SURGICAL OPINION

The Use of Cyanoacrylate in Surgical Anastomosis: An Alternative to Microsurgery

G. M. Bot, K. G. Bot[1], J. O. Ogunranti[2], J. A. Onah[2], A. Z. Sule, I. Hassan[3], E. D. Dung

Department of Surgery, Jos University Teaching Hospital, [1]Faculty of Medical Science, University of Jos, [2]Department of Anatomy, University of Jos, [3]Department of Surgery, Aminu Kano University Teaching Hospital, Plateau State, Nigeria

ABSTRACT

To present anastomosis with cyanoacrylate as a cheap, simple, fast, and available technique for anastomosis in urological, vascular, gynecological, and general surgical procedures. This method may in the future be a good alternative to microsurgery, particularly in centers where facilities are unavailable and the financial implication is unbearable for the patient. Cyanoacrylate is an adhesive or glue that is available in different chemical forms ranging from ethylcyanoacrylate (superglue) to Isobutylcyanoacrylate and octylcyanoacrylate (dermerbond), which is in clinical use. Anastomosis with cyanoacrylate requires the application of stay sutures, a luminal stent and the subsequent application of the adhesive. The adhesives with lower molecular weights produce a rigid and patent region of anastomosis, while the higher molecular compounds produce a consistency close to the normal tissue. This technique presents a surgical method that is socially, culturally, and ethically acceptable, which is affordable to a larger majority of patients in our subregion. Cyanoacrylate anastomosis may in the future present a fast, convenient, simple, and affordable option in the treatment of patients requiring anastomosis. In our subregion where the socio-cultural, psychological, and economic burden of failed anastomosis is high, associated with the low per capital income, this may be a novel option for the management of urogynecological, vascular, neurosurgical, and general surgical procedures requiring either microscopic or macroscopic anastomosis.

Key words: Alternative, anastomosis, cyanoacrylate, microsurgery, limited, resource, subregion

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INTRODUCTION

The use of cyanoacrylate is not widespread despite a number of published studies on the subject.[1] Cyanoacrylate is an adhesive that was first discovered by Dr. Harry Coover and Fred Joyner in the Kodak laboratory.[2] Cyanoacrylates were first synthesized by Airdis in 1949, while Coover *et al.* described their adhesive property and suggested their possible use as surgical adhesives in the 1960s.[3,4] There are different types ranging from ethylcyanoarylate (super glue) to isobutylcyanoacrylate and octylcyanoacrylate (dermabond, which is approved by the food and drug agency of the United State of America). The physical properties of the glue differ based on the molecular weight of the chemical. Even as the low molecular weight ones are more rigid and fairly more toxic, the higher molecular weight substances are stronger, more pliable, and less toxic.[3,4]

An anastomosis is a surgical connection between two structures. It usually means a connection that is created between tubular structures, such as blood vessels or loops of the intestine. The word anastomosis is derived from two Greek words, which literarily means without a mouth, that is, when a tubular viscus (bowel) or vessel is joined after resection or bypass without exteriorization with a stoma, or having been tied off.[1] Anastomoses in the bowel were not undertaken successfully until the nineteenth century. Prior to that period the experience was limited to exteriorization or simple closure of the laceration. In 1826, Lembert described the seromuscular suture technique, which became the main stay in bowel anastomosis. Senn recommended the two-layer closure, while Halsted showed preference for the one-layered closure where the mucosa was not incorporated. Connell later described the single layer of interrupted sutures incorporating all layers of the bowel. This was further modified to the through-and-through continuous single layer with a 'loop-on-the-mucosa' suture, which is otherwise called the Connell stitch. Kocher developed the two-layer closure, inner continuous, and outer interrupted stitches. Currently the single layer extramucosal anastomosis by Metheson of Aberdeen is advocated because it produces the least necrosis, narrowing of lumen, and adequate tensile strength.[1] In vascular anastomosis, which was pioneered by Carrel, an everting anastomosis was advocated, with triangular stay sutures,

Address for correspondence: *Dr. Gyang Markus Bot, Department of Surgery, Jos University Teaching Hospital, PMB 2076 Jos, Plateau State, Nigeria. E-mail: gyangbot@yahoo.co.uk*

to ease the application of the continuous monofilament sutures.[1]

Currently, several suture substitutes have been used such as staples and adhesive glues. The basic principles of bowel, vascular, and urogynecological anastomosis must be taken into consideration. In bowel surgery, locally, at the site of anastomosis, there must be a good supply of blood, inverting sutures applied, accurate tissue apposition, and avoidance of tissue damage, while systemic considerations include prophylactic antibiotics, adequate oxygenation, correction of shock, and good nutritional rehabilitation. In vascular surgery, the considerations include, proximal and distal vascular control, minimal tissue handling, proline-like sutures are used, knotts are secured, the sutures are passed from inside out to fix any arteromatous plaque, and anticoagulants are used.[1]

The use of cyanoacrylate for anastomosis of vessels, the urogenital tract, and bowel have been reported in different experimental models ranging from rat to rabbits, and dogs and monkeys, with varying outcomes.[5-8]

Stricture and ureterocutaneous fistula for the urologist, enterocutenous fistula for the general surgeon, failed arterovenous fistula for the vascular surgeon, mediastinitis from esophageal leak for the cardiothoracic surgeon, and tubal infertility for the gynecologist, are conditions that pose significant management difficulty. However, cyanoacrylate anastomosis may provide a way to overcome these obstacles in the future.

DISCUSSION

The surgical use of cyanoacrylate for surgical apposition of wound edges, hemostasis, and embolization has been documented in humans.[4,9,10] However; the use of cyanoacrylate in surgical anastomosis, to the best of our knowledge, has not been reported in humans and if it has been, then there are very few cases. This technique in experimental animals, however, is well established.

The surgical use of cyanoacrylate in experimental animals is well known. Experimentally, it is used in urology, vascular surgery, gynecology, and gastrointestinal surgery. In urology a study by Merimsky and Baratz on 10 dogs showed that ureteroureteral anastomosis resulted in good anastomosis with no untoward reaction.[7] It was also seen that urethral and spongiosal healing was excellent when Gluban 2 a cyanoacrylate was used for anastomosis. However, when the cyanoacrylated was applied to an incised tunica albuginea it led to irregularity of the layer, with inflammation, necrosis, deformation of spermatogenesis, and partial deformation of the sertoli and leydig cell.[11]

Another study in mongrel hounds shows that cyanoacrylate appears to be unsuitable for use in forming the large-diameter vesicourethral anastomosis required in radical prostatectomy.[8] In vascular surgery, cyanoacrylate might be a good alternative to sutures (in anastomosis of arterovenous shunts and bypass procedures in microsurgery).[12-14] In gastrointestinal surgery, while it appears to be useful in esophageal anastomosis and gastroenterostomy, the usefulness in colonic anastomosis is still questioned.[15-18] Cyanoacrylate may therefore be relevant as a sealant and also for reinforcement of sutures in the colon. Cardiothoracic surgeons have used cyanoacrylate to reinforce bronchial anastomosis after pulmonary resection. Surprisingly, its untoward effect of increased inflammatory reaction is observed to accelerate Wallerian degeneration, and it may therefore have a more beneficial effect compared to sutures for reconstruction of peripheral nerves.[19]

Cyanoacrylate may in the future be used in humans for anastomosis of vessels, intestines and the urethra.

The surgical techniques involved in the use of cyanoacrylate for surgical anastomosis can be divided into two. The first involves the use of cyanoacrylate as the main agent of anastomosis. While in the second it serves as a sealant and for reinforcement of an anastomosis. In the first technique where cyanoacrylate is the main agent of anastomosis, ethical clearance is obtained and the subject anesthetized. The region to be anastomosed is exposed. If a resection has been done the two ends are approximated and apposed with four to six stay sutures and the glue is then carefully applied, to ensure that there is no spillage into the lumen. A period of 45 - 90 seconds is allowed for polymerization. There is the lid technique, which is used in microvascular anastomosis. In this method a combination of sutures and cyanoacrylate is used. At the distal end of the vessel two parallel incisions are made at 180 degrees. Two sutures are placed from the proximal end to the exit at the most distal part of the longitudinal incision. The adhesive is then applied to the proximal vessel and the full-thickness vascular 'lid', and the flap is closed over it on the anterior and posterior surfaces.[20] In the second technique it serves to reinforce and seal the suture anastomosis. In this case a conventional suture is applied after which cyanoacrylate is applied. This is very useful when the risk of anastomotic leak is high (either due to technical competence, degree of contamination and peritoneal soilage or a poor nutritional state of the

patient) or the mortality associated with anastomotic leak is high (e.g., esophageal leak leading to mediastinitis). This method will probably be useful in esophagogastrointestinal surgeries. In esopghageal surgeries, 'the technical goal of all esophageal surgeons is a zero anastomotic leak'.[21] This is because esophagovisceral anastomotic leaks are the bane of thoracic surgeons, associated with 10 – 30% mortality.[22] 'Leak of an anastomosis between two hollow organs is one of the most serious complications a surgeon will ever encounter'.[23]

A review of the literature for vascular, esophageal, tracheal, gastrointestinal, common bile duct, ureteral, vas deferens, and Fallopian tube adhesive anastomosis indicates that reduced suture adhesive anastomosis and sutureless adhesive anastomosis procedures may be performed with less training, reduced operating time, leakage, ischemia, inflammation, necrosis, and better tube patency compared to sutured techniques.[24] While, training in the microsurgical technique would require between 40 and 70 hours, the use of cyanoacrylate has a brief learning curve, such that Dr. Peter Rubin of the University of Pittsburgh stated that it was 'off the shelf and ready to use'. When considering the duration of anastomosis using cyanoacrylate and sutures, studies on the intestine, vessels, vas deferens, and others indicate a statistically significant reduction in operation time. Gurhan *et al.* showed a reduction in operation time between the control and study sample with a timing of 16.2 and 10.7 minutes, respectively.[20] Ang *et al.* had a *P* value of < 0.001 for reduction in vascular anastomotic time;[25] Busato *et al.* had a statistically significant reduction in time of anastomosis, with a *P* value of < 0.05 and timing of 24.6 ± 1.8 minutes and 9.35 ± 0.78 minutes for the control and study group during a vasovasotomy.[26] The patency of anastomosis with cyanoacrylate is better; in a study by Haj *et al.* it was seen that histologically that there were less foreign body granulomas.[5] Takenaka *et al.* clearly showed that cyanoacrylate anastomosis prevents anastomotic neointimal hyperplasia.[27] The patency of the structure involved is very important, the work of Ang and co-workers showed 90% patency when cyanoacrylate was used for anastomosis as opposed to 85% for conventional sutures in vascular anastomosis.[25] Busato *et al.* showed an 80% patency for the cyanoacrylate group and 75% for sutures, following vasovasotomy.[26] The apposition of the wall was without tension, hence, there was less ischemia and reduced risk of necrosis and subsequent anastomotic leak. The tensile strength of the anastomosis was also worthy of note, Intestinal tensile strength was equal for both cyanoacrylate and sutures in the study by Elemen *et al.*[28] However, the review of several studies by Detweiler *et al.* showed a reduction in the burst pressure of the intestine of small pigs and colon of rat on the fourth day, which then returns back to normal by the seventh day, but the mortality was not affected and there was no stenosis.[24] In the vessels there appeared to be a superior tensile strength when cyanoacrylate was used, with similar stiffness, but without adverse effects to the surrounding tissue,[29] these therefore would probably make the development of an aneurysm at the anastomotic site far-fetched.

In the guidelines for the use of dermabond, its use was limited to skin because of its relative toxicity, and was not recommended for use in areas of the body with significant moisture, such as, the foot and hands, except if splinted and wounds were at risk of poor healing.[30,31] Considering the toxicity of cyanoacrylate, the study by Ang showed that when he used dermabond there were less inflammatory cells compared to when sutures were used, and when studied from the first week to the sixth month there was no evidence that 2-octylcyanoacrylate caused toxicity to the vessel wall, hence the toxic profile of these agents should be closely studied.[29] The recommendation that it should not be used in moist areas does not really have a hold in anastomosis, as it is used even in corneal lacerations[32] and it is only affected when there is excessive wound seepage, before the wound is closed, besides when applied for anastomosis the aim is not to get it into the mucosal layer. Although, it may be argued that if it cannot be used for the digit, then the tensile strength is not good enough to hold an anastomosis, studies have shown that the tensile strength is the same with sutures except in the intestine of a pig and the colon of a rat, where there was a reduction in tensile strength, which returned back to equal that of the sutures on the seventh day, with no associate increase in mortality.[24] It was also possible to use stents to ensure the strength on the anastomosis, the stent could be soluble or otherwise.[33] The avoidance of the use of cyanoacrylate in wounds at the risk of poor healing is not rock solid, this is due to the fact that although it is believed that skin strength decreases by 27% after seven days in diabetics, a study has shown that the strength of colonic anastomosis is not influenced by diabetes.[34]

The possible complication of this technique includes leakage either of glue into the lumen or an anastomotic leak; these could be avoided by the application of stay or anchor sutures or by the use of the lid technique described earlier.[5] The application of three layers of cyanoacrylate is also helpful.

Socially and culturally, this method of anastomosis ensures that the failure rate of anastomosis is reduced.

It ensures that families suffer less from the lost of loved ones following anastomotic leak. In the esophagus for example it may reduce the risk of mediastinitis following esophagectomy. It may also reduce the risk of enterocutaneous fistula, with its attendant social problem, which may lead to depression and an inability to do normal social functions, because of the fear of fecal soilage in public, particularly in our environment where colostomy bags are not readily available. Cyanoacrylate has also been used for the treatment of vesicovaginal fistula, which has immense social problems sometimes leading to divorce because of the stench associated with urinary incontinence. Even the surgeons sometimes fear these complications,[21,22] as it could lead to energy sapping repeated surgeries, with poor outcomes, or sometimes it could lead to a form of an albertus syndrome if managed non-operatively, where the patient just keeps on pestering the surgeon by continually asking when the fistula will close.

Economically, anastomosis with cyanoacrylate is by far cheaper than a microsurgical operation. It would cost about fourteen thousand dollars to obtain an operating microscope,[35] which could be used for several patients and between one dollar to nine dollars to obtain a suture. While, super glue cost twenty cents and dermabond cost between twenty-four to thirty-two dollars,[31] with an additional surgical fee (including anesthesia and surgical items) of about three hundred and thirty dollars in most teaching hospitals in Nigeria. It further reduces the economic burden associated with the management of the patient with anastomotic failures, which are associated with a long hospital stay and sometimes repeated surgeries. These patients probably spend more on antibiotic and intravenous fluid resuscitation. In gynecology, it may present an alternative to microsurgery and *in vitro* fertilization, for the management of tubal infertility, in which the cost of treatment, that is, microsurgery or *in vitro* fertilization is unbearably high for the common man.[36]

Ethically, although only 2-octylcyanoacrylate is approved by the food and drug administration of the United State of America for use to appose skin lacerations, results from some experimental studies have shown that cyanoacrylate is not as toxic as it was initially thought to be; hence it is safe.[9,13,37] It will therefore be necessary for this substance to undergo standard experimental and clinical trials aimed at certifying it fit for use in anastomosis

CONCLUSION

The use of cyanoacrylalate presents a possible technique for the future management of urological, vascular, gynecological, general surgical, and some neurosurgical anastomosis in humans, which is cheap, available, simple, and convenient. It may probably be a good alternative to microsurgery, and with further development in the area, this method may probably be economically, socially, culturally, and ethically acceptable in the future.

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