Solid Organ Injuries in Vietnam

Emergency Hemostasis With N-Butyl Cyanoacrylate Adhesive

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The military surgeon occasionally encounters extensive combat wounds of the liver, kidney, or retroperitoneal area where conventional techniques of hemostasis are not adequate. Consequently, extensive resections of the liver, loss of a kidney, or even death may result. At the very least, considerable effort, time and blood are expended in the combat situation where all three are in short supply.

The present report describes the clinical trial of an aerosol tissue adhesive spray developed by the US Army for use in achieving rapid hemostasis of the solid organs of combat casualties. The development and experimental testing of these materials has been reported by Leonard et al[1,2] and Matsumoto and co-workers.[3-5]

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Method

N-Butyl cyanoacrylate is packaged in sterile disposable bottles as a 25% solution in a liquid propellant (carbon tetrafluoride [Freon 14] and dichlorodifluoromethane [Freon 12]). This provides a controllable spray of variable particle size, depending on the rate of spray. Polymerization time is 20 or 30 seconds.

In a life-threatening situation or in one in which an organ would otherwise be sacrificed due to extensive persistent bleeding, the following technique is utilized. Occlusion of the vascular supply to the organ by digital pressure or a vascular clamp achieves temporary hemostasis. Then a sterile polyethylene sheet which accompanies the package of aerosol spray is draped over the area. A hole is cut in the sheeting which exposes the area to be sprayed but shields the adjacent normal tissues. The oozing surface is dried carefully. The spray is applied to the area and is allowed to polymerize on the naked surface, or alternatively, pressure is applied to the adhesive during polymerization. Such pressure may be applied in one of three possible ways: by the use of another polyethylene sheet to which the adhesive will not adhere; by use of a piece of omentum; or by reapproximation or

coaptation of the organ itself, ie, fractures of the liver or kidney. The use of pressure has several advantages: (1) hemostasis from the oozing surface is controlled during polymerization; (2) the layer of cyanoacrylate monomer is thinned to allow more rapid degradation; (3) adhesions to the area are minimized by the use of omentum or by organ reapproximation; and (4) the monomer film is more flexible. If a large area is to be sprayed, as in the wide loss of the retroperitoneal tissues, the spray may be applied to successive small areas in which temporary hemostasis can be achieved by manual pressure. In this way large areas of persistent oozing tissue can be covered with multiple applications.

Polymerization is signalled by the appearance of an opaque dry eschar on the surface of the organ. When polymerization is complete, the occluded vascular supply may be released. If bleeding recurs because hemostasis was not adequate during polymerization, it is best to remove the polymerized adhesive and repeat the procedure. The polymer can easily be removed from the surface of an organ with forceps when its seal to the organ is incomplete.

All patients have been recorded in a registry in the Division of Surgery at Walter Reed Army Institute of Research in order to determine the long-term results of spray application.

Results

The injuries treated with the N-butyl cyanoacrylate spray are summarized in the Table. The spray is particularly useful for achieving hemostasis in the liver, kidney, and the retroperitoneum. In addition, arterial anastomoses of five patients were reinforced with the polymer in order to expedite attending to other wounds in the same patient. One patient in whom liver hemostasis was achieved underwent laparotomy two weeks following application of the cyanoacrylate in order to control bleeding from a subsequent ulceration of the stomach. At this time the liver surface was dry and healing with few adhesions to the area. The following cases illustrate the use of spray and the problems which may be encountered.

Organ Injuries Treated by Cyanoacrylate Aerosol Spray

Organ	No. Patients	Failures
Liver	10	No. 1 mechanical failure of spray action
Kidney	3	No. 1 nephrectomy required due to injury of vascular pedicle
Retroperitoneum	5	No. 1 failure due to inadequate hemostasis
Vascular anastomosis reinforcement	5	No. 1 postoperative pelvic abscess

Report of Cases

CASE 1.—A 21-year-old soldier was admitted to the third Surgical Hospital (MASH), Republic of Vietnam on Aug 20, 1967, with a high velocity missile wound of his lower left thorax. The diaphragm was perforated; the left lobe of the liver was fractured, and the stomach and sigmoid colon were perforated.

After resection of the left lobe of the liver, hemostasis could not be achieved despite multiple sutures, the use of an absorbable gelatin sponge, and prolonged packing. The porta hepatis was occluded with digital pressure; the polyethylene sheet was draped over the wound to protect the remainder of the peritoneal cavity, and the spray was applied to the area of the liver resection. Immediate hemostasis was achieved. The area was drained but no serosanguineous drainage was seen after the first postoperative day and no biliary drainage was seen at any time.

CASE 2.—A 24-year-old soldier was wounded by a bullet which entered the right flank fracturing the right kidney, the right hepatic lobe, gallbladder, and then entered the hemithorax. Right nephrectomy and right hepatic lobectomy were performed. The larger vessels within the liver substance were individually ligated but persistent oozing remained. At this point more than 25 units of blood had been utilized during resuscitation and operation. Blood pressure was 80/40 mm Hg and pulse 120 beats per minute with the patient under anesthesia. Application of cyanoacrylate spray after temporary occlusion of the porta hepatis was followed by complete cessation of bleeding from the liver surface.

CASE 3.—A 24-year-old soldier was wounded in the sacral region and right buttock with fractures of the sacrum and right iliac bones. There was also extensive muscle and soft tissue injury. After debridement of the devitalized muscle, hemostasis, in an area measuring more than a foot square, could not be accomplished. At the time the aerosol spray was utilized, 22 units of blood had been administered, and no blood pressure could be obtained although a faint rapid pulse was palpable. The entire bleeding surface was packed and small areas were uncovered in turn and sprayed; pressure was applied with polyethylene sheeting. Hemostasis was complete. Further transfusion of three units of blood returned the vital signs to normal.

CASE 4.—A 34-year-old soldier was wounded by a single gunshot wound of the left flank. The small bowel was transected in four places; the transverse colon and the left lobe of the liver were perforated, and the lower pole of the left kidney was shattered. After several bowel resections, exteriorization of the transverse colon, and suture control of the bleeding left lobe of the liver, the lower pole of the kidney was resected. The remaining tissue could not be reapproximated with sutures, and oozing from the kidney was so profuse that resection was planned. The renal pedicle was occluded with digital pressure, and the polyethylene was draped across the field excluding the remainder of the peritoneal cavity. After application of the spray and release of the renal pedicle, hemostasis was complete. Results of postoperative intravenous pyelograms revealed absence of the left lower pole of the kidney but normal bilateral renal function had been established.

Comment.—The preceding four cases exemplify the successful use of the hemostatic spray in the liver, retroperitoneum, and kidney. Nineteen of the 23 cases treated up to this time are similar. In four cases,

imperfect results were achieved. Brief summaries of these cases follow.

CASE 5.—A 22-year-old soldier was shot through the right upper quadrant of the abdomen with an exit wound in the left mid-back. The diaphragm was perforated and the right kidney and right lobe of the liver were fractured. The right kidney and right lobe of the liver were resected. Following liver resection, persistent bleeding was apparent from the liver. The large vessels were not individually ligated. Occlusion of the porta hepatis by a vascular clamp did not slow bleeding to a point in which the spray could be applied to the relatively dry liver tissue. In addition, the spray bottle malfunction did not allow controlled application of the spray directly onto the liver surface. However, partial control of the bleeding from the liver surface was obtained in this way. Large bleeding points were then individually ligated, and hemostasis was acceptable.

Comment.—This case illustrates the important principle that large vessels within the substance of the liver should be ligated prior to spray application. Although experimentally, vessels of 1 to 2 mm lumen diameter can be occluded by the spray, rapid flow of blood from larger vessels of the liver whose vascular supply is never completely under control prevents adhesion of the monomer to the liver surface. The spray bottle has been redesigned and no further malfunctions have been encountered.

CASE 6.—A 22-year-old sailor was admitted to the Third Surgical Hospital with multiple fragment wounds of the abdomen and lower extremities. The left kidney was widely shattered in its mid-portion. After debridement continual bleeding could not be controlled. The renal pedicle was shut off with a vascular clamp, and the kidney was delivered into the wound to expose the posterior surface. Application of the spray achieved hemostasis and the vascular clamp was removed. Circulation did not return to the kidney, which appeared congested and cyanotic. Renal vein thrombosis was not found after nephrectomy, but venous thrombosis secondary to renal pedicle occlusion probably caused the difficulty.

Comment.—Prolonged clamping of the renal pedicle and rotation of the kidney into the wound resulted in vascular compromise necessitating nephrectomy. We have since found that digital compression of the renal pedicle is simpler and less dangerous than vascular clamps in these circumstances.

CASE 7.—A Vietnamese National policeman was admitted in severe shock after receiving a high velocity missile wound of the abdomen with an exit wound in the back. The right retroperitoneal area was extensively damaged with laceration of the vena cava below the renal veins and destruction of the right kidney. The vena cava was ligated at the level of the laceration and the right kidney was removed. Continual profuse bleeding from the right retroperitoneal area required the use of 50 units of whole blood. The bleeding could not be stemmed for more than a few seconds with packs. In desperation, the area was packed and the spray applied as the packs were removed. There was no time for the monomer to polymerize before the area was flooded with blood. The patient was exsanguinated.

Comment.—This case exemplifies the situation in which the adhesive did not remain in contact with the tissue due to profuse bleeding. The adhesive polymerizes on the surface of the blood and cannot occlude for bleeding vessels. The monomer must be in contact with the tissue itself for 20 to 30 seconds to achieve hemostasis. Segmental application of the monomer is one solution to this problem as exemplified in case 3.

CASE 8.—A 22-year-old soldier was admitted with a gunshot wound of the abdomen that had transected the sigmoid colon and had done massive damage to the left pelvic retroperitoneum. The area of sigmoid damage was exteriorized and the pelvis was extensively irrigated with saline. The pelvic retroperitoneal tissues continued to bleed, and 4,000 ml of blood replacement were required over the hour prior to spray application. The entire area was packed and the pack was removed in segments with prompt application of the spray. Hemostasis appeared complete and the abdomen was closed. One week postoperatively, there was sudden evidence of intraperitoneal hemorrhage and reoperation was necessary. A laceration of the external iliac artery was found with a pseudoaneurysm formation which subsequently broke down.

The bleeding vessel was not in the area of spray application which appeared dry. A saphenous vein graft was utilized to bridge the gap in the iliac artery, but this broke down in the presence of infection three days later. Ligation of the external iliac artery was required. The patient died with pelvic sepsis after a stormy course two weeks later.

Comment.—The laceration in the wall of the iliac artery was missed during the original resuscitative surgery. Extensive contamination may have contributed to the pseudoaneurysm in this area. Although cyanoacrylate was not applied in the area of the arterial laceration, it did provide a foreign body which may have contributed to the patient's death from pelvic sepsis. This is the only case of infection in the area of adhesive application. Clinical experience indicates that careful search for arterial injury is always necessary in patients with extensive retroperitoneal injuries.

Comment on All Cases

A number of authors report the successful use of methyl 2-cyanoacrylate tissue adhesive for hemostasis of various wounds of the liver, spleen, and pancreas. However, methyl 2-cyanoacrylate has been found to be extremely toxic to tissues and its acceptance has not been widespread. Leonard and his associates have developed a series of higher homologues of the cyanoacrylate monomers which are less histotoxic. Matsumoto et al have developed a series of techniques for the application of these monomers to various surgical circumstances including vascular and intestinal anastomosis, treatment of recurrent pneumothorax, and the repair of bisected kidneys for the removal of staghorn calculi. In the application of these compounds to the control of tissue surface-bleeding, the relative characteristics in respect to wetability, spreadability, and rapidity of polymerization had to be considered. Collins has shown that the

higher homologues wet, spread, and instantly polymerize on the surface of blood and are therefore more effective than the lower homologues in inducing hemostasis. The lower homologues (methyl, ethyl, and propyl cyanoacrylate) do not spread but form droplets on the tissue surface, thus incompletely covering the surface as well as slowing polymerization time. In addition it was found that with the spray application, a very fine uniform film of the higher homologues could be applied rapidly, covering the surface and further hastening polymerization time. Spraying also minimizes the amount of monomer needed and lessens the degree of histotoxicity. N-Butyl cyanoacrylate was chosen from among the other higher homologues because polymerization time is slow enough to allow time for surgical manipulations (20 to 30 seconds), and the film is thick enough to bind heavy tissues together. The Freon propellant itself is not histotoxic and freezing has been minimized by mixing Freon 12 with Freon 14 in the appropriate proportions. Neither the cyanoacrylates themselves nor the freon propellant is bacteriostatic or bacteriocidal. Prior to packaging, the monomer is heat sterilized and the freon is sterilized by filtration. After packaging, gas sterilization is carried out.

Summary

The present report is designed to emphasize not only the advantages, but also the limitations, of an aerosol tissue adhesive utilized for hemostasis in emergency circumstances in a combat zone. It is apparent that the spray is highly effective in achieving hemostasis when other methods fail. If life is threatened or the sacrifice of an organ would be detrimental to recovery, the material is applied. Temporary malfunction of the spray device contributed to one failure. Redesign of the gaskets has alleviated this problem. Two failures occurred when sufficient temporary hemostasis could not be achieved in order to allow the adhesive to bond to the tissue without intervening blood. A third patient lost a potentially salvageable kidney due to excessive manipulation of the vascular pedicle. A fourth patient developed a pelvic infection in a highly contaminated pelvis after rectal transection. The potential danger of inserting any foreign body into a contaminated area is well known and is reemphasized here. In addition to these problems, the higher homologues of cyanoacrylate are only slowly degraded within the body. Although no experimental evidence indicates that this material is potentially carcinogenic, the problem has not been fully investigated. Because of these real and potential problems, and other evidence that the polymer interferes with capillary growth and collagen deposition across the line of adhesion, we feel that the use of the spray should be restricted to life and organ threatening emergency situations at present.

References

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