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Original Research Article

SUPERGLUE IN GI LEAKS: USE OF CYANOACRYLATE GLUE IN GI FISTULAE

Atul Kumar Sood*, Atul Jha, Rahul Jain, Manish Manrai, Prerna Pallavi, Khushvinder Sherry, Mohit Sethia

Army Hospital (Research and Referral), New Delhi – 110010, India

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For Correspondence
Email ID:
atulsooddr@gmail.com

Abstract

Background and Aims: Gastro-Intestinal Fistulae (GIF) on most occasions are iatrogenic and come with significant morbidity and myriad of presentations from asymptomatic individuals to severe sepsis. About a third of GIF heal but most require repeated surgeries adding to the morbidity. We evaluated the feasibility of cyanoacrylate glue injection in the management of non-healing GIF which had failed conservative management of nutrition, antibiotics, and percutaneous drainage.

Methods: Seven patients of non-healing GIF were managed with CAG injection by a sclerotherapy needle via an upper GI endoscopy. The primary endpoint was the closure of the fistula. Feasibility of the procedure was defined as the possibility to reach the opening of the GIF and perform the glue injection. The other parameters noted were the number of injections required the time to achieve complete closure of the fistula and other complications

Results: Feasibility of the procedure was 100%. A median of 01 injections (Range 1-2) was performed in the patients with 71.4% requiring only one injection. The success rate was 100%. The average time required for GIF closure was 8.5 + 3.9 days (range 02-13 days). There were no complications noted in the study. All the patients were followed up for 12 weeks and no mortality was recorded.

Conclusions: Endoscopic injection of CAG appears to be a safe, feasible, reliable and effective modality which offers a minimally invasive technique as an alternative to surgical reoperation in patients with accessible GIFs that are non-healing after standard management.

Keywords: GI Fistulae; Cyanoacrylate glue

Introduction

A Gastrointestinal fistula (GIF) is an abnormal communication between 2 epithelized surfaces with at least one of them pertaining to the GI tract. GIF remains a challenging problem as they come with a myriad of presentations. The manifestations range from an asymptomatic patient to one with sepsis and may be complicated by septic shock and death [1]. Studies have demonstrated a mortality rate of up to 10% [2]. On most occasions (75 – 85%) the etiology of the fistula is iatrogenic and follows a surgical procedure. The incidence of fistulae varies as per the surgery. It is uncommon after an esophageal surgery

(2.7%) and is seen frequently after a pancreatic surgery (25%) [1]. The rest (15% to 25%) are spontaneously occurring fistulae due to various etiologies like radiation, inflammatory bowel disease, diverticular disease, appendicitis and ischemic bowel [3]. Almost a third of fistulae resolve spontaneously with conservative management [4]. In the remaining patients, the options were limited. Surgery is the standard management but is fraught with high morbidity and mortality.

Due to the limited options in non-healing GIFs, the last 10 years have seen in a surge of novel techniques being developed to augment the management of non-healing fistulae. Most of the therapeutic interventions that are being developed include minimally invasive approaches which are either endoscopy based or intervention radiology based. Endoscopic interventions include placement of clips, stents or fibrin glue [2,5,6]. Interventional radiology also offers a similar management and is usually done in patients with fistulae that can't be approached endoscopically [7,8].

Cyanoacrylate glue (CAG) is a standard feature in the armamentarium of a gastroenterologist and is easily available in the endoscopy theatre. The most common use of CAG is an injection of fundal varies through a sclerotherapy needle and has been established as a safe modality of management is basic precautions and protocols are followed. We present the result of our clinical experience with CAG injection in the management of non-healing GIFs after the failure of standard medical therapy.

Materials and Methods

Patient Population: All patients with a persistent non-healing GIFs were prospectively enrolled in the study during a study period of Apr 2016 to Mar 2018. Ethical clearance was taken from the hospital ethics committee. In all cases, standard conservative procedures (nutrition, antibiotics and percutaneous drainage) had failed in achieving closure of the GIF and they were diagnosed as non-healing GIFs. Patients consent (written) was taken after detailed counseling of the patients and their relatives. The counseling included a detailed description of the current clinical condition of the patients, planned procedure and the potential complications of the therapy.

Procedure: The diagnosis of GIF was suspected clinically in presence of persistent drain from the surgical site or occurrence of fever. The patients underwent Contrast-Enhanced Computed Tomography (CECT) of the part. On detection of a collection, a percutaneous drain was placed and the patient was managed with nutrition (through appropriate access) and antibiotics. The response to conservative therapy was assessed by the decrease in the drain output and resolution of clinical symptoms. If the drain persisted for a period of a week with no demonstrable decrease in the drain or the collection, the diagnosis of a non-healing GIF was made. The details of the seven patients are shown in Table 1.

Endoscopy was done for all patients of non-healing GIFs. Procedures were performed by gastroenterologists with 5-10 years of experience. Upper GI endoscopy (Olympus, USA) was used to access the GIF and injection of CAG Endocrinol, Samarth, India) was done using sclerotherapy needle (Interject, Boston Scientific, USA).

On localization of the GIF, the tract was obliterated with an injection of CAG, composed of monomers of n-butyl-2-cyanoacrylate. The glue was injected in 1 ml aliquots. The catheter that was used for glue injection was flushed with non-ionic dextrose solution to prevent glue polymerization within the catheter. The drainage catheter was left in situ to assess the response to the intervention and was removed when the daily drain was less than five ml for three consecutive days. A repeat CECT was done to document resolution of the collection. Image of the fistulous opening of patient no. 1 is shown in Figure 1. In case of persistence of the drain, the second session of glue injection was planned if a fistulogram demonstrated the persistence of the fistula.

Data Analysis: The primary endpoint was the closure of the fistula. Healing/closure of the GIF was defined by a stoppage of the persistent drain followed by imaging of the part which had to document the absence of a collection. Feasibility of the procedure was defined as the possibility to reach the opening of the GIF and perform the glue injection. The other parameters that were noted were the number of injections required the time to achieve complete closure of the fistula and other complications.

Table 1: Patient characteristics

	Age	Sex	Disease	Management	Site of Fistula	Size of fistula	No of Injections	Healing time	Follow up	The total dose of CAG
1.	32	Male	Duodenal Perforation	Omental patch	Duodenum	1.5 cm	01	08 days	12 weeks	2 ml
2.	55	Male	Choledocholithiasis Post ERCP duodenal perforation	Conservative	Duodenum	1.5 cm	01	09 days	12 weeks	2.5 ml
3.	45	Male	Severe Acute Pancreatitis	Necrosectomy followed by ERCP and MPD stenting	Necro-cutaneous fistula	1 cm	02	12 days	12 weeks	1 ml + 1 ml
4.	05	Male	Foreign Body (Coin) Esophagus	Endoscopy – Hemoclip	Esophagus	2.5 cms	01	10 days	12 weeks	1 ml
5.	36	Male	Moderate Severe Pancreatitis	Necrosectomy followed by ERCP and MPD stenting	Necro-cutaneous fistula	1.5 cms	02	13 days	12 weeks	1 ml + 1 ml
6.	28	Male	Perforating duodenal ulcer with GOO	Gastrojejunostomy	Duodenum	1.5 cms	01	02 days	12 weeks	2 ml
7.	58	Male	Fistula at PEG site	Removal of PEG tube and antibiotics	Stomach	1 cm	01	05 days	12 weeks	1 ml

Abbreviations
ERCP: Endoscopic Retrograde Cholangiopancreatography
GOO: Gastric outlet obstruction
PEG: Percutaneous Endoscopic Gastrostomy
MPD: Main Pancreatic Duct

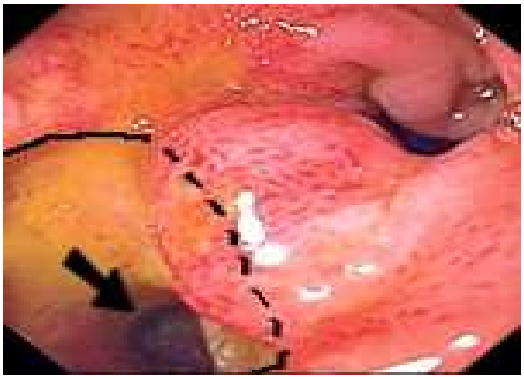

Fig 1: The Fistulous opening of Patient No 1

Results

Seven cases of non-healing GIF were managed with CAG injection over the study period. Feasibility of the procedure was 100% and the fistula was localized in all cases. A median of 01 injections (Range 1-2) was performed in the patients with most (71.4%, 5/7) requiring only one injection. The CAG injection data is shown in Table 1.

The success rate of the procedure was 100% and all the patients with GIF had complete closure of the fistula after the CAG injection. The average time required for GIF closure was 8.5 $\pm$ 3.9 days (range 02-13 days). Two patients (33%) required a repeat injection and both the patients had been a case of severe acute pancreatitis requiring necrosectomy leading to a persistent GIF despite ERCP and pancreatic duct stenting. All other patients had closure with a single injection only. Possibly the inflammation of the pancreatic head played a role in the decreased response to the intervention.

There were no complications noted in the study. All the patients were followed up for 12 weeks and no mortality was recorded. There was no recurrence of the GIF during the follow-up.

Discussion

GIFs mark an important event in the management of patients of gastrointestinal catastrophe. The manifestation of GIFs can be diverse and the spectrum includes patients who range from asymptomatic individuals to patients with sepsis. Nonhealing GIF can pose an even important challenge due to multiple reasons. Firstly the GIF results in increased morbidity and mortality. Secondly, it increases the financial burden of healthcare as it implies an increase in hospital stay and the need for multidisciplinary management both of which increase the cost of the treatment.

Surgical management of non-healing GIFs is a challenge on its own and the resultant surgery comes with significant morbidity. The acceptance for a second surgery by the patient is usually difficult as most of the GIFs are iatrogenic and the patient already has a severe illness. Hence over the last decade, multiple new approaches have been devised to treat these GIFs. These approaches include clips (Hemoclips and OTSC), Loops (Endoloops), Sutures (ENDOCLINCH), Stents (ALIMAX) and tissue sealants (including fibrin sealant and glue injection) [4]. Series have also been published indicating the feasibility of intervention radiology using CAG for management of fistula [9].

Tissue sealants are substances that polymerize and stick together epithelial surfaces following contact with tissue fluid or water. Polymerization is followed by epithelisation which results in fistula closure. Fibrin glue is a type of tissue sealant that has been used more extensively in the management of GIF. Rabago et al used fibrin glue for effective treatment of postoperative fistulas resistant to conservative treatment [10]. Various studies have proven the safety and the benefit of fibrin sealant in the management of entero-cutaneous fistulas [11].

Chemical glue without fibrin is another option for management of GIF. CAG is a readily available sealant in a standard endoscopy theatre and thus is easily available to most gastroenterologists. Cyanoacrylate was the first super glue used for the purpose. Cyanoacrylate use resulted in severe local inflammation and thus was not used in humans. Subsequent studies in animals showed that N-butyl cyanoacrylate and N-octyl cyanoacrylate cause less inflammation when N-butyl cyanoacrylate was used in the closure of cystostomy in dogs [12]. CAG is also bacteriostatic in nature. Hence, CAG has been utilized in humans for management of numerous fistulas like vesicovaginal fistula [13].

CAG has been used in numerous studies by interventional radiologists in the management of non-healing GI fistulas. Bae et al described 11 patients of enteric or biliary fistulae who were managed with percutaneous CAG injection with a high success rate [14]. Mauri et al also used CAG, albeit a different material, for management of non-healing GIFs with a success rate of 88.9% [9]. The authors argued that Glubran-2 has a different chemical structure which produces a more stable polymer leading to less inflammation. Glubran-2 can be easily identified under fluoroscopy and has been shown to have antibacterial properties [15].

We used CAG for management of non-healing GIFs with a high success rate and no complications. CAG injection in the management of GIF, however, has been reported only as case reports and series [16,17,18,19]. In our knowledge, this is the largest study of endoscopic injection of CAG for management of non-healing GIFs. The fact that CAG is easily available in endoscopy theatres and has a high success rate for accessible fistulae with low complication rate makes it an interesting and useful option in the management of non-healing GIFs.

Some limitations of this study have to be taken into account. Firstly this is a study with a limited sample size and larger studies have to be conducted before recommending CAG in the management of non-healing GIFs. But with non-healing GIFs being a rare entity, it might not be feasible to have a large study. Secondly, the amount of CAG to be injected has not been standardized. It was given in aliquots of 1 ml. Thus this study cannot recommend any definite amount of CAG. Thirdly, there was no standard duration after the onset of fistula that CAG was offered. The attempts were made after failure of conservative therapy at varying intervals from the onset of fistula.

Conclusion

Endoscopic injection of CAG appears to be a safe, feasible, reliable and effective modality which offers a minimally invasive technique as an alternative to surgical reoperation in patients with accessible GIFs that are non-healing after standard management.

Conflict of Interest: None

References

1. Girard E, Messager M, Sauvanet A, Benoist S, Piessen G, Mabrut JY et al. Anastomotic leakage after gastrointestinal surgery: diagnosis and management. J ViscSurg 2014;151:441–450
2. Joyce MR, Dietz DW. Management of complex gastrointestinal fistula. Curr Probl Surg 2009;46:384–430
3. González-Pinto I, González EM. Optimizing the treatment of upper gastrointestinal fistulae. Gut. 2001;49(suppl 4):iv22–iv31
4. Kumar N, Larsen MC, Thompson CC. Endoscopic Management of Gastrointestinal Fistulae. Gastroenterol Hepatol. 2014; 10(8): 495–452.
5. Jacobsen HJ, Nergard BJ, Leifsson BG, Frederiksen SG, Agajahni E, Ekelund M et al. Management of suspected anastomotic leaks after bariatric laparoscopic Roux-en-y gastric bypass.Br J Surg 2014;101:417–423
6. Kumar N, Thompson CC. Endoscopic therapy for post-operative leaks and fistulae. Gastrointest Endosc Clin N Am 2013;238:123–136

7. Mauri G, Mattiuz C, Sconfienza LM, Pedicini V, Poretti D, Mel-chiorre F et al. Role of interventional radiology in the management of complications after pancreatic surgery: a pictorial review.Insights Imaging 2014;6:231–239
8. Pedicini V, Poretti D, Mauri G, Trimboli M, Brambilla G, Sconfienza LM et al. Management of post-surgical biliary leakage with percutaneous transhepatic biliary drainage (PTBD) and occlusion balloon (OB) in patients without dilatation of the biliary tree: preliminary results. Eur Radiol 2010;20:1061–1068
9. Mauri G, Pescatori LC, Mattiuz C, Poretti D, Pedicini V, Melchiorre F et al. Non-healing post-surgical fistulae: treatment with an image-guided percutaneous injection of cyanoacrylic glue. Radiol Med. 2017;122(2):88-94.
10. Rábago LR, Ventosa N, Castro JL, Marco J, Herrera N, Gea F. Endoscopic treatment of postoperative fistulas resistant to conservative management using biological fibrin glue. Endoscopy 2002; 34(8):632-8
11. Jorge Avalos-González, Eliseo Portilla-deBuen, Caridad Aurea Leal-Cortés, Abel Orozco-Mosqueda, María del Carmen Estrada-Aguilar et al. Reduction of the closure time of postoperative enterocutaneous fistulas with fibrin sealant World J Gastroenterol. 2010; 16(22): 2793–2800.
12. Davila-Serapio F, Villicana-Benítez JJ, Montejo-Velazquez C, Martínez-Olivera G, Rivera-Cruz JM. Comparison of n-butyl-2-cyanoacrylate tissue adhesive in bladder perforation closure with double-layer suture in a dog model. Rev Mex Urol 2010;70:103-10
13. Sawant AS, Kasat GV, Kumar V. Cyanoacrylate injection in the management of recurrent vesicovaginal fistula: Our experience. Indian J Urol 2016;32:323-5
14. Bae JH, Kim GC, Ryeom HK, Jang YJ. Percutaneous embolization of persistent biliary and enteric fistulas with Histoacryl. J Vasc Interv Radiol 2011;22:879–883
15. Rogalski P, Daniluk J, Baniukiewicz A, Wroblewski E, Dabrowski A. Endoscopic management of gastrointestinal perforations, leaks and fistulas. World J Gastroenterol 2015;21:10542–10552
16. Seewald S, Brand B, Groth S. Endoscopic sealing of pancreatic fistula by using N-butyl-2-cyanoacrylate. Gastrointest Endosc 2004;59:463–470
17. Rotondano G, Viola M, Orsini L. Uncommon cause of early postoperative colonic fistula successfully treated with endoscopic acrylate glue injection. Gastrointest Endosc 2008;67:183–186
18. Billi P, Alberani A, Baroncini D. Management of gastrointestinal fistulas with n-2-butyl-cyanoacrylate. Endoscopy 1998;30: S69
19. Ojima Toshiyasu. Alpha-cyanoacrylate injection for esophageal fistulas. Endoscopy 2014; 46: E62–E63