



## SUTURELESS COLIC ANASTOMOSES WITH CYANOACRYLATES.

Sánchez-Matamoros Martín I, Capitán Morales LC, Sánchez-Matamoros Martín MD,  
Carolina Castellanos, Ortega Beviá J, Oliva Mompeán F.

General and Digestive Surgery Service. Clinical Management Unit. Coloproctology Unit.  
Universitary Hospital "Virgen Macarena". Seville. Spain.

### KEYWORDS

Sutureless colic anastomoses. 2-octyl-cyanoacrylate.  
N-butyl-cyanoacrylate. Cyanoacrylates.

### ABBREVIATIONS

NB2C: N-butyl-2-cyanoacrylate. 2OC: 2-octyl-cyanoacrylate.  
AI: Acute inflammation. CUII: Chronic unspecified inflammatory infiltrate.  
CGII: Foreign body granulomatous inflammatory infiltrate.  
Ede: Oedema. Fi: Fibrosis.

### Correspondence:

Prof. LUIS CRISTÓBAL CAPITÁN MORALES  
Avda. Eduardo Dato, 40, 4º B-2.  
41005 -Seville. Spain.  
E-mail: lcapitan@us.es

### ABSTRACT

**BACKGROUND AND AIMS.** The present research project has been made mainly with the idea of comparing the tensile strength values and histological answers of three types of colon anatomises: sutured with silk and sutureless anastomoses with 2-octyl-cyanoacrylate and N-butyl-2-cyanoacrylate.

**METHODS.** 112 Wistar rats distributed into three groups of 35 animals and a last control group of 7 have been used for this. Group 1: silk, group 2: 2-octyl-cyanoacrylate, group 3: N-butyl-2-cyanoacrylate, group 4: Control group. The following surgical interventions were practiced on them: A cross section of the colon, followed by: group 1: an end-to-end discontinuous suture anastomoses with Silk; group 2: sutureless anastomoses with 2-octyl-cyanoacrylate; group 3: sutureless anastomoses with N-butyl-2-cyanoacrylate. On the 10th, 20th, 30th, 40th and 50th days we proceeded to measure the anastomoses' tensile strength value for each series. In the same period of time we carried out the following anatomic-pathological determinations: a) sharp inflammation; b) oedema; c) non-specific chronic inflammatory infiltrate; d) granulomatous inflammatory infiltrate to foreign bodies; e) fibrosis.

**RESULTS.** The results obtained indicate a greater anastomoses' tensile strength for group 2 and 3. The anatomic-pathological values show a better response to anastomoses with adhesives than with conventional sutures.

**CONCLUSIONS.** All these experimental results lead us to conclude that the cyanoacrylates used to carry out sutureless anastomoses may be an alternative to the handmade conventional anastomoses. Moreover they are easy to be implemented.

### INTRODUCTION

Anastomotic dehiscence are still the most important cause of morbidity and mortality in colorectal resections. Nowadays, anastomotic dehiscence complications following a surgical procedure are located between 0.1 and 30%<sup>1-4</sup>. When the two cut ends of the bowel are sutured together the healing begins with an inflammatory reaction that provokes the replacement of damaged cells by knitting of granulation and fibroblasts and later on by the deposit of conjunctive knitting that requires reconstructing the intestinal wall. The healing of the colon starts with a varying level of collagen in the submucous layer, where its concentration is the highest. The most critical period of the healing is the first 3-5 days. During this time there is an invasion of the colon anastomoses by platelets, macrophages, granules and fibroblasts. This invasion leads to an increase in

the collagenolysis and a decrease in the collagen activity, which infers that the colic anastomoses will be mainly held together by the uniting suture.

The complications of anastomoses leakage are infection and septicaemia consecutive to peritoneal or retroperitoneal contamination due to the faecal content<sup>5</sup>.

Different techniques have been developed to restore the digestive continuity in those cases where it is necessary to resect the colon and perform anastomoses. The experimental possibility to connect sutureless colic anastomoses has been established<sup>6</sup>. This study has been carried out with the aim of comparing the resistance and histological responses of three types of colonic anastomoses: sutures with Silk 5/0 and sutureless anastomoses with N-butyl-2-cyanoacrylate and 2-octyl-cyanoacrylate.

N-butyl-2-cyanoacrylate and 2-octyl-cyanoacrylate was developed in the seventies and was the first's adhesives to have insignificant tissular toxicity and good closing strength. It has been widely used in Europe because of its bacteriostatic power and minimum tissular toxicity in: bone and cartilage unions, medium ear surgery, corneal ulcers, embolization of gastrointestinal varix, neurovascular surgery and closure of superficial wounds<sup>7-11</sup>.

The aim is to verify whether sutureless anastomoses using cyanoacrylates are useful in experimental animals in terms of tensile strength and cicatrization of the anastomoses as it shows biological tolerance, appraised in degrees of histological inflammation and cicatrization in live intestinal tissue.

## MATERIALS AND METHODS

### MATERIAL

1. Animals. 112 white female Wistar rats with an average weight of 200 g. were used under the following experimental conditions: Approximate temperature 21°C, circadian rhythm, 40 to 60% humidity and nutrition with special fodder for rats. The animals were kept on a fast 24 hours before the operation, with access to water "ad libitum". 24 hours after surgery the habitual alimentation of the rats was continued.

The Wistar rats were distributed into three groups of 35 animals and a control group of 7. Each group, in its turn, was subdivided into five series of 7 animals depending on the time they were going to be sacrificed postoperatively (10, 20, 30, 40 and 50 days).

Group 1.- 35 animals. Anastomoses with Silk. Group 2.- 35 animals. Anastomoses with N-butyl-2-cyanoacrylate. Group 3.- 35 animals. Anastomoses with 2-octyl-cyanoacrylate. Group 4.- Control group. 7 animals.

The resistance or tensile strength (measured with an extensometer) and the following anatomopathological determinations were studied in each series: chronic and acute inflammation (unspecified and foreign body type granulomatous), oedema and fibrosis.

2. Anastomoses material. Three types of materials were employed: Silk (S), N-butyl-2-cyanoacrylate (NB2C) and 2-octyl-cyanoacrylate (2OC).

3. Measuring apparatus of resistance. A set of four extensometric gages arranged in a Wheatstone bridge structure, lodged on a flexible metal strap has been used. The gages are fixed onto the strap with an adhesive which provides solidification by polymerization and is arranged in such a way that the compensation of the section, to which Poisson's principle refers, is obtained. The reader in volts in the measurer is converted, by means of a conversion factor, into Kilograms-strength and corresponds to the traction force that is applied in the test. The circuit is equipped with a zero-setting system which permits balance on the bridge for later tests.

### METHODS

1. Anaesthetic methods. The animals were anaesthetized by means of intraperitoneal injection of Ketamine, 0.2 cc dosis per 100 gr. of weight.

#### 2. Surgical methods.

a) Group with Silk. After performing a medium laparotomy, the intestinal loops were revealed and once the colon was located a transversal section was carried out followed by its terminal-end anastomoses with discontinuous suture with

silk 5/0. The abdominal wall was closed with silk 2/0, in continuous suture in peritoneum block and aponeurosis and skin separately.

b) Group with NB2C. After performing the transversal section of the colon, three loose stitches with Polyglycolic Acid were applied to triangle and approximate the section ends, applying NB2C on the three lines which constitute the union of the extremities. A complete closure of the union was obtained in this way.

c) Group with 2OC. We proceeded in a similar way to the previous group, although 2OC was used (Figure 1).

3. Method to obtain samples and measurement of tensile strength of sutures. Employing the same anaesthetical method as in the operations, once the rat was sacrificed on the corresponding postoperative day and properly fixed to the workbench, we proceeded to remove the corresponding region to the intestinal anastomoses. One centimetre, marked by two fine hypodermic needles, was measured with a precision micrometer, leaving the anastomoses just in the middle, and after its section, it was placed between two supports on the resistance measurer, fixing it with two serrated clamps. The apparatus was started until the anastomoses broke; the referred value in the voltmeter is the tensile strength or resistance expressed in grams/centimetres, given that the fragment of anastomoses measured exactly one centimetre.

We proceeded the same way in the control group, extracting one centimetre of the descending colon without previous intervention, which allowed us to obtain the tensile strength of a normal colon.

4. Anatomopathological method. The anastomotic region of the sample used after measuring resistance was fixed in tamponed formol at 10%.

With the object of studying the existence or not of acute inflammation (AI), chronic unspecified inflammatory infiltrate (CUII) and foreign body type granulomatous inflammatory infiltrate (CGII), oedema (Ede) and fibrosis (Fi), the 3 µ thick histological cross sections were processed in paraffin and stained with Hemotoxiline-Eosine.



Figure 1.- Application of 2-octyl-cyanoacrylate.

5. Statistical methods. The parametric ANOVA Test was performed for a tensile strength factor and the T for Student Test for a sample to compare with normal colon.

In the case of obtaining a non-normal variable, such as the anatomopathological, the comparison was carried out by means of the Kruskal-Wallis Test. On the other hand, the multiple comparisons were performed by means of the U for Mann-Whitney reducing the global significance level from  $\cdot$  to 0.005 so as to be able to maintain a global significance level of  $\alpha = 0.05$ .

The dichotomic variables (obstruction/non obstruction) were compared with the Chi-squared Test in the causes of mortality.

6. Mortality studies. All the animals for each group, according to the days elapsed from the operation to the taking of resistance measurements, were observed, noting the number of deaths to determine survival.

## RESULTS

1.- Tensile strength. The arithmetical mean (gr/cm) and the typical deviation of the values obtained for the different groups were calculated, with the results that show themselves in the Tables I and Figure 2.

It has been verified that the tensile strength value in the technically conventional groups as well as in the sutureless anastomosis groups increased progressively in time from 10 to 50 days.

2.- Anatomopathological results. The values of the elements studied have been expressed through a scale of 0 to 3 and the arithmetical mean has been found. (Figure 3)

### 2.1.- Silk group (Table II).

In this group an acute inflammatory component was globally observed in most cases, even in series V, sometimes, with formation of authentic perianastomotic abscesses. The chronic inflammatory reaction was seen in every series.

The suture material caused a foreign body type granulomatous reaction in every case, more evident in series II, IV and V.

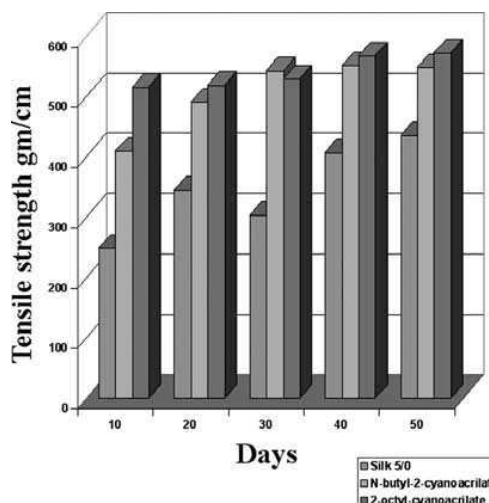


Figure 2.- Results of tensile strength.

Table II

### ANATOMOPATHOLOGICAL RESULTS. SILK GROUP.

	AI	Ede	UCI	CGII	Fi
Series I	1.43	0.57	0.86	1.43	1.14
Series II	1.16	0.17	0.83	1.83	1.17
Series III	1.16	0.17	1.17	1.50	1.00
Series IV	1.67	0.17	1.33	1.83	1.67
Series V	1.83	0.00	1.17	1.67	1.83

Table I

#### 1.1. Colic anastomoses with Silk.

	Series I	Series II	Series III	Series IV	Series V
Mean	248.9	345.6	304	407.7	436.5
Typical deviation	2	15	36.5	16.5	12.5

#### 1.2. - Colic anastomoses with N-butyl-2-cyanoacrilate.

	Series I	Series II	Series III	Series IV	Series V
Mean	410.14	491.33	543.3	552	549.14
Typical deviation	38.62	59.28	68.38	38.68	33.06

#### 1.3. - Colic anastomoses with 2-octyl-cyanoacrilate.

	Series I	Series II	Series III	Series IV	Series V
Mean	516.2	519.4	530.16	568.28	572.28
Typical deviation	41.96	80.15	64.76	27.30	29

#### 1.4. - Control group. The mean was 541.1 gr/cm (typical deviation 2.6)

Insofar as the formation of connective tissue we observed that it increased as the postoperative time did.

**2.2.- N-butyl-2-cyanoacrylate group (Table III).**

The acute inflammatory reaction was relevant in the first series.

Although the unspecified chronic inflammatory reaction existed it was not very important; however the chronic granulomatous was.

**2.3.- 2-octyl-cyanoacrylate group (Table IV)**

**3.- Mortality study. (Table V)**

It has been verified that the three groups showed a total mortality of 12.38 % which oscillated between 11.42% for S and NB2C groups and 14.28% for 2OC group during the observation period. In the following table the total number of deaths and the causes for each animal in each group.

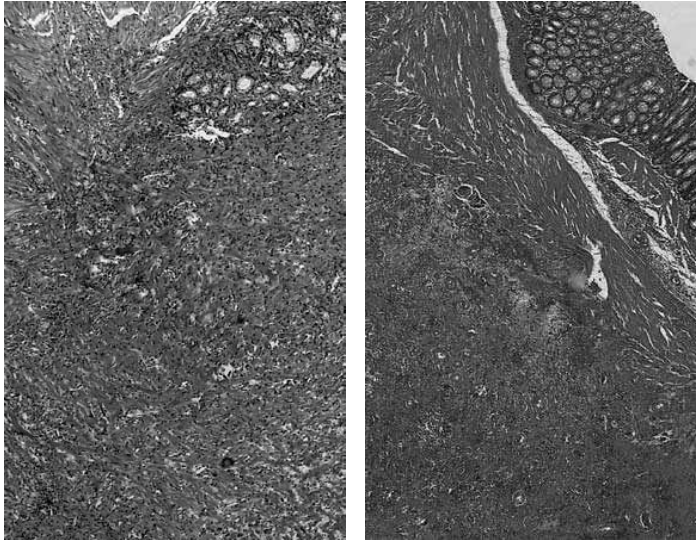


Fig 2.a (H.Ex10)

Fig 2.b (H.Ex10)

Figure 3.-  
Anastomoses with 2-octyl-cyanoacrylate (fig 2.a.) and with N-Butyl-cyanoacrylate (fig 2.b.) in 50 days time.

Table III

**ANATOMOPATHOLOGICAL RESULTS.  
N-BUTYL-2-CYANOACRYLATE GROUP.**

	AI	Ede	UCII	CGII	Fi
Series I	2.14	0.00	1,14	1.42	0.00
Series II	1.00	0.00	1.00	2.00	0.60
Series III	0.83	0.00	1.16	1.66	1.33
Series IV	0.00	0.00	2.00	1.80	0.16
Series V	0.16	0.00	1.33	1.66	0.50

Table IV

**ANATOMOPATHOLOGICAL RESULTS.  
2.3. 2-OCTYL-CYANOACRYLATE GROUP.**

	AI	Ede	UCII	CGII	Fi
Series I	2.20	0.00	1,00	1.40	0.60
Series II	2.00	0.00	1.80	2.00	0.20
Series III	1.50	0.00	1.30	2.00	0.33
Series IV	1.71	0.00	1.28	2.28	0.24
Series V	1.00	0.00	1.28	0.28	0.00

Table V

**MORTALITY STUDY**

	Total number of deaths	Causes	Number of deaths
Colic anastomoses with Silk 5/0	4	Immediate postoperative	2
		Wall dehiscence	1
		Sepsis due to abscess in abdominal wall	1
Colic anastomosis with NB2C	4	Anastomotic leakage	1
		Intestinal obstruction	3
Colic anastomosis with 2OC	5	Anastomotic leakage	2
		Intestinal obstruction	3

## DISCUSSION

In this experimental study we have endeavoured to verify the efficiency of N-butyl-2-cyanoacrylate and 2-octyl-cyanoacrylate used as sutureless colonic anastomoses as opposed to conventional technique with Silk 5/0 in rats. We studied the tensile strength the sutures are able to support and the anatomopathological repercussions relating to cicatrization such as acute inflammation, oedema, unspecified chronic inflammatory infiltrate and foreign body type granulomatous, and anastomotic fibrosis.

Insofar as the tensile strength, it has been verified that in any of the groups whether they are conventional technique or sutureless anastomosis their value increases progressively in time from 10 to 50 days. NB2C and 2OC show a much greater tensile strength than the other group (S) as from 10 days with clear statistically significant differences with them; NB2C reach the normal colon mean at 30 days and 2OC reach the normal colon mean at 40 days. Significant statistical differences are only found at 10 days between both cyanoacrylate.

Kirkegaard<sup>12</sup> carried out a comparative study between sutured colonic anastomoses or those performed with isobutylcyanoacrylate in rats, concluding that there are no significant differences between either tensile strength; something which contrasts to our results, perhaps due to a cyanoacrylate ester with different alcohol in its structure.

As regards to the anatomopathological study, beginning with the acute inflammatory reaction, the 2OC group obtained the highest values.

Fariás-Lamas et al<sup>13</sup> in a study realized with 2-octyl-cyanoacrylate, N-2-butyl-cyanoacrylate and fibrinogen in rates, concluded that an increase exists in the bursting pressure in the groups treated with fibrinogen, which expressed increase of the tensile strength of the anastomosis and that pressures were similar on having treated the anastomosis with any of the synthetic adhesives.

Insofar as N-butyl-2-cyanoacrylate is concerned, there is a significant statistical difference at 40 and 50 days when compared to S group, the acute inflammatory reaction being less in the former. In the statistical study they did not find significant differences for both types of cyanoacrylates.

According to the previous results, we can refute the conclusion established by Nash and Belleger<sup>14</sup> in their study on cat intestine using conventional suture and N-butyl-2-cyanoacrylate, which affirms they obtain a greater inflammation at 7 days in sutures than in adhesive, although the inflammation persisted at 28 days in the latter as opposed to what happened in sutures.

We have not obtained statistically significant differences in the group of the 2-octyl-cyanoacrylate in the values of sharp inflammation for with any of the other series of our enclosed study in the comparison with the N-butyl-2-cyanoacrylate.

Matera<sup>15</sup> reveals the great inflammatory and granulomatous reaction of anastomoses performed with cyanoacrylate in a study with dogs.

Oedema did not appear in the group treated with 2OC and NB2C. It appeared in S group, although it diminished until disappearing at 50 days, without any significant differences among the results at different periods of time.

The unspecified chronic inflammatory infiltrate (U.C.I.I.) in all groups and at all times was evident, obtaining the lowest values for S. Except for this last technique, there is a clear

increase in said anatomopathological parameter in time, if the results at 10 and 50 days are compared. As regards to the statistical study, no significant statistical differences amongst the different groups have been found.

Granulomatous chronic inflammatory infiltrate of foreign body type (G.C.I.I.) was observed in all the groups.

The results were ratified by papers such as Matera<sup>15</sup> and Oliver<sup>16</sup> who affirm that cyanoacrylates act as foreign bodies.

Insofar as N-butyl-2-cyanoacrylate and 2-octyl-cyanoacrylate we did not gather significant differences with S group and neither for both types of cyanoacrylates.

With respect to the fibrosis parameter, it was observed how the cicatrices became more and more compact in all groups from 10 to 50 days, i.e. the value of said parameter increases; this reaches its minimum values in the case of 2-octyl-cyanoacrylate.

It has been verified how the three groups showed a total mortality rate of 12.38% which oscillated between 11.42% for Sand NB2C groups and 14.28% for the 2OC group during the observation period. According to the results it can be observed how the cause of greater mortality is constituted by the intestinal obstruction which took place in anastomoses performed with the adhesive but did not appear in those with conventional suture; that is why it is thought that as the former have a greater tendency to form adhesions, these could be the cause of the obstruction.

The statistical study taking as a dichotomic variable obstruction/ non obstruction and the three independent techniques did not show significant statistical differences. On the other hand, grouping the techniques into conventional and adhesives, significant statistical differences did appear. Therefore, we can affirm that the adhesives used as an alternative to conventional suture in colon anastomoses are more inclined to the formation of adhesions and, as a consequence, to the formation of intestinal obstruction than sutures.

At the sight of the results, it is thought that cyanoacrylates can be used as an alternative to conventional manual anastomoses to confect a sutureless anastomoses from the experimental point of view.

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