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Use of Cyanoacrylate N-Butyl Versus Subcuticular Suture in the Dermal Closure Following Cesarean Delivery: A Randomized Controlled Trial

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Abstract

Background: Currently the use of tissue adhesives for surgical wound closure has multiplied; however, its use in cesarean sections is still not well determined. The objective of this study was to compare the surgical wound healing following cesarean sections between N-butyl cyanoacrylate (Tisuacryl) and suture (Monocryl 2-0).

Methods: A randomized, non-blinded controlled clinical trial was conducted from October 2017 to March 2018 at the Instituto Nacional de Perinatologia. Forty women undergoing cesarean delivery were randomly assigned to skin closure group using a random number table: 20 with N-butyl cyanoacrylate (Tisuacryl) (cases group) and 20 with Monocryl (control group). Scars were evaluated at 24 h, 1 week, 1 month and 3 months. Primary objective was to evaluate the esthetics of the scar with the scar cosmesis assessment and rating (SCAR) scale. Secondary objectives were skin closing time, the satisfaction of the patient and the satisfaction of the surgeon.

Results: Demographic characteristics, including average age, body mass index and number of pregnancies, were similar in both groups. The skin closing time showed a significant decrease with a P value of 0.000 between Tisuacryl and Monocryl (54.95 ± 10.353 s in the first group vs. 407.5 ± 72.61 s). The esthetic evolution of surgery using the SCAR scale showed a better evolution in the first visits (weekly and monthly) in the Monocryl group (2.05 ± 0.60 and 1.68 ± 0.477) vs. Tisuacryl (2.77 ± 0.685 and 2.55 ± 0.74) with a P value of 0.001 in SCAR 1 (first visit) and 0.000 in SCAR 2 (second visit). However, no significant differences were observed in the last result at 3 months (SCAR 3). Similarly, no significant differences were observed regarding the satisfaction of the surgeon or the patient.

Conclusions: The results of skin healing with Tisuacryl vs. Monocryl were similar in terms of the esthetics and satisfaction of the patient or the surgeon. Therefore, the use of each one depends on surgeon/patient preferences and the availability of materials.

Keywords: Cesarean section; Cyanoacrylate; Monocryl; Skin healing

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Introduction

Throughout the history of mankind, man has had the need to face edges of war wounds, hunting or accidental, so they have used different elements for the closure of wounds in order to face the edges with the lowest possible tension, without causing ischemia and to allow healing as biological as possible [1]. The healing process is a sequence of events that depends on the cellular dynamics of the injured and surrounding tissue which allows the liberation of growth factors and cytokines which culminates with the repair in three phases: acute or inflammatory, cell proliferation and tissue remodeling. Healing of first intention occurs after approximating wound edges with sutures, ribbons or some mechanical device [2]. Most sutures have shown a greater or lesser degree of reaction due to the microtrauma that implies its application and therefore the tissue responds according to the healing process mentioned above. The closure of wounds with suture, staple, adhesive tape or tissue adhesive, differs from each other with the degree of inflammatory reaction, infection rate, mechanical properties and cosmetic results [3, 4]. Currently, there is no evidence on the best method for skin closure in cesarean sections, so the method selection is based on the preference of the surgeon.

Nowadays, the most commonly used items are non-absorbable sutures with an average withdrawal time of 7 - 12 days [1]. Surgical suture is defined as products that are made with synthetic, absorbable or nonabsorbable strands, purified ribbons of animal intestines, silk filaments, textiles, steel, or others that, in addition, must be inert, non-antigenic, apyrogenic and non-toxic, which are used with the purpose of joining the ends of a wound and favoring its healing [5]. Monocryl (Poliglecaprone 25) is a synthetic, absorbable, sterile mono-

filament surgical suture synthesized from epsilon-caprolactone and glycolide copolymer. It is absorbed by hydrolysis, maintains tensile strength for at least 28 days and is completely absorbed in 90 - 120 days [6].

Tissue adhesives are synthetic, biocompatible biomaterials, compounds based on cyanoacrylate of N-butyl or octyl, and its cyanoacrylic composition gives it bactericidal characteristics. Its design was specific for the biological closure of surgical wounds or recent trauma seeking a faster healing process since it sets in the presence of biological fluids which gives it a marked hemostatic character when adhering strongly to the tissues [7]. Regarding the bactericide spectrum, it was observed that it inhibits the growth of all gram-positive microorganisms with a bactericidal effect above 70%, but among gram-negative microorganisms, it only inhibits the growth of *E. coli* and *E. fecalis* with bactericidal effect of 60% and 40%, respectively [8].

Tissue adhesives provide firmness for up to 8 days in the closure of surgical wounds. These substances have a specific density of 1.05 g/mL and soluble in methyl ethyl ketone and toluene. They are transparent, of similar appearance and viscosity to water, absorbable and polymerized on contact with the endothelium, and once applied, they are resistant to most organic solvents except the dimethyl formaldehyde that dissolves the polymers. It must be stored cold (5 °C), applied fresh and used in the first 72 h after exposure to the environment [9].

It should be applied topically; the speed of polymerization is variable, from instantaneous to 55 s after being applied depending on the monomer used and the application method. They exert their adhesiveness by polymerizing small amounts of esters in biological tissues at room temperature, unlike other tissue adhesives that require heat to catalyze [4, 10, 11].

So far, the application of cyanoacrylate is restricted in patients with pathologies that may alter the natural process of healing, coagulation, idiosyncrasy reaction, atopy, known or suspected skin allergies, dermatitis, and with infected wound or potential risk of infection, in mucous membranes with constant secretion or hypersecretion, wounds with inadequate hemostasis, as well as areas exposed to tension or direct pressure [12].

Specifically, Tisuacryl was developed by the Biomaterials Center of the University of Havana (BIOMAT). It is a liquid material, blue, with viscosity similar to that of water, synthesized based on 2 N-butyl cyanoacrylate which gives it bactericidal characteristics. It requires to be stored at low temperatures (2 and 8 °C) to extend its useful life. Initially it was developed for traumatic or surgical wounds no larger than 3 cm; however, currently it can be used in larger wounds using approximately 0.15 mL for wounds of 30 cm. Like the rest of the cyanoacrylates, the Tisuacryl forges with biological fluids to undergo polymerization that gives it strong adhesion, as well as hemostatic character. It is a biodegradable material, so it is not necessary to remove it later. The preclinical tests to which it was submitted are skin irritation test, implantation, acute oral toxicity, irritation to the oral mucosa, histotoxicity, cytotoxicity, adhesiveness, *in vitro* genotoxicity, dermal irritability, solubility and sterility; currently, it has sanitary authorization for use in humans in the cutaneous application [13].

Before applying the N-butyl cyanoacrylate, it is necessary to properly clean the wound and dry the area, avoiding the presence of wet areas or bleeding sites as this will accelerate the polymerization process and increase the risk of dehiscence. The dose to be used will depend on the extension of the wound, and only the neck of the plastic ampule should be slid over the edge of the wounds to get the tissue to adhere. If surplus material is placed, a dense, flexible and fragile polymer layer will be created and it can be easily removed, which can cause dehiscence. In case of accidental application in unwanted sites, the material can be removed with acetone or common nail polish remover [13].

Because adhesion is instantaneous, it is important to place the edges of the wound in a proper position to result in more esthetic healing; this is achieved with a confrontation of the lower planes as close as possible and in some cases the use of tweezers at the ends of the wound can facilitate this process [13].

In several studies, the significant reduction in pain and the speed of wound repair have been observed, which could substitute the need for sutures. Moreover, the cost reduction when using 0.15 mL in wounds of up to 30 cm, besides that it does not require sterilization or special applicators since it is an inert substance, makes it an excellent option for skin closure [13].

To date, there are no controlled randomized studies comparing the closure of cesarean wounds using Monocryl vs. Tisuacryl using the scar cosmesis assessment and rating (SCAR) scale together with the scale of visual satisfaction of surgeon and patient for the evaluation of postsurgical results. The SCAR scale is a validated and reliable instrument that evaluates the evolution of postoperative linear wounds first developed in Philadelphia in 2016 [14]. This scale evaluates six items by the same observer and two items of the patient. It gives a rating from 0 to 15 with 0 being the best possible scar and 15 the worst. The items evaluated by the observer are: scarring, erythema, depigmentation, suture marks, hypertrophy or atrophy of the wound and general inspection, while those evaluated by the patient are pain and pruritus. Prior to its publication, studies were carried out to verify the validity, feasibility and inter- and intra-observer reliability of the same, proving to be an adequate scale for the evaluation of surgical wounds [14].

The most recent publication in April 2017 in the AJOG reports a randomized study comparing the closure of cesarean wounds with subdermal suture vs. tissue adhesives using the patient and observer scar assessment (POSAS) scale, in which it is concluded that wound closure with both methods is similar in both safety and final cosmetic result, so the use of both will be determined by the preferences of the patient and the surgeon [15].

This is a prospective study comparing surgical wound closure of cesarean sections using N-butyl cyanoacrylate (Tisuacryl) vs. suture (Monocryl 2-0).

Materials and Methods

A single-institution, prospective, analytical, unblinded, randomized clinical trial was conducted, in which 40 patients

undergoing cesarean section (20 cases and 20 controls) were selected in the period from October 2017 to March 2018 at the Instituto Nacional de Perinatologia. Sample size was not calculated because in the absence of studies comparing both methods in the same way, it was decided to conduct a pilot study of 20 patients per group. Patients scheduled for elective cesarean section who wished to participate in the study, were randomized to having skin closure of their cesarean section wound with either N-butyl cyanoacrylate or subcuticular running suture (Monocryl 2-0) using a random number table computer-generated by the main investigator. In all cases the procedure was explained to the patients and informed consent was requested from the protocol prior to performing the surgery; the risks and benefits of participating in the protocol were explained. All the cesarean sections were performed by the same group of attending obstetricians and senior residents. This project was submitted to the Institutional Research and Ethics Committee and was approved with the number 2017-2-106. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

The inclusion criteria were patients of the Instituto Nacional de Periatologia with skin injury secondary to cesarean sections. The exclusion criteria were antecedents of cyanoacrylate allergy, severe malnutrition, uncontrolled diabetes mellitus, infected wounds or with high risk of infection, morbid obesity and history of keloid scarring. The criteria for elimination were patients who did not wish to participate in the study or those who did not attend follow-up.

In all cases, antibiotic prophylaxis with cephalosporin was administered 30 min prior to the procedure; in case of allergy to cephalosporins, clindamycin was administered. In patients with previous cesarean section, the scar was removed. The tissues were opened using a sharp technique with scissors and with electrocautery when indicated. In both groups, after closing the rectus fascia, subcutaneous cellular tissue was closed with Vicryl 2-0 simple points to achieve a better skin coping. In the Tisuacryl group after closing the subcutaneous cellular tissue, wound was cleaned and dried well to avoid wet areas or bleeding sites. The edges of the surgical wound were aligned, and the neck of the plastic ampule slid over the edge of the wound. Once the cyanoacrylate was hardened, the wound was covered with an abdominal pad. For the suture group with Monocryl after closing the subcutaneous cellular tissue, Monocryl 2-0 suture was taken with needle holder and the skin was closed using a blind suture technique, and the wound was covered with an abdominal pad.

To evaluate the skin facing time in the Monocryl group, the time was clocked in seconds from needle holder taking to the placement of the abdominal pad. In the Tisuacryl group, the time was clocked from the time the cyanoacrylate was applied to the placement of the abdominal pad as reported in a previous study [1]. Each patient was followed up at 24 h, 1 week, 1 month and 3 months after the procedure with scheduled appointments for wound revision in the emergency area.

For the evolution of wound esthetics, the SCAR scale was used to evaluate six items by the same observer and two items of the patient. It grades from 0 to 15 with 0 being the best possible scar and 15 the worst. To have a similar image in each patient, two photographs of the wound were taken in each visit 15 cm away from the skin, while the patient was in the dorsal decubitus position, the photographs were taken in the same room to avoid modifications due to the exposure of light, the camera of the Apple iPhone 7 with automatic adjustment without flash was used in all the reviews, and the same evaluator completed the scale in each visit.

To measure the satisfaction of the patient and the surgeon, the visual satisfaction scale was used, which evaluates 1 dissatisfied to 5 completely satisfied. The visual satisfaction of the surgeon was evaluated by the same surgeon observing the photographs of each session.

The primary objective was to evaluate the esthetics of the scar with SCAR scale. Secondary objectives were to evaluate skin facing time, patient satisfaction and surgeon satisfaction.

Statistic analysis

Data were analyzed using statistical software SPSS. The results were obtained in the following way. The description of the sociodemographic variables was carried out with descriptive statistics. The differences in the proportions of the dichotomous variables between the groups were analyzed with X^2 test. The differences in means of the quantitative variables were analyzed with Student's *t*-test in normal distribution, and with nonparametric tests when no normal distribution was observed. We calculated the power analysis based on the assumption that a 25% (3-point) difference in SCAR score would influence our clinical decision regarding the preferred method for skin closure.

Results

Forty patients scheduled for elective cesarean section were recruited from October 2017 to March 2018 and were randomly assigned 20 patients to each group. Two patients from the Tisuacryl group lost follow-up, so two additional patients were recruited in this group.

The demographic characteristics are shown in Table 1. The average age, body mass index, number of pregnancies, deliveries and abortions or previous cesarean sections were similar in both groups.

The specific characteristics of the population studied were number of previous abdominal surgeries (0 - 4) and type of incision (middle line/Pfannenstiel) (Table 1).

The results that were evaluated between the groups of Tisuacryl and Monocryl were facing time, esthetic evolution of the wound using the SCAR scale, satisfaction of the patient and surgeon (Table 1).

Regarding facing time, a significant decrease was observed with a P value of 0.000 between Tisuacryl and Monocryl (54.95 ± 10.353 s in the first group vs. 407.5 ± 72.61 s). The esthetic evolution of surgery using the SCAR scale showed a better evolution in the first two visits (weekly and monthly) in the Monocryl group (2.05 ± 0.60 and 1.68 ± 0.477) vs. Tisuacryl (2.77 ± 0.685 and 2.55 ± 0.74) with a P value of 0.001

Table 1. Demographic Characteristics, Specific Characteristics and Results Between Two Groups

	Tisuacryl	Monocryl	P
Demographic characteristics			
Age (years)	29 ± 5.75	28 ± 6.34	0.49
Weight (kg)	76.2 ± 11.01	78.16 ± 16.42	0.45
Body mass index (kg/m^2)	30.5 ± 4.45	30.78 ± 4.94	0.97
Number of pregancies			
1	7	6	0.84
2	4	5	0.82
3	6	5	0.81
4	4	3	0.92
5	1	0	0.39
6	0	1	0.39
Number of previous vaginal births			
0	19	16	0.49
1	2	1	0.92
2	1	3	0.88
Number of previous abortions			
0	14	10	0.48
1	4	7	0.41
2	4	2	0.92
3	0	1	0.39
Number of previous cesarean section			
0	12	13	0.92
1	5	6	0.96
2	4	1	0.70
3	1	0	0.39
Number of previous abdominal surgeries			
0	13	18	0.74
1	5	2	0.67
2	3	0	0.45
3	1	0	0.39
Type of incision			
Middle line	22.7%	18.2%	0.76
Pfannenstiel	77.3%	72.7%	0.22
Facing time (s)	54.95 ± 10.353	407.5 ± 72.61	0.000
Esthetic score of the wound (SCAR)			
SCAR 1	2.77 ± 0.685	2.05 ± 0.60	0.001
SCAR 2	2.55 ± 0.74	1.68 ± 0.477	0.000
SCAR 3	1.75 ± 0.91	1.15 ± 0.50	0.035
Satisfaction			
Patient	4.68 ± 0.46	4.63 ± 0.5	0.257
Surgeon	4.22 ± 0.70	4.7 ± 0.45	0.055

SCAR: scar cosmesis assessment and rating.

in SCAR 1 (first visit) and 0.000 in SCAR 2 (second visit). However, no significant differences were observed in the final result at 3 months (SCAR 3). Similarly, no significant differences were observed regarding the satisfaction of the surgeon or the patient (Table 1).

Discussion

The clinical variables of the patients were similar, so it was concluded that the samples were homogeneous. Speaking about the benefit of skin closure with N-butyl cyanoacrylate (Tisuacryl), there was a decrease in the facing time, whereas in the traditional closure group (Monocryl suture), there was better esthetic evolution in the first and second revisions (SCAR 1 and 2). There were no significant differences in the evaluation at 3 months of the procedure (SCAR 3), nor in the satisfaction of the patient or the surgeon regarding the use of one or the other for skin closure.

It is concluded that Tisuacryl is better in terms of reduction of surgical time without difference in terms of evolution or satisfaction of patients or surgeons, which agrees with previous studies. Due to the above, it can be considered in surgeries where the surgical time should be shortened. In terms of costs, it was observed that, on average, the price to the public of suture (Monocryl) is $162.40 vs. $450.00 of the N-butyl cyanoacrylate (Tissuacryl) which implies a higher unit cost; however, if the reduction of surgical time is considered in the long term, it would imply cost reduction at the institutional level.

As reported by Montes de Oca et al in the article published in 2009 "Effectiveness between tissue adhesive (cyanoacrylate) vs conventional suture for the closure and repair of superficial wounds caused by trauma" performed with 30 patients with superficial skin wounds caused by trauma, divided into two groups, the first handled with cyanoacrylate and the second with conventional suture (polypropylene) with similar demographic characteristics, there was a significant decrease in the time of closure, the average for group 1 was 20.06 ± 16.56 s and was 440.86 ± 345 s in group 2 [1]. In another study conducted by Orozco-Razon et al in 2002, 62 patients were divided into two groups. In group 1 cyanoacrylate was placed and in group 2 traditional suture with nylon was used, reporting a closing time of 402 s (6.7 min) in cyanoacrylate vs. 1,260 s (21 min) in suture with nylon [16]. In our study, it was reported that the average time for cyanoacrylate was 54.9 ± 10.353 s vs. 407.5 ± 72.61 s for Monocryl, which shows a significant decrease in facing time with the use of tissue adhesives which may represent a decrease in surgical times.

Unlike Montes de Oca and Orozco Reason who reported a significant difference in the esthetic results in the previously cited studies, in our study no significant differences were found in the final esthetic result at 3 months of follow-up.

Finally, similar to the report by AJOG 2017 [15], it is concluded that the choice of technique for skin closure should be determined by the preference of the surgeon and the availability of materials since wound closure with both methods is similar in both safety and final cosmetic outcome. It can be concluded that, thanks to the ease of use, rapidity of application, less trauma and comfort for patients by not requiring withdrawal of points, N-butyl cyanoacrylate is considered an excellent option for the closure of cesarean wounds. It is not intended to replace the cesarean wound closure; however, the use of cyanoacrylate in well selected patients can be recommended, following rules of use and used by trained personnel.

The limitation of the study is the small sample size, so studies with a larger sample size should be carried out. Also, another limitation of the study is the learning curve in the application of N-Butyl cyanoacrylate in this institution, so it is suggested to carry out new studies with the acquired knowledge.

Conclusions

It is concluded that the Tisuacryl is better in terms of decreased surgical time as it has significantly shorter facing time than Monocryl; however, Monocryl has better esthetics results within the first week and first month with no difference after the third month. There is no difference in terms of evolution or satisfaction of patients or surgeons, so the choice of technique for skin closure in cesarean sections should be determined by the preference of the surgeon and the availability of materials. Likewise, it can be concluded that, thanks to the ease of use, rapidity of application, less trauma and comfort for the patients by not requiring withdrawal of points, the N-butyl cyanoacrylate is considered an excellent option for closing cesarean wounds, so our team will prefer the use of N-butyl cyanoacrylate in cesarean sections.

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Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

The patient signed informed consent.

Author Contributions

JAMG performed research including data collection, and wrote the paper. MSGE statistically analyzed the data, and

created tables. NRP designed research, study and provided expert clinical knowledge to revise critically. JMGE designed research, study and provided expert clinical knowledge to revise critically. MAOR performed research including data collection. CMSR performed research including data collection.

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