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Effectiveness of Collagen–Gentamicin Implant for Treatment of "Dirty" Abdominal Wounds

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Abstract. The purpose of this work was to compare the efficacy and safety of the collagen–gentamicin sponge with conventional treatment (wound open, maintaining a close observation, and cleaning it daily with antiseptics) for the prophylaxis of infection in "dirty" abdominal wounds. Seventy-three patients with dirty abdominal wounds caused by gastrointestinal tract surgery were studied. The patients were randomized in two groups: group A, open wounds, treated with local cleansing, metronidazole 20 to 40 mg/kg/day IV and gentamicin 5 mg/kg/day IV for 7 days. Group B, primary closure with collagen–gentamicin implant plus metronidazole 20 to 40 mg/kg/day IV for 7 days. Surgical wound infections were significantly reduced by the collagen–gentamicin implant. Polymicrobial infections were observed in group A, whereas the infections were caused only by a single organism in group B. In conclusion, the collagen–gentamicin implant is effective and well tolerated in the treatment of "dirty" surgical abdominal wounds because it significantly reduces the wound infection rate ($p < 0.01$) and shortens healing time ($p < 0.001$) and the period of disability.

Abdominal wound infections comprise one of the most frequent complications in patients submitted to complicated abdominal surgery [1]. One of the internationally accepted classifications on this matter is that proposed by the National Research Council Ad Hoc Committee on Trauma in 1964, which was later adopted by the American College of Surgeons. This classification considers the following categories: (1) clean wounds; (2) contaminated clean wounds; (3) contaminated wounds; and (4) dirty wounds [2].

Dirty wounds carry a risk of infection in up to 45%, regardless of all measures taken to reduce the incidence of this complication, such as the improvements in surgical techniques, asepsis and antisepsis, and the use of perioperative antimicrobial agents. The germs most frequently found in surgical wound infections are the gram-negative anaerobes such as *Escherichia coli, Klebsiella* sp., *Proteus* mb and *Pseudomonas aeruginosa,* among others; therefore aminoglycosides should be included in the treatment regimens for these infections [3].

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It has been observed that primary closure of dirty abdominal wounds at the end of the intervention increases the risk of infection and the risk of dissemination of this infection to adjacent structures such as adipose tissue, fasciae, and muscles. This complication is associated with a mortality rate of up to 25%. The most frequent method for preventing these complications consists in leaving the wound open, maintaining close observation, and cleaning it daily with antiseptics, until the presence of infection has been ruled out and it can be safely closed within 3 to 5 days. This procedure avoids delays in the diagnosis of wound infection and reduces the possibility of complications such as necrotizing fasciitis.

This study was designed to determine how to reduce the infection rate of dirty surgical wounds. The study population was composed of patients with dirty wounds in whom a collagen sponge soaked with gentamicin was placed within the wound to obtain high concentrations of this aminoglycoside in the wound's tissues and thus facilitate its healing.

The collagen–gentamicin implant is composed of highly purified type I collagen obtained from bovine tendon, which acts as a vehicle for the antimicrobial gentamicin. Collagen is absorbed slowly by the tissue 6 to 10 days after its application [4]. The purpose of the implant is to provide a high concentration of local gentamicin at the site of implantation, 300 to 900 μg/ml. The sponge, $10 \times 10 \times 0.5$ cm, contains 130 mg gentamicin sulfate. There are previous reports about the efficacy of these collagen–gentamicin implants in orthopedic surgery, for treatment of osteomyelitis and soft tissue infections, but it has not been used as a prophylactic measure in abdominal wound infections caused by complicated gastrointestinal tract (GI) surgery [5].

Materials and Methods

A total of 73 patients with dirty abdominal wounds derived from the lower GI tract (i.e., preoperative perforation of the GI tract) were enrolled in the study. Patients were randomly assigned to one of two groups. Treatment of group A consisted in leaving the wound open and cleaning it daily with a povidone solution (with iodine); this method was referred as "traditional"; and if no

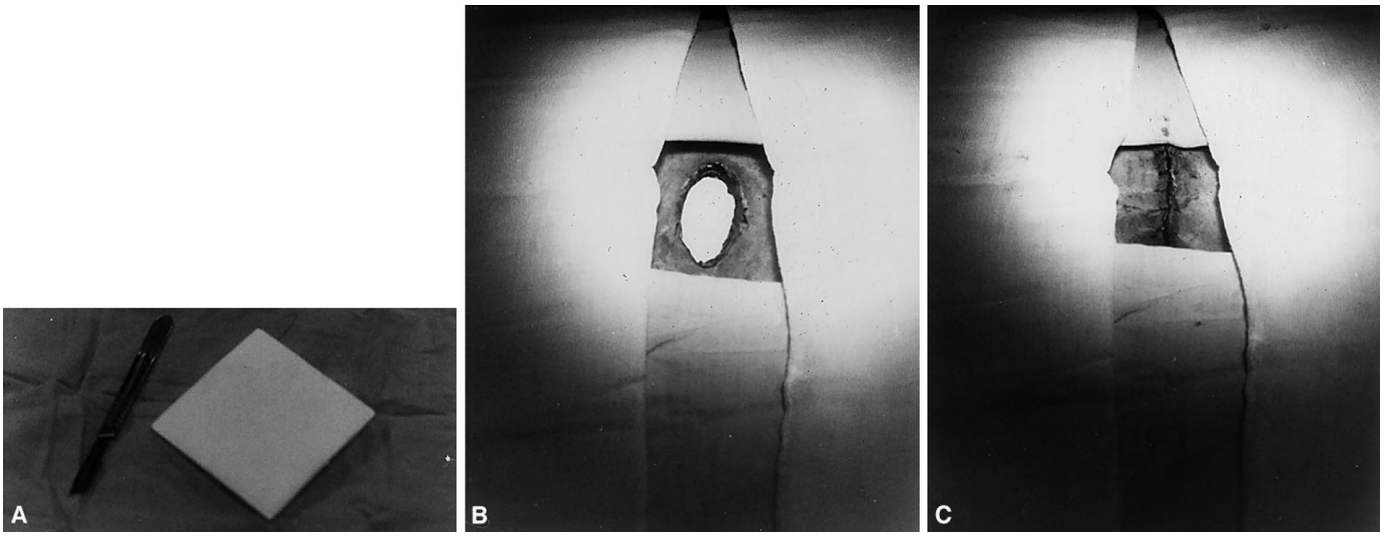

Fig. 1. Implant of collagen/gentamicin (**A**) is put into the wound above the aponeurosis (**B**), and the wound is sutured (**C**).

Table 1. Patients excluded from the study.

Characteristics	Reason for exclusion
45-Year-old man with complicated colonic diverticular disease	Required antimicrobial therapy not in study
27-Year-old woman with complicated acute appendicitis	Discontinued antimicrobial therapy
29-Year-old woman with perforated ileitis by *Salmonella*	Required another antimicrobial scheme
72-Year-old man with complicated acute appendicitis	Developed pneumonia and required another antimicrobial therapy
68-Year-old woman with complicated colonic diverticular disease	Died during postoperative period
78-Year-old man with perforated colonic cancer and bilateral pneumonia	Required more antimicrobial therapy; died during postoperative period
45-Year-old woman with perforated cholecystitis	Discontinued antimicrobial therapy

infection was apparent by the third day the wound was closed with adhesive tape. The antimicrobials administered to these patients were metronidazole 20 to 40 mg/kg/day and gentamicin 5 mg/kg/day, both administered intravenously for 7 days. Patients in group B received the collagen–gentamicin implant, and their wounds were closed immediately after surgery (Fig. 1); they received only metronidazole 20 to 40 mg/kg/day for a period of 7 days.

For comparison of the groups regarding infection, we used the chi-square test with $\alpha = 0.001$. For the wound healing time, Student's t-test with $\alpha = 0.001$ was applied.

Results

Seven patients were excluded from the study mainly because of postoperative complications and in two cases because of the administration of additional antimicrobials not allowed in the protocol. Therefore the final study population consisted of 66 patients (Table 1).

Group A was composed of 32 patients: 21 males (66%) and 11 females (34%), with a mean age of 44.1 years (range 17–75 years). Group B comprised 34 patients: 15 males (44%) and 19 females (56%) with a mean age of 48.4 years (17–83 years).

The main pathologies that caused the clinical picture of acute abdomen are listed in Table 2. Patients in group A had been sick for an average of 70 hours, and those in group B had been sick for an average of 87.4 hours. A total of 43.75% of patients from group A developed infection (14/32 patients), whereas only 8.82% of patients in group B were affected by this complication (3/34 patients, $p < 0.001$, chi-square) (Fig. 2).

Table 2. Major pathology that leads to "dirty" abdominal wounds.

	Group A		Group B	
Condition	%	No.	%	No.
Acute appendicitis	72	23	63	21
Colon perforation	12	4	10	3
Gallbladder perforation	6	2	13	4

The mean hospitalization time was 7 days in the group on conventional treatment (A) and 5.45 days in the group treated with the collagen–gentamicin implant (B). There was a statistically significant difference in the wound healing time between groups: 15.20 days in the conventional treatment group versus 10.31 days in the group with the collagen–gentamicin implant ($p < 0.001$ with Student's t-test). Tables 3 and 4 show the ratio of patients's length of hospital stay and wound healing time.

Forty percent of patients in group B experienced drainage of serous fluid through a surgical wound or dehiscence. This effect was transitory in all cases. The germs isolated from purulent secretions of infected wounds are shown on Table 5. It is of note that it was possible to isolate two or more bacteria from the

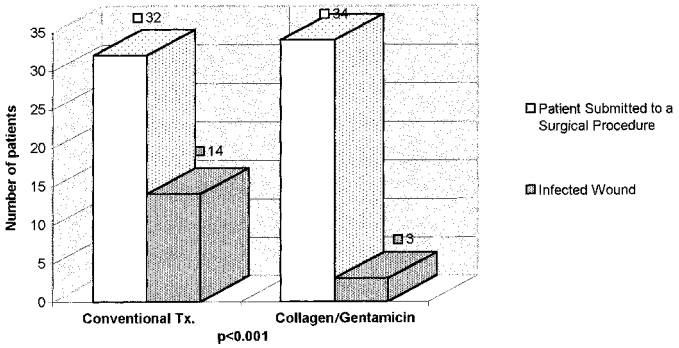

Fig. 2. Incidence of infection among "dirty" abdominal wounds. Comparison between conventional treatment based on cleaning the wound and leaving it open and the use of a collagen/gentamicin implant with primary closure of the wound. $^{*}p < 0.001$, chi-square test.

Table 3. Length of hospitalization.

	Group A		Group B	
Hospitalization (days)	Patients (no.)	Average time (days)	Patients (no.)	Average time (days)
<7	23	4.22	29	4.03
8–15	5	11.0	3	9.33
>15	4	21.0	2	22.00

Table 4. Wound healing time.

Healing duration (days)	Group A		Group B	
	Patients (no.)	Average duration (days)	Patients	Average duration (days)
<7	6	7	21	7
8–15	8	10.5	4	12
>15	12	13	8	22
>20	6	52	1	42

Table 5. Germs isolated from secretions of the infected wounds.

Microorganism	Group A (%)	Group B (%)
Escherichia coli	54	66
Streptococcus	23	—
Pseudomonas	23	—
Candida	15	—
Proteus	15	—
Klebsiella	8	—
Enterococcus	8	—
Enterobacter	8	—
Staphylococcus	—	34

patients in group A, whereas all cases of infection in group B were monomicrobial.

Discussion

Acute suppurative peritonitis secondary to inflammatory conditions of the GI tract, especially acute appendicitis, continues to occur frequently, and surgeons are concerned about the treatment of dirty abdominal wounds and the consequent increase in hospitalization time and high costs of antimicrobial therapy. In the present study, a reduction in the incidence of surgical wound infection from 44% with conventional treatment to 9% with the use of the collagen–gentamicin sponge was noted. We consider that this result is due to the high local concentration of the aminoglycoside, gentamicin in this case, which inhibits the growth of gram-negative bacteria, the most common type of bacteria found in wounds.

Other clinical trials have shown the usefulness of collagen not only as a carrier for gentamicin but also due to its effects on healing and the hemostatic process [6]. We believe that the reduction in healing time observed in the wounds of the patients who received the collagen–gentamicin implants was caused mainly by the absence of infection associated with the positive effects of collagen on the healing process. In 13 patients (40%) in group B the wound healing time was more than 7 days because partial dehiscence of the wound by serous liquid drainage. This serous liquid drainage fluid observed was most prominent among those with thick adipose tissue; therefore it may be adequate to use a closed drainage system to aspirate the excess transudate in these patients. It is important to note that no bacteria were isolated from this serous drainage fluid.

Conclusions

The collagen–gentamicin implant is effective for treatment of "dirty" abdominal wounds caused by GI tract surgery, as it significantly reduces the incidence of infections and the length of hospital stay. These effects provide an earlier return to daily and work activities.

Résumé

Le but de cette étude a été de comparer l'efficacité et la sûreté d'une éponge collagène imbibée de gentamycine à celle d'un traitement conventionnel (plaie laissée ouverte, observation de près, et nettoyage quotidien par des antiseptiques) dans la prophylaxie de l'infection dans des incisions abdominales «sales». Soixante-trois patients ayant une incision abdominale «sale» en rapport avec une intervention gastro-intestinale ont été randomisés pour constituer deux groupes: le groupe A a été traité en laissant la plaie ouverte, des soins locaux, la métronidazole en intraveineux, 20 à 40 mg/kg/jour et la gentamycine en intraveineux 5 mg/kg/jour pour sept jours pendant 7 jours alors que le groupe B a eu une fermeture primitive, un implant collagène-gentamycine plus la métronidazole intraveineux 20 à 40 mg/kg/jours pendant 7 jours. Le taux d'infections de la plaie chirurgicale a été réduit de façon significative par l'utilisation de l'implant collagène-gentamycine. Dans le groupe A, on a observé des infections polymicrobiennes alors que dans le groupe B, les infections étaient en rapport avec un seul organisme. En conclusion, l'implant collagène-gentamycine est efficace et bien tolérée dans le traitement des incisions chirurgicales abdominales «sales» car il permet une réduction significative du taux d'infection ($p < 0.01$), abrège le temps de cicatrisation ($p < 0.001$) et la période d'incapacité.

Resumen

El objetivo del presente trabajo fue comparar la eficacia y seguridad del la esponja de colágeno-gentamicina con el tratamiento convencional (herida abierta, observación cuidadosa y lavado diario con antisépticos) en la profilaxis de la infección en heridas abdominales "sucias". Se estudiaron 73 pacientes con heridas abdominales sucias resultantes de cirugía sobre el tracto gastrointestinal. Los pacientes fueron randomizados en dos grupos: Grupo A, heridas abiertas, tratadas con limpieza local, Metronidazol IV 20 a 40 mg/kg/día y Gentamicina IV 5 mg/kg/día por 7 días, y Grupo B, cierre primario con implante de Colágeno-Gentamicina más Metronidazol IV 20 a 40 mg/kg/día por 7 días. El implante de Colágeno-Gentamicina resultó en una disminución significativa de las infecciones de la herida quirúrgica. En el Grupo A se observaron infecciones polimicrobianas, mientras que en el Grupo B las infecciones fueron causadas por un microorganismo único. En conclusión, el implante de Colágeno-Gentamicina es efectivo y bien tolerado en el manejo de heridas abdominales "sucias", por cuanto reduce significativamente la tasa de infección de herida ($p < 0.01$), acorta el tiempo de cicatrización ($p < 0.001$) y reduce el periodo de incapacidad.

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Invited Commentary

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The authors studied the rate of infected incisional wounds in patients operated for peritonitis from appendicitis ($n = 44$) and colon ($n = 7$) and gallbladder ($n = 6$) perforation. In one group of 34 patients the incisional wounds were left open (I assume only the skin was not sutured while the fascia was closed); in the second group of 32 patients 130 mg of gentamicin contained in a 5 cm^3 collagen sponge was implanted epifascially into the subcutaneous tissue, and the skin was closed. The overall surgical site infection (SSI) rate was 26%. The authors claim that the gentamicin–collagen wound implant reduced the SSI rate from 41% to 9%. They do not, however, tell us their definition of wound infection. There is strong evidence that patients in the nonsponge group (I) should not have experienced wound infections at all if these wounds had been left open to heal by secondary intention, as initially planned. Why did the authors close the wounds on the third postoperative day? On the third postoperative day, open wounds are heavily contaminated, and wound-healing processes have not formed sufficient granulation tissue (e.g., local host defense) to eliminate bacteria that colonize such wounds. Closing contaminated wounds before host defenses are established produces ideal conditions for wound infection, so the comparison used in the otherwise laudable study seems unfair.

Results of prospectively randomized studies in the literature tell us that the SSI rates would have been approximately 7% to 9%, exactly the same rate the authors observed in group II, if they had chosen to close the wounds of group I primarily and had administer the right antibiotic preoperatively. The lowest SSI rates are obtained with preoperatively started intravenous antibiotics. In 262 patients with acute appendicitis, preoperative administration of metronidazole or clindamycin against obligate anaerobes combined with a third-generation cephalosporin resulted in wound infection rates of less than 5% [1]. This comparison is permitted because in the present study 67% had appendicitis.

In their introduction the authors mentioned a series of Enterobacteriaceae including *Pseudomonas* as being gram-negative anaerobes. True obligate anaerobic bacteria that would be typical for the diseases described in this paper are not mentioned. One may assume that the bacteriologic methods used did not focus on isolation of obligate anaerobes. Bacteriologic methods, however, have not been described. It is difficult for the reader to accept the report as being representative. For example, the list of wound isolates in their Table 5 includes 15% of *Candida* and 23% of *Pseudomonas. Pseudomonas* does not tolerate anaerobic conditions, is not found in human bowel, and is not a pathogen of peritonitis. It is likely that these microorganisms contaminated the

open wound postoperatively. The bacteriology of Table 5 therefore suggests heavy exogenous contamination, rather than endogenous flora of peritonitis that contaminated the wounds at the time of the initial operations and that would have been amenable to antibiotic prophylaxis. This paper does not prove that a gentamicin/collagen sponge implant inserted into the incisional wound is of any benefit to the patient.

The lesson of this paper is that one should not close on the third day after operation a granulating wound that was left open for healing by secondary intention.

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