STERNAL CYANOACRYLATE GLUING IN MEDIASTINITIS; EFFECTS ON INFECTION, STABILITY AND BONE HEALING

T. N. OĞUŞ , MD,
M.H. US *, MD,
H. OĞUŞ *,* MD,
S. ÇİÇEK, MD,
S. ÖZKAN* , MD,
Ö.Y. ÖZTÜRK*, MD,
Ö. IŞIK, MD

From:
Department of Cardiovascular Surgery, Maltepe University, Faculty of Medicine, Istanbul, Turkey.
*Department of Cardiovascular Surgery, and Anesthesiology-Reanimation, Gülhane Military Academy of Medecine, GATA , Istanbul, Turkey
** Anesthesiology-Reanimation Clinic, Kosuyolu Heart and Research Center

Adress for reprints:
Dr. Temuçin N. OĞUŞ
Nuhkuyusu C. Pişkinler S. Aykent Sitesi D Blok D:20
Altunizade – Üsküdar 81190
Istanbul -Türkiye
Tel:+90 216 4341827
e-mail:
togus@superonline.com

It is crucial to determine stability, histocompatibility and antibacterial properties of the cyanoacrylate used for sternal fixation.
Clinical study: In 17 cases of mediastinitis, debridement and rewiring the sternum, was applied as the treatment method (Group I). Eighteen cases of mediastinitis was treated with same method added sternal cyanoacrylate gluing (Group II). A comparative study was done; the follow-up period was 36,7±4 and 18,5±6,9 months in Group I and II respectively. Animal study: In 10 rats, an upper sternotomy was made and the sternal bone was contaminated. Direct wound closure was made in 4 rats (Group A), in 6 animals, wounds were closed after applicating cyanoacrylate in sternal split (Group B). In this prospective study, all rats alive were sacrified at 3rd and 8th week and sternums were examined.
Clinical study: In Group I, six patients required additive interventions due to recurrent sternal detachment and osteomyelitis (35,3%). In Group II no osteomyelitis was occurred, three patients required reintervention related to cyanoacrylate hystotoxicity. Hospital stay was higher in Group I compared to Group II (24,1±4,7 vs 14,2±4,0 days respectively). Experimental study: Group A animals were died of sepsis. In Group B all rats survived the procedure. At 3rd week, histologic evaluations showed that cyanoacrylate was not degraded, and no infection or foreign body reaction was observed. At 8th week, the histologic examination showed that cyanoacrylate was completely degraded and replaced by connective tissue.
Cyanoacrylate is effective to diminish the sternal complications and their related cost and hospital stay of mediastinitis.

Key words: ***Cyanoacrylate, hystocompatibility, osteomyelitis, mediastinitis, sternotomy.***

Postoperative mediastinitis after cardiac surgical procedures remains a serious complication associated with tremendous morbidity, cost and mortality. Although the reported incidence range from 0,15% to 8% (1) its associated mortality rate varies from 14% to 47% (2). Early diagnosis and treatment is essential and may prevent the spread of infection with its devastating sequela. The optimal treatment of mediastinitis is still controversial with operative treatment varying from simple debridement and drainage to extensive myocutaneous or omental plastic procedures (3-5). However failure rate and the need for repeat procedures are still substantial after these procedures (6,7).

Although cyanoacrylate glue derivatives have been used as surgical adhesives for many years; its use in mediastinitis (8) and sternal dehiscence is relatively new (9) with promising early results.

In this study we assesed the tissue response, adhesion and antimicrobial properties of cyanoacrylate in an animal model and report our early and mid term clinical results with cyanoacrylate use in mediastinitis.

MATERIAL AND METHODS

A-Clinical study

One thousand three hundred eighty nine adult median sternotomies were performed from April 1996 to July 1998. Mediastinitis occurred in 17 patients (1,2%) (Group I). Group I patients were treated with debridement and sternal refixation. Two thousand three adult median sternotomies were performed from August 1998 to April 2001. Mediastinitis occured in 18 patients (0,8%) (Group II). Group II patients were treated with debridement, cyanoacrylate application to sternum and refixation. This treatment modality was approved by the institutional ethics committee and informed consent was obtained from all patients. Cefazolin was used for routine antibiotic prophylaxis perioperatively. We retrospectively reviewed all cases of sternal wound complication., and Patients demographics, operative procedures and intraoperative variables are documented in table I.

Table-I Patients' charactheristics and perioperative variables.

	Group I	**Group II**
Age	62,58±5,16	60,66±5,86
Male / Female	16 / 1	16 / 2
Accompanying diseases		
DM	8 (47%)	9 (50%)
COPD	8 (47%)	11 (61%)
CRF	2 (11,7%)	2 (11,1%)
LVD	8 (47%)	12 (66,6%)
Surgical procedures		
CABG	15 (88,2%)	15 (83,4%)
Valve replacement+CABG	2 (11,8%)	3 (16,6%)
Operation time (min.)	142,3±34	155,8±23,8
CPB time (min.)	81±27,5	90,8±19,1
ACC time (min.)	46,4±21,8	61,4±14,7
Intubated time (hour)	24,2±21,8	24,8±12,6
Low cardiac output syndrome*	6	6
IABP usage	2	4

* Low cardiac output state over postoperative 24th hour. Abbreviations: SD: Standard deviation. DM: Diabetes mellitus, COPD: Chronical obstructive pulmonary disease (Forced expiratory volume in first second< %75 of predicted value), CRF: Chronically renal failure (dialyze dependent patients), LVD: Left ventricular dysfunction (ejection fraction <35 %), CABG: Coronary artery bypass grafting, IABP: intraaortic balloon pump.

A clinical diagnosis of mediastinal infection was made on the basis of wound discharge, sternal instability, spreading wound erythema and systemic features of infection such as pyrexia or leukocytosis. Antibiotic management was started systemically before debridement with vancomycin and an aminoglicozide. Thereafter, the antibiotic regimen was adapted to the results of bacterial susceptibility.

The surgical procedure in Group I patients included wide excision of the original skin incision, removal of all suture materials, sternal wires and nonviable tissue. The sternum was debrided back to bleeding bone. The medistinal tissue was carefully debrided until gentle bleeding of the tissue occurred and the wound was than washed out with warm normal saline. Irrigation catheters were placed if needed and the sternum was closed with simple interrupted 6 or 7 No steel wires. In this group, if sternal fractures impede primary closure, rewiring was done by Robiscek's method (10). Deep interrupted polypropylene sutures were used to close the superficial fascia and skin en-block.

Patients in Group II were treated by radical debridement, and sternal refixation as described above. However, commercially available cyanoacrylate glue (Cyanoacrylacid ethylester; Lely Turbo Inch., Istanbul/Turkey) was used to decrease the number of wires used and to prevent recurrent osteomyelitis. Cyanoacrylate glue was applied to the fractures and along the two sides of sternum; and sternum was closed with three or four 7 No steel wires. Skin and subcutanous tissue were closed en-block with heavy polypropylene sutures. Chest corset was routinely used in both two groups for 1 month postoperatively.

B- Animal model

The study design was approved by the Ethics Committee of Gülhane Military Medicine Academy (GATA) - Ankara, Turkey. And the study was carried out in GATA-Haydarpaşa medical school- İstanbul.

Ten wista albino adult rats with either sex, weighting 260 to 300g were selected for the study. The animals were fed a normal diet and received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the national society for Medical Research and the "Guide For The Care and Use of Laboratory Animals" Prepared by the National Academy of Sciences and published by the National Istitutes of Health (NIH) Publication No 85-23, revised 1985.

Ketamine 2 to 4 mg/kg was administered intraperitoneally. In each animal, sternum was exposed through a superior midline incision, and a superior midline sternotomy of 1,5 cm was done with the scissors. After ensuring the hemostasis with a sponge, 0,5 ml of S. Aureus bovine bouillon culture obtained from infected patients was injected in to the exposed sternal edges and the spongiosa. The sternum was left open and; subcutanous tissue and skin was closed en-block in 4 animals (Group A). In six animals (Group B) one drop of cyanoacrylate glue was applied to the open sternal surfaces and the wound closed in the same maner described for Group A. All animals were put in to the separate cages after completion of the procedure and followed-up, and then sacrified at the end of 3rd week (n=3) and 8th week (n=3) postoperatively. The sternum was removed and cross-sections were taken from the cyanoacrylate applied regions. The sections were stained with silver-nitrate; hematoxylene-eosine and Masson to assess the inflammatory response and foreign body reaction; recognise the connective tissue appearance and the effect of cyanoacrylate in the adjacent tissues.

RESULTS

A- Clinical study

The most frequent sign of mediastinal infection were leucocytosis (13 patients in Group I (76%) and 16 patients in Group II (88 %)). Sternal instability, drainage from the sternal wound and increased pain were the other common signs in both Groups.

Group I patients: All but 2 patients had bacterial growth from their mediastinal tissue samples. In 10 patients, Staphylococcus aureus was the significant pathogen. In 4 patients the pathogen was Klebsiella and Proteus in another. There was no mortality in this group.

Closed drainage and irrigation was used in four of 17 patients. Chronic suppurative fistula formation due to osteomyelitis developed in 6 patients (35,3%), 4 of which were treated with wire extirpation and local debridment. The other 2 patients needed wide sternal resection and bilateral pectoralis major muscle flap due to persistant osteomyelitis and dehiscence. The hospital stay after the first revision was 24,06±4,98 days (range 17 to 33 days). However, the treatment period required for cure lasted up to 99,8±26,7 days (range 30 to 720 days) due to multiple interventions to 6 patients with chronical osteomyelitis fistulas. The sum of the hospital stay in this group was 51,88±40,7 (range 17 to 150) days. Reintervention data and hospital stay are documented in Table II.

Group II patients: 16 patients had bacterial growth from their mediastinal tissue samples. In 10 patients, Staphylococcus aureus was the significant pathogen. In 3 patients the pathogen was Klebsiella; Proteus [1], Pseudomonas [1], and Enterobacter [1], were also isolated sporadically.

There was no mortality. No patients required plastic surgical intervention. Three patients (17%) required reintervention due to profuse serous drainage after the revision. There was no sternal dehiscence or osteomyelitis, in a second revison; simple debridement of cyanoacrylate was done. Hospital stay after the first revison was 14,1±3,9 days (range 10-24 days). All patients achieved excellent functional and cosmetic results and were discharged with closed stable sternums. There were no recurrent wound complications and no reintervention after discharge. Variables of revision procedures are shown in Table II.

B – Animal study

All animals in Group A died of sepsis in 4 to 7 days after the procedure.

All six rats in Group B survived the procedure and were sacrificed at the end of the 3rd week (n=3) and 8th week (n=4).

At 3rd week, there were no skin erythema or subcutanous seroma formation in all of the animals. Microbiologic cultures showed no growth. Bone was intact with no adhesion to the surrounding tissue. Glued sternal edges could be separated by force, and semitransparent, dirty white cyanoacrylate polymers were seen macroscopically. Silver nitrate stain showed destabilized crystalloid cyanoacrylate polymers (Figure 1) and

Table II. Variables of revision procedures.

		Group I	Group II
Postoperative first revision day		10,5±5,5 (ranged 5 to 28)	12,9±4,1 (ranged 6 to 21)
Revision number	1	11	15
	2	4	3
	>3	2	-
Osteomyelitis after 1st revision		6	-
First Hospitalisation period (day)*		24,06±4,98 (ranged 17 to 33)	14,1±3,98 (ranged 10 to 24)
Dewiring in the first 6 months		7	-
Dewiring after the first 6 months		2	-
Late fistula and revision (>1 year)		2	-
Total hospitalisation period (day)**		51,88±40,7 (ranged 17 to 150)	14,1±3,98 (ranged 10 to 24)
Time lasted for complet cure of sternal infection (day/patient)		99,8±26,7 (ranged 30 to 720)	14,1±3,98 (ranged 10 to 24)
Follow up period (month)		36,76±4 (ranged 31 to 44)	18,5±6,9 (ranged 6 to 31)

*The time period between the first revision and first hospital discharge of the patient; patients were discharged after stopped parenteral antibiotic treatment and daily wound care.
**Sum of the re-hospitalisation periods required for complete cure of the infection.

Figure 1. Third week microscopic view of the sternum: cyanoacrylate cristals were destabilized during cross section and staining (arrow). No destruction nor toxicity was observed in cyanoacrylate applied region. In adjascent tissues, Havers' canals were intact with normally arranged viable spongious bone cells. Silver nitrate stain (X20).

Figure 2. Third week microscopic view of the sternum. The polymers were washed-out during preparation. Increased fibroblastic activity at the adjascent spongious bone tissue can be seen (black arrow) with also increase of connective tissue and angioneogenesis (white arrow) in intercellular area. No inflammatory process indicating foreign body reaction was observed. H&E stain (X10).

preserved original bone structures on the adjacent tissues. Hematoxylene-eosin (H&E) stain showed increased fibroblastic activity at the adjascent tissues and no foreign body reaction (Figure 2) directed to cyanoacrylate.

At 8th week, both the cutaneous and subcutanous layers healed completely with a thin scarred tissue. There were no sternal adhesion to surrounding tissues, and the sternum could not be separated by force. H&E stain showed a formation of connective tissue filled in to the cyanoacrylate applied space and no more cyanoacrylate particles could be detected (Figure 3). Masson staining showed that the connective tissue consisted of collagen fibers which are almost arranged longitudinally between the two edges of the divided sternum (Figure 4).

DISCUSSION

Although the incidence of mediastinitis in

Figure 3. Eight week microscopic view of the sternum. Cyanoacrylate applied area is filled by a dense connective tissue. Cyanoacrylate polymers was entirely degraded and absorbed. Angiogenesis found to be decreased compared to of 3rd week findings. H&E stain (X4).

Figure 4. Eight week microscopic view of the sternum. Arrangement of collagen fibers and connective tissue cells (fibroblasts and osteoblasts). Masson stain (X20)

patients undergoing median sternotomy for open-heart surgery is low; the consequences for the individual patient and cost remain substantial. There is no concensus regarding the optimal management of poststernotomy mediastinitis. Whatever is the used procedure, recurrence after the revision remains a formidable problem, requiring more extensive procedures. Major plastic surgical procedures such as pectoral muscle or omental flaps carry higher risks due to extent of the operation (11). They assessed the functional and cosmetic results of 202 flaps performed in 133 patient. They reported a 7,5 % primary early failure rate. An abdominal or thoracic contour abnormality was found in 85%.

Pairolera and associates (6) reported the results of wound debridment with or without sternectomy followed by a pectoral muscle flap. Patients had an average of 1,6 previous attempts at operative management (range, zero to ten) and 13,2% had a recurrence of the wound infection. These results may suggest that there seems not a single procedure existing that could be applied successfully to all cases of mediastinitis.

Cyanoacrylate glue derivatives have been used as surgical adhesives and/or filling materials finding application in the fields of dental medicine, neurosurgery, plastic and reconstructive surgery, ophtalmology and finally in cardiac surgery (9,12). It gains adhesion quickly and has strong adhesive power. The cyanoacrylate derivatives were found to have an antibacterial effect on various microorganisms (13).

Cyanoacrylate applied to the contaminated wound edges has bactericidal and bacteriostatic effects (14). More recently, we and others (8,9) showed the antimicrobial properties of cyanoacrylate on various organisms. Caroli and associates (15) reported that cyanoacrylate is effective in bone stabilization and consolidation without a foreign body reaction. Amarante and associates (16) showed that n-butyl-2-cyanoacrylate is effective as plates and screws in the fixation of created osteotomies of the upper facial skeleton in animals. Histologic analysis demonstrated bony fusion and there was no statistical difference found in the comparison of maximum torque to failure between analogous plated and glued fragments.

Both by the antimicrobial effects and the promising results, its use on fractured bones prompted us to use cyanoacrylate to restore sternal integrity, to control infection and prevent recurrent osteomyelitis. Both the clinical and animal components of our study confirmed that cyanoacrylate prevents bacterial attachment and proliferation in bone tissue.

In the reported studies on bone, there were no observation of histotoxicity or foreign body reaction resulted by the application of cyanoacrylate. However, the application of cyanoacrylate in different tissues, can cause various amounts of foreign body reactions characterized by giant cell granulomatous responses (17). Toriumi and colleagues (18) reported that cyanoacrylate does not resultin any reaction when applied to areas deprived of vascularity, but on the other hand causes a strong foreign body reaction in high vascular areas like subcutaneous tissues.

In three of our patients, overuse of cyanoacrylate resulted in mediastinal and subcutanous spread of the glue which caused profuse serous drainage. These patients were taken to the operating room and excess cyanoacrylate particles were cleared and sternum rewired. The drainage stopped and there were no recurrent infections. We think that cyanoacrylate causes a strong foreign body reaction or histotoxicity on highly vascular tissues resulting in seroma formation. After this experience, we have limited the amount of cyanoacrylate to 2 ml, resulting with no more patients having this problem. Using a spray form of cyanoacrilate or an applicator that provide a thin layer application on the sternal edges, may prevent this complication.

In our experimental study on rats, as there were no foreign body reaction and sternal infection; it can be assumed that cyanoacrylate has a potent antimicrobial effect and histocompatible for bones. On the other hand, cyanoacrylate which was found to be not degraded at 3rd week, is a disadvantage for maintaining enough bone stability. In our study, we have not approximated the sternal

edges by using any suture in order to not to interfere with the foreign body reaction. Leaving the separated edges of the sternum resulted a large amount of cyanoacrylate between them and this excessive amount, could prevent early degradation and absorption of cyanoacrylate and might be the reason for late ossification. The sternal fixation seems to be ensured only by connective tissue consisted of collagen fibers at 8th week on the rats. This finding shows that overuse of cyanoacrylate in order to filling the sternal defects, may delay sternal ossification but may not cause sternal instability.

CONCLUSION

Our results suggest that, the use of cyanoacrylate glue is a valuable adjunct in the management of poststernotomy mediastinitis in order to prevent osteomyelitis and sternal dehiscence. Its use is safe and effective to reduce the cost and hospital stay by removing the necessity of reintervention procedures including the flap sternoplasty.

REFERENCES

1- Baskett RJ, Mac Daugall CE, Ross DB. Is mediastinitis a preventable complication? A ten-year review. Ann Thorac Surg 1999;67:462-5.

2- El Oakley RM, Wright JE. Postoperative mediastinitis: classification and management Ann Thorac Surg 1996;61:1030-6.

3- Demmy TL, Park SB, Liebler GA, Burkholder JA, Maher TD, Benckart DH, Magovern GJ. Recent experience with major sternal wound complications. Ann Thorac Surg 1990;49:458-62.

4- Jeevanadam V, Smith CR, Rose EA, Malm JR, Hugo NE. Single state management of sternal wound infections. J Thorac Cardiovasc Surg 1990;99:256-62.

5- Seguin JR, Loisance DY. Omental transposition for closure of median sternotomy following severe mediastinal and vascular infection. Chest 1985;88:684-6.

6- Pairolero PC, Arnold PG, Harris JB,. Long term results of pectoralis major muscle transposition for infected sternotomy wounds. Ann Surg 1991;213:583-9.

7- Calvat S, Trouillet JL, Nataf P, Vuagnat A, Chastre J, Gibert C. Closed drainage using redon catheters for local treatment of poststernotomy mediastinitis. Ann Thorac Surg 1996;61:195-201.

8- Ogus T, Emir M, Cicek S, Isik O. Prevention of recurrent osteomyelitis using cyanoacrylate gluing in mediastinitis [letter] Ann Thorac Surg 2000;70:1761-2.

9- Demirtaş MM, Çimen S, Ketenci B, Günay R, Akçar M, Özler A. Late follow-up of cyanoacrylate usage in cardiothoracic surgery. Asian Cardiovasc Thorac Ann 1999;7:195-9.

10- Rrobicsek F, Daugherty HK, Cook JW. The prevention and treatment of sternum separation following open-heart surgery. J Thorac Cardiovasc Surg 1977; 73:267-8.

11- Ringelman PR, VanderKolk CA, Cameron D, Baumgartner WA, Manson PN. Long-term results of flap reconstruction in median sternotomy wound infections. Plast Reconst Surg 1994;93:1208-14.

12- Robicsek F, Rielly JP, Marroum MC. The use of cyanoacrylate adhesive (krazy glue) in cardiac surgery. J Card Surg 1994; 9:353-6.

13- Blum GN, Nolte NA, Robertson P. In vitro determination of antimicrobial properties of two cyanoacrylate preparations. J Dent Res 1975;54:500-3.

14- Quinn J, Maw J, Ramotar K, Wenckebach G, Wells G. Octylcyanoacrylate tissue adhesive versussuture wound repair in acontaminated wound model. Surgery 1997;122:69-72.

15- Caroli A, Marcuzzi A, Limontini S, Maiorana A. An experimental study of a

cyanoacrylate biological adhesive in view of its use in the fixation of various fractures of the fingers. Ann Chir Main Memb Super 1997;16:138-45.
16- Ammarante MT, Constantinescu MA, O'connor D, Yarenchuk MJ. Cyanoacrylate fixation of the craniofascial skeleton: an experimental study. Plast Reconstr Surg 1995;95:639-46.
17- Green AR, Milling MA, Green AR. Butylcyanoacrylate adhesives in micro vascular surgery: an experimental pilot study. J Reconstr Microsurg 1986; 2:103-5.
18- Toriumi DM, Raslan WF, Friedman M, Tardy ME. Variable histotoxicity of histoacryl when used in a subcutaneous site: an experimental study. Laryngoscope 1991;101:339-43.