at admission (hr) | | |
| < 24 | 5 | 8 |
| 24–48 | 6 | 5 |
| 48–72 | 4 | 6 |
| > 72 | 7 | 4 |
| Full term | 20 | 19 |
| Preterm | 2 | 4 |
| Birth weight (g) | | |
| < 2000 | 3 | 4 |
| 2000–3000 | 15 | 14 |
| > 3000 | 4 | 5 |
| Preoperative Pneumonitis | 2 | 2 |

The difference in the two groups is not statistically significant

Table 2 Associated anomalies

| Anomaly | Group A glue + (<i>n</i> = 22) | Group B glue- (<i>n</i> = 23) | Total |
|-------------------------------|------------------------------------|-----------------------------------|-------|
| Musculoskeletal ^a | 3 | 2 | 5 |
| Genitourinary ^b | 1 | 2 | 3 |
| Gastrointestinal ^c | 1 | 2 | 3 |
| Total | 9 | 9 | 18 |

Cardiac anomalies included five cases of ventricular septal defect and one case each of right side aortic arch and azygos veins abnormality with tetralogy of Fallot. These patients were excluded from the study

^a Three cases of radial bone defect, one case of sacral agenesis, and one case of lumbosacral meningocele

^b Two cases of hypospadias and one case of hydronephrosis

^c One case each of low ARM, high ARM and common cloacae

times more frequent in group B than in group A, which was statistically significant ($p = 0.017$). An anastomotic leak occurred in 100% of patients in group B in whom the gap between the two esophageal pouches was > 3 cm and in 33% of the patients in group A; in patients having a gap of 2.1 to 3.0 cm, an anastomotic leak was seen in about 5.5% and 41.1% of group A and group B patients, respectively (Table 3). Overall, an esophageal stricture was observed in 24.4% of cases. The incidence of esophageal stricture was almost three and half times higher in group B than in group A (Table 4), which was statistically significant ($p = 0.028$). The survival rate for our series was 82% (Table 4). Recurrent fistula was observed in only one patient (in group B).

Discussion

Esophageal atresia with or without TEF has been described as the epitome of pediatric surgery. Thomas Gibson is

Table 3 Anastomotic leaks vs. gap length ($n = 45$)

| Gap length (cm) | Group A: glue+ ($n = 22$) | Group B: glue- ($n = 23$) |
|----------------------|--------------------------------|--------------------------------|
| 2.0 ($n = 5$) | 0/1 | 1/4 (25%) |
| 2.1–3.0 ($n = 35$) | 1/18 (5.5%) | 7/17 (41.1%) |
| >3 ($n = 5$) | 1/3 (33%) | 2/2 (100%) |
| Total ($n = 45$) | 2/22 (9.1%) | 10/23 (43%) |

The incidence of leak was lower in group A (2/22) than in group B (10/23) and the difference was statistically significant ($p = 0.017$, Fisher's exact test)

credited with the first description of EA/TEF in 1697 [4]. It then took more than 200 years for the first reports of two patients to survive multiple-stage procedures, as described by Ladd [5] and Leven [6]. In 1943, Haight and Towsley [3] reported the first survivor following a primary anastomosis. At present, in most developed countries the presence of associated major congenital anomalies determines survival [7]. This, however, is not the case in developing countries, where many other factors continue to contribute to the persistently high mortality rates [8]. Currently, cardiac and chromosomal abnormalities are the most significant causes of death. In the present study, the two groups were comparable in terms of other associated anomalies. Infants with a birth weight < 1500 g, major congenital cardiac abnormalities, severe associated anomalies, preoperative ventilator dependence, and/or a long gap are at increased risk. In the present series, the two groups were comparable regarding these parameters. In developing countries such as India, the age at the time of presentation to the tertiary center is also important because most deliveries are conducted by untrained personnel, leading to a delay in diagnosis, which may increase the chances of infection and hence the morbidity and mortality of these patients. This, then, could explain the abnormally high mortality in our series.

Esophageal anastomosis leak is one of the most common and dangerous complications of surgery for EA/TEF. Anastomotic leakage into the mediastinum occurs in 14% to 21% of infants who have undergone a surgical EA repair. Leaks result from the small, friable lower segment, ischemia of the esophageal ends, excess anastomotic tension [9], sepsis, poor suturing techniques, type of suture [10, 11], excessive mobilization of the distal pouch [12], and increased gap length [9, 11]. To minimize the incidence of anastomosis leak, fibrin glue was tried based on studies of different sites that have indicated that fibrin glue enhances wound healing [13, 14]. In the present series, the overall incidence of anastomotic leak was 26.6%, which is comparable to that of other reported series [7, 8], although in our series we selected only cases where the gap between the two esophageal pouches was ≥ 2 cm (long-gap cases [10]). The incidence of anastomotic leak was five times

higher in group B than in group A: 9.1% and 43.0% in groups A and B, respectively, with the difference statistically significant ($p = 0.017$). These data suggest that fibrin glue when used as a sealant to an esophageal anastomosis can decrease the chances of anastomotic leak.

Another advantage of fibrin glue is that healing occurs with minimal fibrosis. Anastomotic stricture is one of the most common complications following surgical repair of EA, being observed in 30% to 40% of patients after a successful repair [15]. A number of predisposing factors have been implicated in the pathogenesis of esophageal anastomotic stricture, including two-layer anastomosis [15], increased gap length [9], anastomotic tension [16], type of suture [17], anastomotic leak [9, 17], and gastroesophageal reflux (GER) [15, 17]. We used Vicryl 5.0 for a single-layer anastomosis, and the distal esophageal pouch was dissected only when the gap was ≥ 3 cm. Esophageal stricture was diagnosed by clinical assessment and radiologic studies; the overall incidence of esophageal stricture in the present series was 24.4% (9/37), which is lower than in other reported series [17, 18]. The incidence of esophageal stricture in group B was almost three and half times higher than in group A, with the difference statistically significant ($p = 0.028$). These data suggest that use of fibrin glue may induce better healing of the anastomosis with minimal fibrosis even in the presence of adverse conditions such as anastomotic line tension, sepsis, and esophageal leak. In the present series, six of nine (66.7%) anastomotic strictures occurred after esophageal leaks (Table 4). Anastomotic strictures after esophageal leaks vary from 70% to 100% in most of the reported series [17, 19, 20], and in the present series esophageal stricture developed in six of nine (66.7%) patients who survived after the esophageal leak (Table 4). Only 50% of patients developed an esophageal stricture in the glue group, whereas in the nonglue group 71% of the patients developed esophageal stricture after anastomosis leak. These results suggest that the use of fibrin glue enhances healing of the anastomosis when used at the anastomosis site. During the follow-up, two patients with an esophageal stricture required surgical intervention (both were in group B), and the rest responded to dilatation [18], as reported in another study.

The incidence of recurrent fistula was 2.5%, which is comparable to that in other series due to the lack of adequate facilities, we were not able to determine the incidence of GER in our patients. In a developing country such as India, most babies are delivered in a primary care center or at home with the help of trained or untrained personnel, which delays the diagnosis. Almost all of the patients were referred to us after having been fed prior to the diagnosis (88% in our study), and most of them had low birth weight (57% in present study), which increases the chances of pneumonitis and infection and may be the main reason for the high mortality in our series.

Table 4 Mortality and esophageal stricture in two groups ($n = 45$)

| Parameter | Group A: glue+ ($n = 22$) | Group B: glue- ($n = 23$) | Total |
|--|--------------------------------|--------------------------------|---------------|
| Patients survived | 20/22 (90.9%) | 17/23 (73.95%) | 37/45 (82%) |
| Patients died | 2 (9.1%) | 6 (26.05%) | 8/45 (18%) |
| Esophageal leak | 2/22 (9.1%) | 10/23 (43%) | 12/45 (26.9%) |
| Esophageal stricture | 2/20(10%) | 7/17 (41%) | 9/37 (24.4%) |
| Esophageal stricture developed after leak/total stricture | 1/2 (50%) | 5/7 (71%) | 6/9(66.7%) |
| Esophageal stricture vs patients alive after esophageal leak | 1/2 (50%) | 5/7 (71%) | 6/9 (66.7%) |

Although the mortality was three times higher in group B than in group A, it was not found to be statistically significant. The difference in esophageal stricture was found to be statistically significant ($p = 0.028$ using Fisher's exact test)

Mortality in group B was three times that in group A, but the difference was not statistically significant because of the small sample size. Our results show that fibrin glue, when used as a sealant for esophageal anastomosis, can decrease the chances of esophageal leak and esophageal stricture and can improve the survival of these patients.

Conclusion

Fibrin glue when used as a sealant for esophageal anastomosis during primary repair of long-gap esophageal atresia with tracheoesophageal fistula appears safe in the clinical setting and may lower the chances of esophageal leak and anastomosis-site stricture. Hence, it can lower the mortality and morbidity rates for these patients.

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