COMPARATIVE STUDY BETWEEN SUTURED INTESTINAL ANASTOMOSIS AND THAT REINFORCED WITH CYANOACRYLATE TISSUE ADHESIVE

By

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ABSTRACT

Background: This experimental study evaluated the effectiveness and safety of using cyanoacrylate tissue adhesive for reinforcement of intestinal anastomosis and as a protective seal to prevent leakage.

Methods: Twenty healthy adult model rabbits weighting 2000 ± 100 gm were included in this study. They were divided into two groups. Group I (experimental group) underwent intestinal resection anastomosis with one interrupted vicryl layer sutures , and N- butyl -2- cyanoacrylate as a tissue adhesive for reinforcement of anastomosis, while in group II (control group) the anastomosis was performed with one interrupted vicryl layer without cyanoacrylate . After 15 days the ileum was gently removed and assessed for wound infection, anastomotic leakage, adhesions, and for anastomotic stricture. The assessment also included pathological evaluation for inflammatory cell infiltration and collagen deposition.

Results: There was no statistically significant difference in anastomotic leakage, adhesions and anastomotic stricture. There was significantly lower inflammatory reaction and collagen deposition in the experimental group (I) when compared with the control group (II).

Conclusion: In this study we confirmed the effectiveness of N – butyl -2- cyanoacrylate for reinforcement of intestinal anastomosis, as an immediate sealing of the tissues and as support to the physiological wound healing process.

INTRODUCTION

Intestinal anastomosis is defined as the creation of a connection between two intestinal segments to re-establish intestinal continuity (1). Techniques for intestinal anastomosis include hand-sewn suture techniques, stapled techniques, and sutureless anastomosis. Various tissue sealants have been tested including fibrin glue, with or without a collagen patch, platelet-rich plasma or cyanoacrylate adhesives (2).

The tissue adhesive N-butyl-2-cyanoacrylate (Histoacryl) is used in many fields of surgery. It had positive effects in terms of increasing anastomotic burst pressures (ABP) both with and without the initial ischemia- reperfusion insult. However, it had the adverse effect of significantly increasing the number of intra-abdominal adhesions (3).

Factors associated with poor intestinal anastomosis healing may be local factors including tissue hypoperfusion, anastomotic tension, poor apposition of wound edges, local infection, radiation injury or distal obstruction, or systemic factors including malnutrition, blood transfusion, hypovolemic shock, immunodeficient state, poorly controlled diabetes or jaundice (4).

Parallel to the research on factors that might negatively impact anastomosis healing, researchers are also exploring new materials and techniques that could prevent or minimize the risk of anastomosis dehiscence. The basic and seemingly simple aim of sutured or stapled anastomosis construction is to secure an appropriate edge-to-edge apposition for healing. It is necessary to achieve optimal distance, freedom from tension and suitable suture or staple tightness to ensure appropriate blood perfusion to the connected parts of the intestine (5).

Cyanoacrylate tissue adhesives provide another option and alternative approach to traditional suture techniques. Considering their mechanical, physical and biological properties, tissue glues should facilitate an optimal bond between anastomosed sections of the intestine with negligible negative effects on intestinal wall perfusion (5, 6).

The aim of this experimental study was to evaluate the effectiveness and to explore the technical and biological potential of cyanoacrylate tissue adhesive

for reinforcement of intestinal anastomosis and as a protective seal to prevent leakage.

MATERIALS AND METHODS

The present study is a comparative experimental study, conducted at excremental laboratory at the department of general surgery, faculty of medicine, Zagazig University in the period between February 2013 and July 2013.

Materials:

Twenty healthy adult model rabbits weighting 2000±100 gm were included in the study. They were divided into two groups; group I (experimental group) underwent intestinal resection anastomosis with one layer sutures, and N-butyl-2-cyanoacrylate as a tissue adhesive for reinforcement of the anastomosis, while in group II (control group) the anastomosis was performed with one layer sutures without using N-butyl-2-cyanoacrylate.

Methods:

- **Preoperative preparation:**

All rabbits received tetracycline (12.5mg/kg IM per day) 5 days prior to surgery and were premedicated with buprenorphine (0.03 mg/kg) and midazolam (1.3 mg/kg) 15min before anaesthetic induction.

- **Surgical procedure**

Rabbits were induced with 5% isoflurane followed by 2-4% isoflurane maintenance with 3L/min delivered via a tight-fitting face mask.

The ventral side of the rabbit was shaved and the skin disinfected with surgical betadine. A 5-7 cm incision was made on the ventral midline and the ileum was isolated and resection anastomosis was done in group I (experimental group) with one interrupted 4/0 vicryl layer sutures , and reinforced with N- butyl -2-cyanoacrylate (fig 1,2), while in group II (control group) the anastomosis was performed one interrupted 4/0 vicryl layer without cyanoacrylate.

The ileum was placed back into the abdominal cavity, and muscle layer closed with 2/0 vicryl (polyglactin) single interrupted sutures, and skin layer closed using 3/0 vicryl (polygelatin) sutures.

- **Postoperative care:**

After surgery rabbits were given post-operative analgesia (buprenorphine 0.03 mg/kg IM) . All rabbits received tetracycline (12.5 mg/kg IM per day) for 7 days after surgery.

After 15 days the animals were anaesthetized and ileum gently removed and assessed (fig 3).

- **Postoperative evaluation:**

Gross evaluation: by examining the anastomosis for wound infection, anastomotic leakage, anastomotic stricture and adhesion formation. The adhesions around the anastomosis were evaluated as 0, no adhesions; 1, mild adhesions, mainly between the anastomosis and omentum; 2, moderate adhesions, between the omentum and anastomosis and between the anastomosis and a loop of small bowel; and 3, severe, extensive adhesions, including abscess formation.

Anastomotic stricture was evaluated as follows: none, no pre-anastomotic colonic dilatation and stool passes freely; mild, solid stool passes, but mild pre-anastomotic colonic dilatation; moderate, solid stool not passing, but liquid stool passes; severe, no stool passes, but infused fluid passes.

Pathological evaluation: Inflammatory cell infiltration, fibroblasts, neovascularization, and collagen deposition were graded from 0 to 3, as follows: 0, no alteration; 1, mild; 2, moderate; and 3, dense.

- **Statistical analysis**

Continuous data were expressed in the form of mean ± SD while categorical data were expressed in the form of count and percent. Comparison of continuous data was performed utilizing student t test, while categorical data were compared using Chi-square test. P value less than 0.05 was considered statistically significant.

RESULTS

Wound infection, anastomotic leakage and peritonitis were not observed

in group I (experimental group). There was a single death in group II (control group), which occurred on the 7th post-operative day. The cause of death was anastomotic leakage and peritonitis, with no significant statistically difference between them as shown in table (1).

Table (1): Wound infection and anastomotic leakage in the studied groups.

	Experimental group N =10	Control group N=10	Chi-square test	
			X^2	P
Wound Infection	-	-	0.0	1.0
Anastomotic Leakage	-	1	0.0	1.0

Adhesion formation was present in 8 cases in group I (experimental group) and 6 cases in group II (control) as shown in table (2), with no statistically significant difference between the studied groups

Table (2): Frequency and severity of adhesions in the studied group.

	Experimental group N =10	Control group N=10	Chi-square test	
			X^2	p
None	2	4		
Mild Adhesion	3	3		
Moderate Adhesion	4	3	1.8	0.63
Severe adhesion	1	-		

Anastomotic stricture was present in 5 cases in group I and in 2 cases only in group II, with no statistically significant difference between the studied groups as shown in table (3)

Table (3): Frequency and severity of strictures in the studied groups.

	Experimental N =10	Control N=10	Chi-square test	
			X^2	P
None	5	8		
Mild stricture	2	1		
Moderate stricture	1	1	3.2	0.39
Severe stricture	2	-		

Upon pathological examination, there was significantly lower inflammatory reaction and collagen deposition in the experimental group (I) when compared with the control group (II) as shown in table (4) , (fig 4-7).

Table (4): The pathological outcomes.

	Experimental group N =10	Control group N=10	Student t test	
			t	p
Inflammatory infiltration	1.2 ± 0.78	2.0 ± 0.81	-2.2	0.038*
Neo-vascularization	1.3 ± 0.82	1.5 ± 0.7	-0.58	0.56
Collagen deposition	0.0	0.6 ± 0.51	-3.67	0.005*

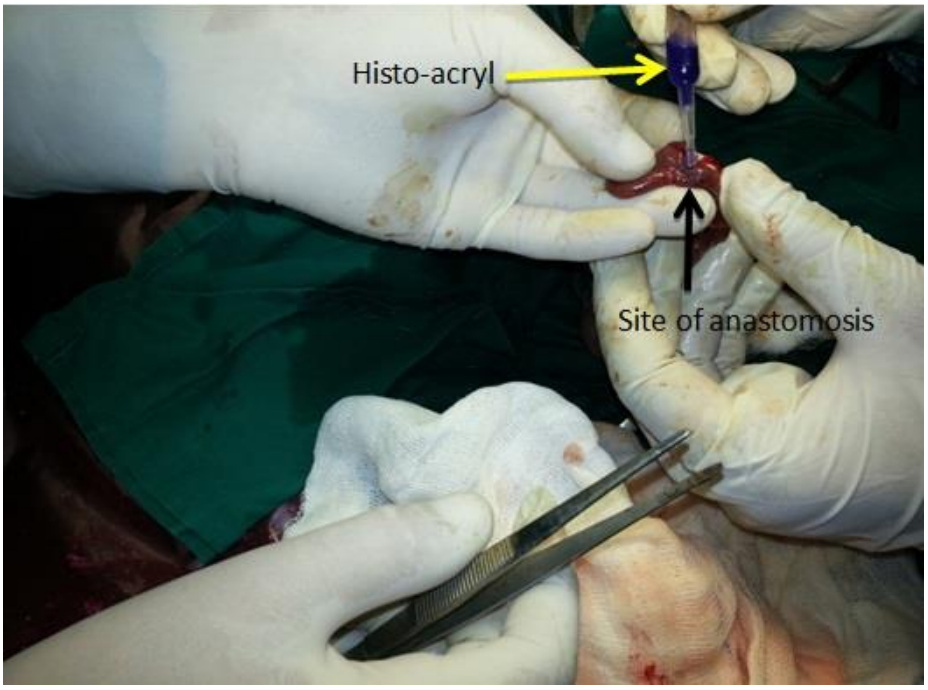

Fig (1): Application of histoacryl over the site of intestinal anastomosis.

Fig (2): Thin film of histoacryl coats the whole circumference of the anastomosis.

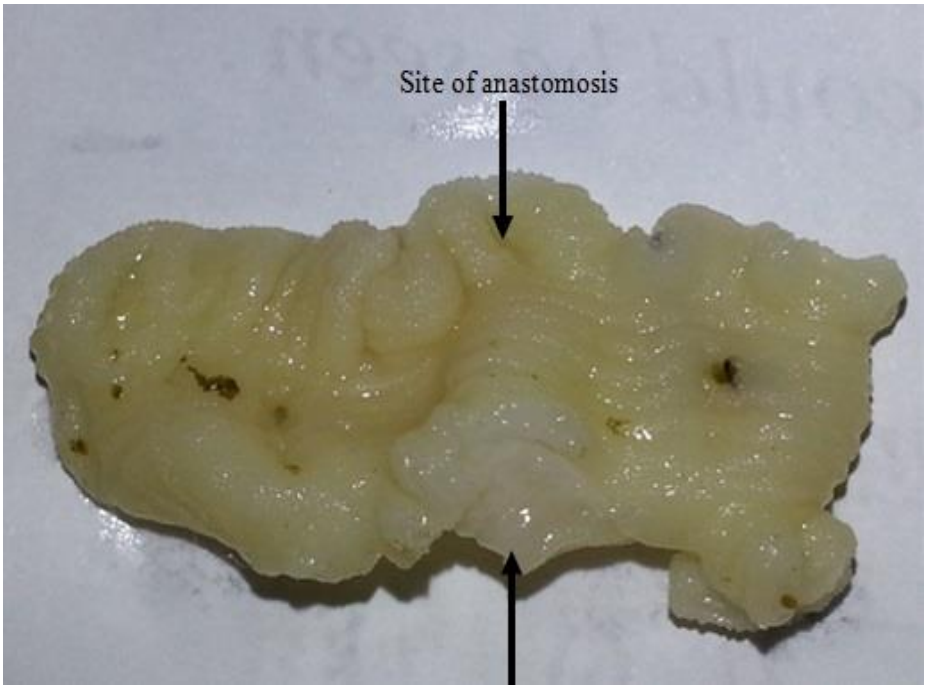

Fig (3): Gross picture of the intestinal lumen of rabbit after resection anastomosis with Histoacryl reinforcement.

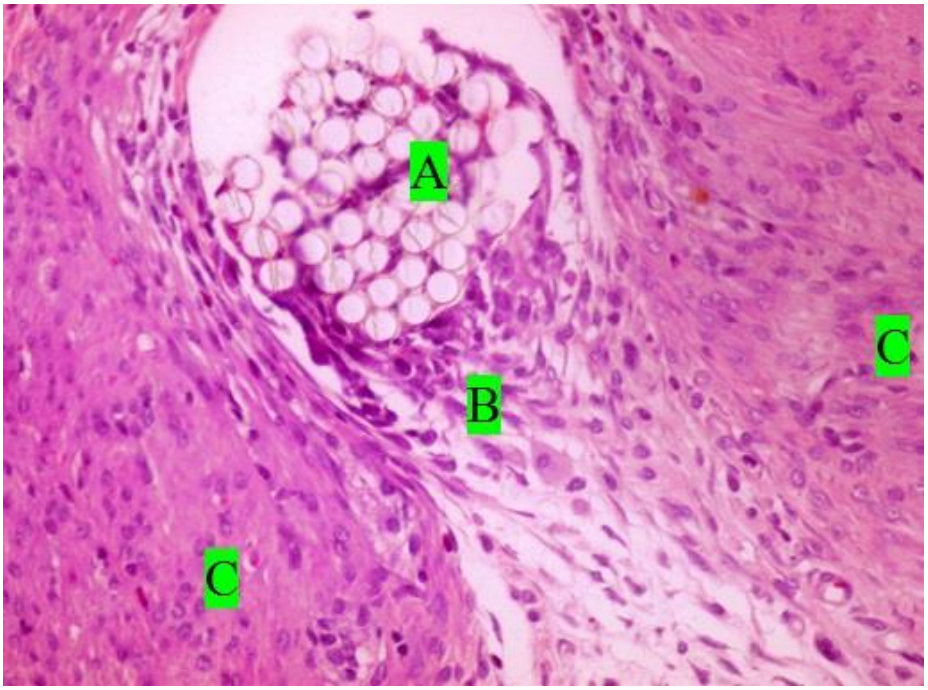

Fig (4): Suture material (A) covered by a few inflammatory cells (B) and a layer of granulation tissue (C) at site of usual resection anastomosis.

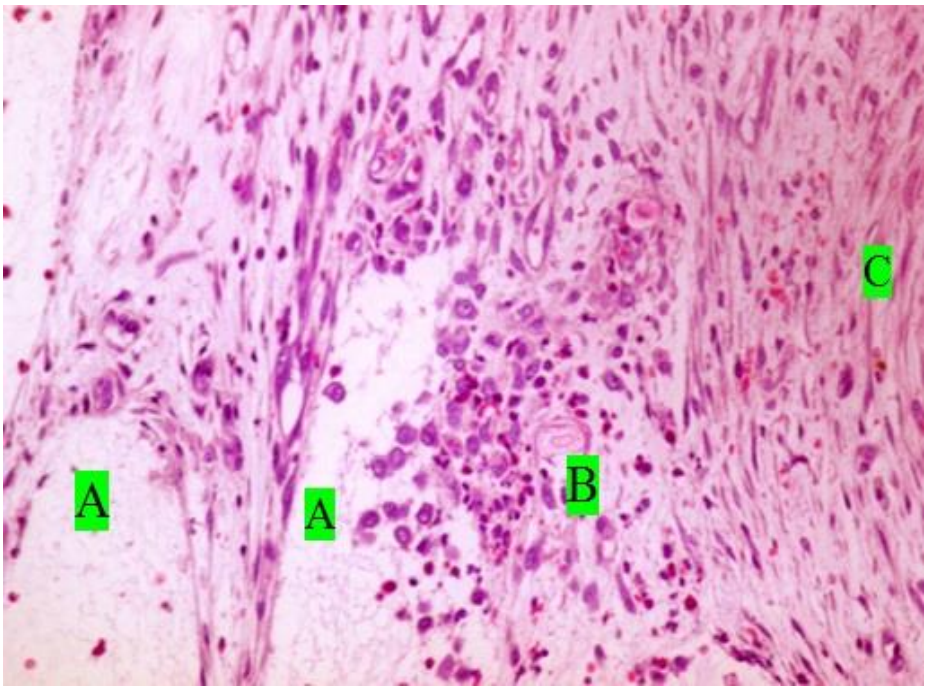

Fig (5): Histoacryl (A) surrounded by layer of few inflammatory cells (B) covering a layer of granulation tissue (C) at site of resection anastomosis.

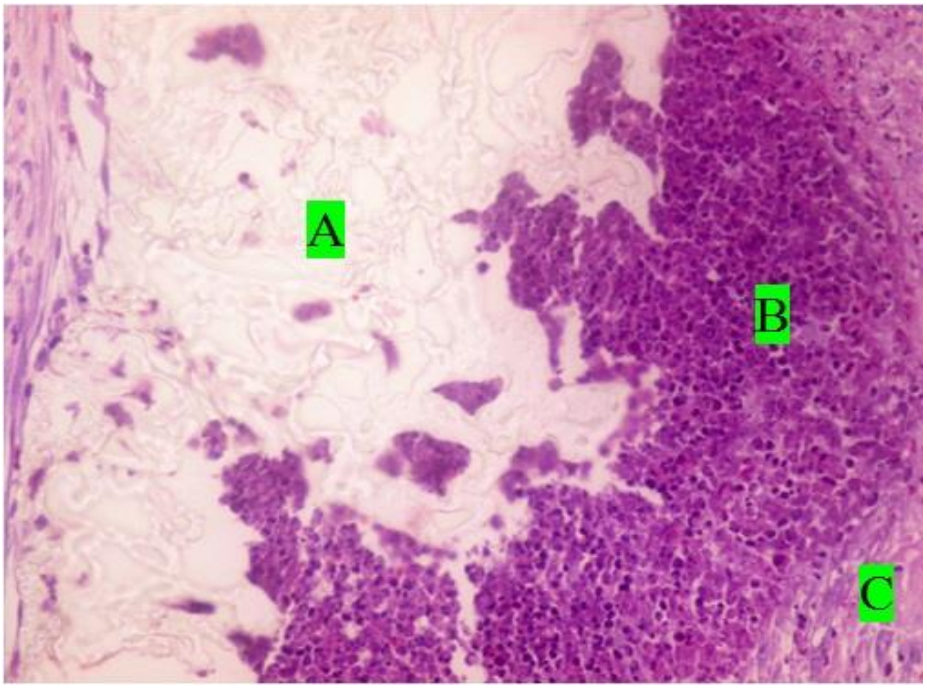

Fig (6): Histoacryl (A) as a tissue adhesive material covered by inflammatory cells (B) and a layer of granulation tissue(C) at site of resection anastomosis.

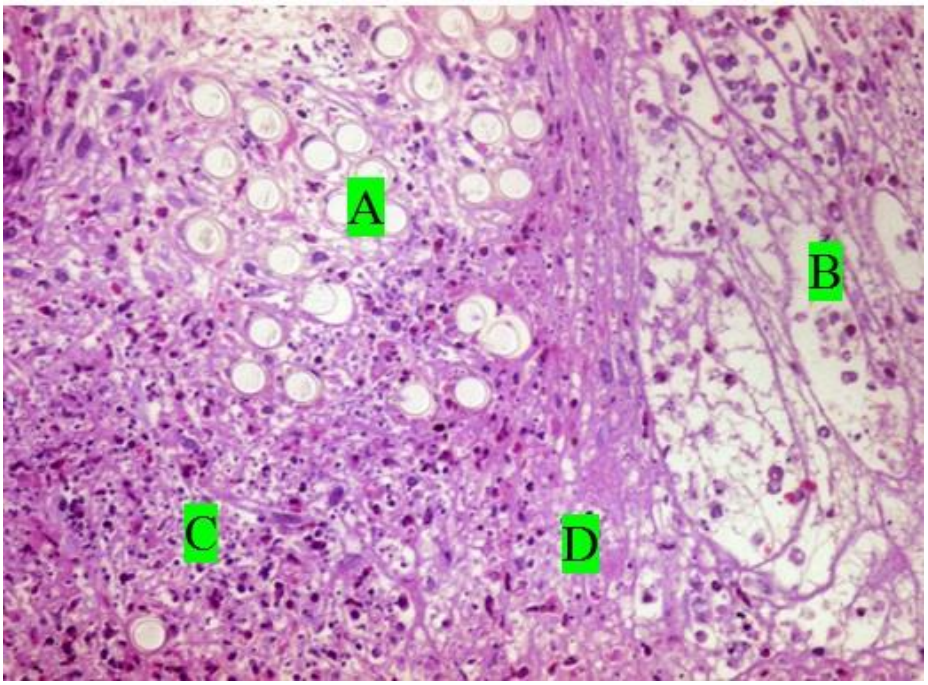

Fig (7): Suture material (A) surrounded by a few inflammatory cells (C) and a layer of granulation tissue (D) that is formed at site of resection anastomosis covered by a layer of Histoacryl (B).

DISCUSSION

The present study aimed to assess the efficacy of Histoacryl as reinforcement tool for resection anastomosis and to study the pathological effects of Histoacryl on anastomosis suture line.

To get this target accomplished, we performed an experimental comparative

study. Twenty model rabbits were included in the study. They were divided into two groups; group I (experimental group) underwent intestinal resection anastomosis with Histoacryl as an adjuvant, while in group II (control group) resection anastomosis was performed without Histoacryl.
The operated animals were evaluated postoperatively grossly by examining the anastomosis for wound infection, anastomotic leakage, anastomotic stricture, adhesion formation and pathologically for inflammatory cell infiltration, neovascularization, and collagen deposition.

Regarding wound infection and anastomotic leakage, our study showed no case of wound infection or anastomotic leakage in the studied groups except one case of leakage and death in group II with no statistically significant difference between them. This is in accordance with Bae and his colleagues who evaluated the effectiveness and safety of using cyanoacrylate adhesive for sutureless colonic anastomosis and as a protective seal to prevent leakage. In their study, no anastomotic leakage was observed in any group (7).

In respect to anastomotic adhesions, there was no statistically significant difference between the studied groups regarding frequency and severity of adhesions. This is in agreement with the study of Bae and his colleagues. However, Soares and Souza found that Adhesion formation was more extensive in the cyanoacrylate group on the seventh postoperative day comparing with suture group (p=0.007) (8).

Considering, anastomotic strictures, the present study found a higher frequency of strictures in the experimental group. However, the difference wasn't statistically significant. This data finds support in the study of Weiss and Haj who found no statistically significant difference between glue and suture group regarding stricture formation (9).

Comparison between the studied groups regarding pathological outcomes had revealed significantly lower inflammatory infiltration and collagen deposition in the experimental group when compared with the control group. This is in harmony with the study of Escalante-Pina and colleagues who undertook a study to evaluate 2-octyl cyanoacrylate (2OCA) glue and suture for wound closure in the small bowel. This was a comparative and experimental study. Ten domestic dogs underwent a 2.0-cm small bowel closure of two wounds. All of these had closure with 2OCA in the first wound. The controls (second wound in the same dog) were closed with suture. Four weeks later the wounds were observed to evaluate the repair. Wound closure time and macrophage count were lower with the 2OCA glue than in the suture group. The authors concluded that 2OCA glue has the strength to seal a small bowel wound. The inflammatory response to the glue is less than that of the suture at 4 weeks. These properties may make it a suitable material for replacing suture in a small bowel wound (10).

CONCLUSION

In conclusion, our findings provide further evidence that N-butyl-2-cyanoacrylate may be considered safe for clinical employment in intestinal anastomosis. Our study showed no case of wound infection or anastomotic leakage with the use of cyanoacrylate tissue adhesive. There was significantly lower inflammatory infiltration and collagen deposition in the experimental group. In this study, we confirmed its effectiveness as reinforcement for intestinal anastomosis upon which the glue yields immediate sealing of the tissues and supports the physiological wound healing process.

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مقارنة بين التوصيل المعوي بالطرق التقليدية و بطريقة إستخدام لاصقات الأنسجة (سيانو اكريلات) كمقوي للتوصيل المعوي

لقد تم استخدام السيانوأكريلات في مجالات طبية للأول مرة في عام ١٩٦٠ و ذلك بالرغم من إحتوائه علي مادة الغراء ، ولقد ظهرت فائدته في جراحات التجميل ، المخ و الأعصاب ، جراحة الأسنان . ومع ذلك ما زال هناك جدلا حول قوة و أمان السيانوأكريلات في عملية التوصيل المعوي . ولذلك فإن الدراسة العملية تهدف إلي تقييم كفاءة السيانوأكريلات (الهستوأكريل) كمادة مقوية للتوصيل المعوي ، وكذلك دراسة تأثير الهستوأكريل علي الخلايا الموجودة في منطقة التوصيل المعوي وللوصول إلي هذا الهدف فقد تم عمل دراسة مقارنة عملية بإستخدام عشرون نموذج من الأرانب .

وتم تقسيمها إلي مجموعتين :-

المجموعة الأولى (المجموعة التجريبية) وتم عمل التوصيل المعوي بها و إضافة الهستوأكريل كمادة مقوية للتوصيل المعوي .

المجموعة الثانية (مجموعة المراقبة) تم عمل التوصيل المعوي بها بدون إستخدام الهستوأكرين و تم إخضاع الحيوانات التي أجريت لها عمليات التوصيل المعوي للتقييم لمكان التوصيل من حيث العدوى في مكان التوصيل أو التسريب من مكان التوصيل أو ضيق منطقة التوصيل أو تكوين الإلتصاقات بين أجزاء الأمعاء وكذلك دراسة الخلايا المتكونة في منطقة التوصيل من حيث تواجد خلايا الإلتهاب و الخلايا الليفية و تكوين الكولاجين .

وفيما يتعلق بالعدوى أو التسريب في مكان التوصيل فلقد أوضحت الدراسة أنه لم تكن هناك إحصاءات تذكر ولم تظهر هذه الأعراض ، فيما يتعلق بالإلتصاق المعوى لا يوجد اختلاف احصائى يعتد به بين المجموعتين فى تواتر وشدة الالتصاق. ولقد لوحظ بالعين المجرده وجود ضيق في مكان التوصيل في مجموعات الإختبار و بالمقارنة بين المجموعتين من حيث تواجد خلايل الإلتهاب و تكوين الكولاجين تبين أن وجودها في المجموعة التجريبية أقل بكثير عنه في المجموعة الثانية

ولذلك فقد تبين أن الهستوأكريل كمادة لاصقة يقدم العديد من المزايا التي تساعد علي تقوية التوصيل المعوي .