

# Effect of Local Gentamicin Application on Healing and Wound Infection in Patients with Modified Radical Mastectomy: a Prospective Randomized Study

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This study investigated the effects of Gentacoll implants on healing in patients ( $n = 44$ ) undergoing modified radical mastectomy and axillary dissection. Group I, the Gentacoll group ( $n = 22$ ), underwent surgery followed by insertion of  $10 \times 10 \times 0.5$  cm Gentacoll implants (280 mg collagen sponge plus 200 mg gentamicin sulphate) into the axillary area and under the flap area of the breast before wound closure. Group II, the control group ( $n = 22$ ), underwent surgery without the application of Gentacoll. Neither group received oral or parenteral

post-operative antibiotic therapy. Outcome measures included wound infection, seroma formation, total drainage volumes, drain removal time and duration of hospital stay. Post-operative infection rate, seroma formation, drainage volumes and duration of hospital stay were significantly reduced in the Gentacoll group compared with the control group. In conclusion, the application of Gentacoll significantly improved post-operative outcomes in patients undergoing modified radical mastectomy.

**KEY WORDS:** GENTACOLL; GENTAMICIN; ANTIBIOTICS; BREAST CANCER; MODIFIED RADICAL MASTECTOMY; COLLAGEN SPONGES; POST-OPERATIVE INFECTION

## Introduction

Gentacoll comprises biologically absorbable collagen sponges that are impregnated with gentamicin enabling its local application. The implants consist of equine type I collagen in a highly purified form. In addition to the effect of gentamicin, it is also reported that the collagen material itself has a haemostatic effect and increases wound healing.<sup>1</sup> Gentacoll has been shown to

reduce post-operative infectious complications and to have various beneficial effects on healing in different types of surgical applications.<sup>2 - 10</sup> In a previous randomized controlled trial (the local collagen-gentamicin for prevention of sternal wound infections [LOGIP] trial) of almost 2000 patients, the addition of local collagen-gentamicin implants between the sternal halves at sternal closure reduced the

incidence of post-operative wound infections compared with intravenous prophylaxis alone.<sup>11</sup> Since the success of the LOGIP trial, Gentacoll has been used routinely in almost all cardiac surgeries.<sup>2</sup> There has, however, been concern that the introduction of this antibiotic prophylaxis could rapidly induce antibiotic resistance among causative microbiological agents, with subsequent loss of the prophylactic antibiotic effect.<sup>2</sup> Thus, the clinical use of Gentacoll has not been widely accepted in other areas of surgery, particularly in those operations that are considered 'clean' (i.e. operations that are elective, non-emergency, non-traumatic and primarily closed, with no acute inflammation and no break in the technique, and where the respiratory, gastrointestinal, biliary and genitourinary tracts have not been entered).<sup>2</sup> To date, there has not been a published study on the efficacy and safety of Gentacoll in breast cancer surgery. The present study was performed to evaluate the effect of the local application of Gentacoll in breast cancer patients undergoing modified radical mastectomy surgery.<sup>8,9</sup>

## Patients and methods

### PATIENT POPULATION

After obtaining approval from the Ethics Committees of Samsun Ondokuz Mayıs University (Samsun, Turkey) and Mustafa Kemal University (Serinyol, Turkey), female patients who were diagnosed with breast cancer and underwent modified radical mastectomy with axillary dissection between June 2006 and June 2009 were enrolled sequentially into the study. Patients with inflammatory breast cancer who had neoadjuvant radiotherapy or who had chronic diseases (e.g. diabetes) or immune suppression were excluded from the study. All participants provided written informed consent.

### TREATMENT GROUPS

At each site, patients were randomly allocated to one of two groups. Group I underwent modified radical mastectomy during which Gentacoll was applied to the axillary area and under the flap area of the breast before closure of the surgical wound. Two pieces of Gentacoll were used for each area, each comprising  $10 \times 10 \times 0.5$  cm collagen from equine tendons (280 mg) plus gentamicin sulphate (200 mg) (Fig. 1). Group II underwent modified radical mastectomy without the application of the Gentacoll. Neither group received oral or parenteral antibiotic therapy after the surgery. Vacuum drains were applied into the axillary area and beneath the flap in both groups. Drains were removed when the drainage volume was  $< 20$  ml/day.

Patients in both groups were followed up 7 days after discharge from hospital, and at 1, 3 and 6 months after surgery. Wound infection, seroma formation, drain removal time, total drainage volumes and duration of hospital stay were recorded.

### STATISTICAL ANALYSES

The mean  $\pm$  SD of the data were calculated and all analyses were carried out using the SPSS® statistical package, version 13.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Drainage volumes, wound infection, seroma formation and removal times of drains for the two groups were compared using Student's *t*-test and a Z-test. A *P*-value  $< 0.05$  was considered to be statistically significant.

## Results

A total of 44 female patients diagnosed with breast cancer who underwent modified radical mastectomy with axillary dissection were enrolled into the study. The mean age  $\pm$  SD was  $51.38 \pm 2.41$  years in the Gentacoll group (group I;  $n = 22$ ) and  $50.68 \pm 2.17$  in the control group (group II;  $n = 22$ ); no



**FIGURE 1:** Photographs showing how Gentacoll was applied to the axillary area of the breast and under the flap area of the breast during modified radical mastectomy procedures in female patients with breast cancer: two pieces of Gentacoll, each 10 × 10 × 0.5 cm and comprising 280 mg collagen from equine tendons plus 200 mg gentamicin sulphate, were applied into each area before surgical wound closure

statistically significant difference. The surgical procedures undertaken, pathological stages, histological diagnoses and lymph node counts of the patients are shown on Table 1.

Mean ± SD drainage volumes were significantly lower in the Gentacoll group

compared with the control group at all times ( $P < 0.05$  for each comparison; Table 2). The mean ± SD drain removal time was significantly shorter in the Gentacoll group compared with the control group ( $P < 0.05$ ; Table 3). No wound infection occurred in the Gentacoll group and this was significantly

**TABLE 1:**  
 Surgical procedures undertaken, pathological stage, histological diagnosis and lymph node counts for female breast cancer patients who underwent modified radical mastectomy with or without the application of Gentacoll

|                                                          | Gentacoll group<br>(n = 22) | Control group<br>(n = 22) |
|----------------------------------------------------------|-----------------------------|---------------------------|
| Right modified radical mastectomy                        | 10                          | 9                         |
| Left modified radical mastectomy                         | 12                          | 13                        |
| Pathological stage <sup>a</sup>                          |                             |                           |
| Stage I                                                  | 5                           | 6                         |
| Stage II                                                 | 8                           | 7                         |
| Stage III                                                | 9                           | 9                         |
| Histological diagnosis                                   |                             |                           |
| Invasive ductal cancer                                   | 18                          | 19                        |
| Invasive lobulary cancer                                 | 4                           | 3                         |
| Metastatic lymph node count                              | 4.21 ± 0.71                 | 2.14 ± 1.24               |
| Reactive lymph node count in modified radical mastectomy | 22.32 ± 1.24                | 21.16 ± 1.34              |

Data show numbers of patients or mean ± SD.

<sup>a</sup>Tumour, node, metastasis cancer staging.<sup>12</sup>

**TABLE 2:**  
Post-operative drainage volumes for female breast cancer patients who underwent modified radical mastectomy with or without the application of Gentacoll

| Post-operative day | Drainage volume (ml)  |                     |
|--------------------|-----------------------|---------------------|
|                    | Gentacoll<br>(n = 22) | Control<br>(n = 22) |
| Day 1              | 70.66 ± 11.45*        | 187.16 ± 12.61      |
| Day 3              | 43.70 ± 9.93*         | 120.51 ± 12.68      |
| Day 7              | 13.43 ± 5.24*         | 52.51 ± 9.78        |

Data show mean ± SD.

\**P* < 0.05 compared with the control (Student's *t*-test and Z-test).

better than for the control group (*P* < 0.05; Table 3); two patients in the control group had to be rehospitalized and were administered parenteral antibiotic therapy, and a further two needed to use enteral antibiotics for 2 weeks. Seroma occurred in one patient in the Gentacoll group and in five patients in the control group (*P* < 0.05; Table 3). The mean ± SD seroma volume was significantly lower in the Gentacoll group compared with the control group (20.1 ± 10.6 ml versus 115.4 ± 12.3 ml, respectively; *P* < 0.05). The mean ± SD hospital stay was significantly shorter in the Gentacoll group compared with the control group (*P* < 0.05; Table 3).

## Discussion

The aim of the present study was to evaluate the effect of Gentacoll, a biologically

absorbable collagen sponge impregnated with gentamicin that enables its local application, on wound healing, infectious complications and duration of hospital stay in breast cancer patients undergoing modified radical mastectomy. The application of Gentacoll was found significantly to reduce the rate of post-operative early and late wound infections and the duration of hospital stay in these patients.

Despite modern surgical techniques, knowledge of the pathogenesis of surgical site infections (SSIs) and the use of peri-operative antibiotic prophylaxis, the incidence of SSIs has not decreased, but has remained at the same level over the last decade.<sup>13</sup> More effective preventative methods are needed and are likely to become even more important in the future due to the growing

**TABLE 3:**  
Post-operative outcomes for female breast cancer patients who underwent modified radical mastectomy with or without the application of Gentacoll

| Post-operative measure              | Gentacoll<br>(n = 22) | Control<br>(n = 22) |
|-------------------------------------|-----------------------|---------------------|
| Drain removal time (days)           | 4.9 ± 1.49*           | 9.2 ± 1.28          |
| Development of wound infection      | 0*                    | 4                   |
| Development of seroma               | 1*                    | 5                   |
| Mean length of hospital stay (days) | 5.12 ± 1.1*           | 9.83 ± 1.6          |

Data show numbers of patients or mean ± SD.

\**P* < 0.05 compared with the control (Student's *t*-test and Z-test).

population of elderly sick patients.<sup>13–17</sup>

The advantages of locally applied gentamicin are: (i) it does not impair renal function; (ii) the risk of developing resistant pathogens is small; and (iii) it has the capacity to kill bacteria by inhibiting protein synthesis.<sup>18</sup> It is also capable of destabilizing the lipid bilayer membranes of bacteria.<sup>13,19</sup> Systemically administered gentamicin may be toxic but, when administered locally, even at very high concentrations, the serum concentrations remain well below toxic levels.<sup>20</sup>

Local gentamicin application has been studied in various fields. For example, de Bruin *et al.*<sup>10</sup> used gentamicin during abdominoperineal resection and reported that it reduced perianal wound infections after radiotherapy in these patients. Based on their results, they recommended the local application of gentamicin in the sacral cavity in patients who undergo abdominoperineal resection after short-term radiotherapy.

In a prospective randomized study, Picó *et al.*<sup>19</sup> investigated wound infections after appendectomy procedures using conventional treatment compared with using reabsorbable antibacterial sutures or gentamicin-impregnated collagen sponges. They concluded that the use of sutures impregnated with antiseptic and/or the use of a gentamicin-containing collagen sponge significantly reduced wound infection rates in children undergoing appendicectomy compared with children in the control group. The beneficial effect on wound healing also decreased the duration of the hospital stay.<sup>19</sup>

Gentamicin is effective against *Staphylococcus epidermidis* and by using locally applied gentamicin even the growth of resistant isolates is inhibited.<sup>13–17</sup> The preventative effect of locally applied gentamicin against wound infections in 'dirty wounds' has been studied by Rutten and Nijhuis<sup>21</sup> in abdominal surgeries. Similarly,

Vogel and Lenz<sup>22</sup> studied the effect of Gentacoll on pilonidal sinus surgery managed with primary closure, which usually results in high recurrence and wound infection, and concluded that it significantly reduced post-operative infection and recurrence rates. In an unpublished study, we investigated the effect of Gentacoll in pilonidal sinus surgery and reached similar conclusions. Although not technically 'dirty' surgery, wound infections after radical mastectomy and axillary dissection gain a special importance, as simple agents may cause serious complications due to axillary dissection. Thus, the primary objective of the present study was to reduce post-operative infection. To our knowledge, there are no published data concerning the effects of local Gentacoll application on wound healing in patients with modified radical mastectomy.

The Gentacoll group in the present study had significantly fewer SSIs and no additional antibiotic therapy was required. A significantly shorter hospital stay was also observed in the Gentacoll group compared with the control group. Thus, it is assumed that the beneficial effects of Gentacoll could indirectly reduce the cost of post-operative care.

Consistent with other studies,<sup>19,21,22</sup> the present study showed that Gentacoll reduced post-operative infections, seroma formation and duration of hospital stay in breast cancer patients undergoing modified radical mastectomy. Gentacoll sponges also reduced drainage volumes and drain removal times. These promising preliminary results need to be confirmed in larger, prospective studies and the issue of the potential development of antibiotic resistance as a result of the use of Gentacoll sponges also needs to be addressed.

## Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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