

## Triclosan-coated polyglactin-910 for closure of infected abdominal wall of rats with peritonitis

Ação do fio de poliglactina-910 impregnado com triclosan na sutura da parede abdominal infectada em modelo de peritonite em ratos

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### ABSTRACT

**Purpose:** Antibacterial-coated sutures have been reported to reduce the incidence of surgical site infections both in experimental and clinical studies. The aim of the present study was to evaluate the performance of coated polyglactin 910 suture with triclosan (Vicryl Plus) and traditional polyglactin suture (Vicryl) with regard to surgical abdominal wound infections following abdominal sepsis by cecal ligation and puncture. **Methods:** Twelve Wistar rats weighing  $285\pm 15$ g were randomly distributed on Vicryl plus group (n=6) and Vicryl group (n=6). The variables to be evaluated were: (1) tensile strength of the tissues at the site of the suture (2) the histopathological aspects with counts of inflammatory cells; (3) bacteriology - growth of Gram-positive and Gram-negative bacteria. **Results:** On the fifth postoperative day bacterial cultures of the secretions collected from abdominal wounds revealed growth of *Staphylococcus aureus* and *Klebsiella sp.* A significant difference was observed in the mean colony forming units of Gram-positive and Gram-negative bacteria in wounds sutured with noncoated (Vicryl) versus triclosan-coated sutures (Vicryl Plus). In the Vicryl group, the average tensile strength was  $533.8\pm 75.8$  gf/mm<sup>2</sup>, significantly lower than in Vicryl Plus group ( $854.0\pm 51.7$  gf/mm<sup>2</sup>). Statistical analysis revealed a significant difference ( $p<0.0001$ ). The density of the inflammatory reaction was significantly higher ( $p=0.003$ ) in the Vicryl group rats ( $1033.26\pm 153.97$ ) than the in Vicryl Plus group ( $723.29\pm 96.5$ ). **Conclusion:** This study demonstrated the in vivo efficacy of Coated Vicryl Plus suture, that prevented bacterial colonization and reduced the inflammatory response, allowing tissue healing even in infected wounds.

**Key words:** Vicryl. Vicryl plus. Polyglactin. Triclocan. Wound infection. Rats.

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## RESUMO

**Objetivo:** Fios de sutura impregnados com antimicrobianos têm sido empregados para reduzir a incidência de infecções de sítio cirúrgico, tanto em estudos experimentais quanto clínicos. O objetivo do presente estudo foi avaliar o efeito tópico do fio de poliglactina 910 impregnado com triclosan, comparando-o com o fio de poliglactina tradicional em infecções de feridas cirúrgicas após sepse abdominal por ligadura e perfuração cecal. **Métodos:** Doze ratos Wistar, pesando  $285 \pm 15$ g, foram distribuídos aleatoriamente em grupo Vicryl Plus—impregnado com triclosan (n=6) e grupo Vicryl (n=6). As variáveis avaliadas foram: (1) bacteriologia (2) resistência à tensão dos tecidos no local da sutura; (3) histopatologia com avaliação da reação inflamatória. **Resultados:** No quinto dia pós-operatório culturas bacterianas das secreções coletadas das feridas de parede abdominal revelou crescimento de *Staphylococcus aureus* e *Klebsiella sp.* O nº de unidades formadoras de colônias de bactérias Gram-positivas e gram-negativas foi significativamente maior em feridas suturadas com Vicryl, do que com Vicryl Plus. No grupo Vicryl, a resistência tênsil média foi de  $533,8 \pm 75,8$  gf/mm<sup>2</sup>, significativamente menor do que no grupo Vicryl Plus ( $854,0 \pm 51,7$  gf/mm<sup>2</sup>). A análise estatística revelou uma diferença significativa ( $p < 0,0001$ ). A densidade da reação inflamatória foi significativamente maior ( $p = 0,003$ ) nos ratos do grupo Vicryl ( $1033,26 \pm 153,97$ ) do que no grupo de Vicryl Plus ( $723,29 \pm 96,5$ ). **Conclusão:** Este estudo demonstrou a eficácia in vivo do fio Vicryl Plus, que preveniu a colonização bacteriana e diminuiu a resposta inflamatória, permitindo a cicatrização dos tecidos mesmo em feridas infectadas.

**Descritores:** Vicryl. Vicryl plus. Poliglactina. Triclocan. Infecção da ferida. Ratos.

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## INTRODUCTION

Antibacterial-coated sutures have been reported to reduce the incidence of surgical site infections both in experimental and clinical studies<sup>1-4</sup>. A polyglactin suture, coated with the antiseptic chemical substance triclosan [5-chloro-2 (2,4-dichlorophenoxyphenol)], the Vicryl Plus, acts as a bacteriostatic by inhibiting enzymes involved in the bacteria's fatty acid synthesis<sup>5</sup>. Experimentally, triclosan has been shown to inhibit the growth of selected Gram-positive and Gram-negative bacteria<sup>1,2</sup>. Favourable effects of Vicryl Plus have been found with regard to sternal wound infections following cardiac surgery<sup>4</sup>. Reduced surgery site infection rates of Vicryl Plus have also been reported following other types of major surgery<sup>6,7</sup>. In contrast, other studies have not demonstrated positive effects of Vicryl Plus<sup>8,9</sup>.

It is a fact that most surgical infections (SSI) are intimately related to sutures. According to the Centers for Disease Control (CDC), 66% of all surgical infections are exclusively located in the incision, superficial or deep<sup>10</sup>. An observational study analyzing the infection rates associated to 12 high-prevalence diseases found that 69%

of all infections were superficial. In order to avoid the suture of being a risk factor of SSI, a new antibacterial suture has been introduced in the market: Polyglactin 910 coated with triclosan, a broad-spectrum antiseptic that has been widely used in humans<sup>11</sup>. This new suture has shown in vitro antibacterial efficacy against *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin resistant, *Staphylococcus aureus*, vancomycin resistant, *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Escherichia coli*<sup>12,13</sup>. This effect has also been demonstrated in vivo in a guinea pig model developed, in which sutures in skin wounds were directly colonized with *S. aureus*<sup>14</sup>.

The aim of the present study was to evaluate the experimental performance of coated polyglactin 910 suture with triclosan and traditional polyglactin 910 suture with regard to surgical abdominal wound infections following abdominal sepsis by cecal ligation and puncture.

## **METHODS**

This study was conducted at the Division of Experimental Surgery, Center for Health Sciences, Federal University of Rio Grande do Norte, Brazil. The experimental protocol and the care of the animals were in accordance with the Animal Welfare Act and Brazilian Law 11.794/2009 and with the Guide for the Care and Use of Laboratory Animals, USA, 1996. This project was approved by the Institutional Animal Care and Use Committee of UFRN, Brazil.

The sample was composed of 12 male healthy Wistar rats, weighing  $285 \pm 15$ g, randomly distributed on Vicryl plus group (n=6) and Vicryl group (n=6). The variables to be evaluated were: (1) tensile strength of the tissues at the site of the suture (2) the histopathological aspects with counts of inflammatory cells, collagen and foreign body reaction (3) bacteriology - growth of Gram-positive and Gram-negative bacteria involved in healing tissues.

### **Operative procedures**

The animals were anesthetized with an intramuscular injection of 0.1 ml/100g body weight of a solution consisting of 1.0 ml of ketamine (50 mg/ml) and 1.0 ml xylazine (20 mg/ml). All of them were subjected to cecal ligation and puncture (CLP). After laparotomy, the cecum was exposed, ligated with 2-0 silk, one cm distally to the ileocecal valve to avoid intestinal obstruction. Four punctures were performed with a 22-gauge needle, squeezed gently to force out a small amount of feces, and then it was returned to the abdominal cavity. The abdomen was closed with 4-0 nylon sutures. All procedures were performed under aseptic conditions.

After 24 hours, the rats were reoperated, and the incision made in the same place at the previous one. Then these wounds were contaminated by secretions present

in the abdominal cavity and sutured with simple stitches using polyglactin 910, which will be tested in each group. In animals of group Vicryl the suture of musculoaponeurotic layer was performed with Vicryl 4-0; the abdominal wall of rats from Vicryl Plus group was sutured with Vicryl Plus 4-0. Postoperative pain control was done with dipyrone s.c. at a dose of 10mg/kg.

Five days after the second surgery, the rats were subjected to another laparotomy under anesthesia. Using a sterile swab, samples were taken of material extracted from infected abdominal wounds, which were plated on blood agar medium (for growth of Gram-positive) and McConkey agar medium (for growth of Gram-negative bacteria). Data were expressed as mean±standard deviation colony forming units (CFU). Later, rectangular fragments of muscle-aponeurotic layer were removed, having its center at the suture zone. Finally, the animals were euthanized with a lethal dose of anesthetic (thiopental 100mg/kg, sc). Once removed, these fragments were tested for tensile strength (gf/mm<sup>2</sup>) by using a tensiometer – (EMIC, Brazil), equipped with the Software 2.0 for Windows.

Fragments of muscle-aponeurotic tissues were used for histological slides, stained with hematoxylin and eosin. The quantitative analysis of inflammation was performed using an image analyzer. The total area of the microscopic fields was observed using an optical microscope (Olympus P-50), whose images were captured on digital camera and scanned by Image Pro-Plus software, version 3.0 (Media Cybernetics - LP, USA). Five random microscopic fields were evaluated. The slides were examined for quantification of cells, collagen and other elements of the inflammatory reaction.

Statistical analysis was processed by BioEstat 6.0 Software. For comparison between groups we used analysis of variance and Student t test for paired samples, considering significance  $p < 0.05$ .

## RESULTS

On the fifth postoperative day bacterial cultures of the secretions collected from abdominal wounds closed with two different sutures revealed growth of *Staphylococcus aureus* and *Klebsiella sp.* A significant difference was observed in the mean colony forming units of Gram-positive and Gram-negative bacteria isolates in wounds sutured with noncoated (Vicryl) versus triclosan-coated sutures (Vicryl Plus), as seen in table 1 ( $p < 0.0001$ ).

**Table 1** – Colony forming units (CFU) in infected wounds closed with respective sutures.

Sutures	Vicryl	Vicryl Plus	p value
CFU	127.142.8±7.559.3	78.571±10.690.4	<0.0001

Mean±standard deviation

These data suggest that triclosan-coated sutures (Vicryl Plus) were significantly effective in reducing the microbial CFU in infected abdominal wounds.

**Table 2** – Tensile strength of abdominal wall sutured with Vicryl or Vicryl Plus (test performed at 5<sup>th</sup> postoperative day).

Sutures	Vicryl	Vicryl Plus	p value
Tensile strength (gf/mm <sup>2</sup> )	533.8±75.8	854.0±51.7	<0.0001

Mean±standard deviation

## DISCUSSION

Surgical site infections (SSI) remain a serious problem in the surgical community. Of the nearly 27 million surgical procedures performed annually in the United States, SSIs occur in 2–3%, with the majority (60%) of these infections being confined to the incision<sup>15</sup>. Evidence suggests that the suture knot may be the central repository for bacteria that contaminate the wound. As such, it provides a nidus or scaffold for bacterial colonization and replication that can ultimately result in SSI. The most common organisms responsible for SSI include *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin-resistant *S. aureus* (MRSA), and methicillin-resistant *S. epidermidis* (MRSE)<sup>16</sup>. Therefore, active inhibition of these organisms at the surgical site may help reduce the overall rate of postoperative infections<sup>17</sup>. Some relevant publications from experts have shown great interest in these sutures<sup>2,18</sup>. Their efficacy remains unproven and there are concerns regarding the safety of these sutures as one trial had shown an increased risk of wound dehiscence<sup>19</sup>.

There is an increasing recognition of the importance of evaluation of surgical innovations. The absence of demonstrable benefit of sutures-which are more closely related to a drug than most other surgical innovations-emphasizes the inappropriateness of such an approach and supports the need of high quality, prospective trials before such innovation are adopted into practice. Before that, experimental studies like this are mandatory.

Because the suture knot is believed to be the principal site of bacterial colonization in the wound, coated polyglactin 910 suture with triclosan (Vicryl Plus Antibacterial Suture®,) was developed in order to impregnate the suture material with antibacterial activity against the most common putative pathogens that may cause SSI. Triclosan has been used as a safe and effective antimicrobial agent for more than 30 years. During this time, it has been proved to be effective against both methicillin-sensitive and methicillin-resistant *S. aureus* (MRSA)<sup>20</sup>. Coated polyglactin 910 suture with triclosan has demonstrated antibacterial activity in vitro against *S. aureus*, *S.*

epidermidis, MRSA and methicillin-resistant *S. epidermidis* (MRSE). In vivo, coated polyglactin 910 suture with triclosan demonstrated antibacterial activity against *S. aureus*, resulting in a statistically significant 30-fold reduction in the number of organisms<sup>14</sup>. Furthermore, triclosan has been proved to be nontoxic in a variety of test systems, and does not affect tissue reaction, healing response, or the absorption profile of coated polyglactin 910 suture with triclosan, compared to the traditional coated polyglactin 910 suture without triclosan<sup>11</sup>.

In the presence of contamination, the sutures are potentially a reservoir of bacterial colonization, and constitutes an established risk factor that acts as coadjuvant to the development of surgical infection. This situation could not be controlled by surgeons, since active antibacterial sutures were not available. The results of the present study support the use of an antiseptic-coated suture to secure a safe wound environment. In view of the results obtained in the present study, an efficacy profile may be established (see Tables 1 and 2), defining Coated Vicryl Plus antibacterial suture as an adequate option for suturing in general, digestive anastomoses, subcutaneous suturing and skin closure, among other applications.

In our model, the microbiological study showed that Coated Vicryl Plus suture effectively reduced the number of bacteria present in the wounds, and the best effect was seen to *Staphylococcus aureus* and *Klebsiella* sp. In the presence of infection, Coated Vicryl Plus suture modulated inflammatory response, with normalization of the tissue healing process. These results, transferred to the clinical setting, indicate that Coated Vicryl Plus suture may offer effective prophylaxis against surgical infection. This suture would afford in situ protection of the wound against most microorganisms that cause surgical infection, at least up to a certain level of contamination which in any case would be covered particularly by clean and clean-contaminated surgery. Wound closure with triclosan-impregnated sutures resulted in 66.6% reduction in positive culture from tissue adjacent to the steel implant, thereby showing that the antibacterial influence extends to the surrounding tissue<sup>3</sup>. In addition, these sutures may have an immunomodulatory effect that is favorable to tissue healing as the healing factors such as hydroxyproline and transforming growth factor- $\beta$  and inflammatory mediators such as tumor necrosis factor- $\alpha$  in contaminated wounds closed with triclosan-impregnated sutures approached that of clean wounds<sup>1</sup>. In the present study we simulated a case of wound infection produced by a polymicrobial abdominal sepsis after cecal ligation and puncture.

In conclusion, this study demonstrates the in vivo efficacy of Coated Vicryl Plus suture. This suture prevents bacterial colonization and reduces the inflammatory response, allowing tissue healing even in infected wounds.

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