The use of a gentamicin-collagen sponge (Garamycin sponge) with NPWT for the treatment of difficult wounds in patients with Chron's disease. A case series

Bartosz Jan Grzechulski, Tomasz Banasiewicz

CASE REPORT

***Abstract*—Negative pressure wound therapy (NPWT) is extremely important in the treatment of difficult wounds in patients with proctological diseases, including patients with Crohn's colitis. Despite the many advantages of this therapy, it has some limitations, including the lack of bactericidal activity. Hence, NPWT is combined with antibacterial products. One of them is the gentamicin-collagen sponge, presented in three cases described below. The combination of the gentamicin-collagen sponge with NPWT may be beneficial in difficult wounds with high risk of an infection, and also in patients with impaired wound healing.**

***Keywords*—NPWT — negative pressure wound therapy, NPWTi — Negative pressure wound therapy with instillation, gentamicin-collagen sponge, Crohn's colitis**

Introduction

TREATMENT of wounds in proctological diseases is a constant challenge for modern medicine and a significant financial burden of health care.[1] Moreover, such wounds seriously affect the patient's mental state, leading to a significant reduction in the quality of life. Patients with proctological diseases are at especially high risk of wound infection. These are patients with metabolic and oncological diseases, treated with immunosuppressive drugs, operated in an infected field, or with surgeries lasting more than 3 hours. Patients with Crohn's colitis, in whom immunosuppressive treatment and other risk factors frequently impede wound healing, are particularly difficult to treat. In order to achieve a significant improvement in the healing of such wounds, these patients require the use of specialized dressings. One such dressing system that has revolutionized the treatment of difficult, complicated, and chronic wounds over the last dozen years is the negative pressure wound therapy (NPWT).

According to recent recommendations of the European Wound Management Association (EWMA) regarding NPWT (EWMA Document: Negative pressure wound therapy. Overview, challenges, and perspectives), the use of negative pressure therapy already covers more than 100 clinical indications.[2–5] The basic and most important mechanisms of NPWT have remained the same since the publications of Argentina and Morykwas,[2] which were thoroughly discussed in 1997. The treatment strategy is based on the TIME mechanism (T — tissue management, I — infection and inflammation control, M — moisture balance, E — epithelial edge advancement). Wound healing is both a multidirectional and a phased process. Negative pressure applied within the wound indirectly influences autolytic processes, which means that devitalized tissues are evacuated faster from the wound bed (T — tissue management). NPWT increases the blood supply to the wound bed, thus increasing its oxygenation. It changes the profile and number of cytokines, as well as the bacterial load, which inhibits inflammation and infection (I – infection and inflammation control). Tight wound closure optimizes the environment in terms of hydration and pH value. This ensures that the wound bed is neither dry nor excessively hydrated (M — moisture balance). Thanks to the micro- and macro-deformation mechanisms, the edges of the wound, which are important in the epithelial phase, are brought closer together, and their quality allows for proper epithelization (E — epithelial edge advancement).[6, 7]

The main advantage of NPWT is the stimulation of tissue perfusion and the granulation process, resulting in a significant acceleration of wound healing. It should also be emphasized that the treatment with negative pressure alone does not have a bactericidal effect, thus it may not be sufficient in the case of infected wounds. Therefore, the use of NPWT in combination with products and drugs containing antibacterial substances is increasingly used as a promising method of treating wounds with high biological stress.[8, 9] Usually, such combinations include solutions, in particular antiseptics, hence the method is called negative wound pressure therapy with instillation (NPTWi). However, it is possible to combine negative pressure therapy with other drugs with antibacterial effects, including dressings.

One such advanced dressing system is the combination of NPWT with the gentamicin-collagen sponge (Garamycin®

Manuscript received 02.02.2023; revised 21.04.2023. This work did not receive any financial support.

Author affiliations: Department of General, Endocrinological Surgery and Gastrointestinal Oncology, Poznan University of Medical Sciences, Poznan, Poland , **(BJG, TB)**

*Correspondence to: Bartosz Jan Grzechulski: bartosz.grzechulski@gmail.com

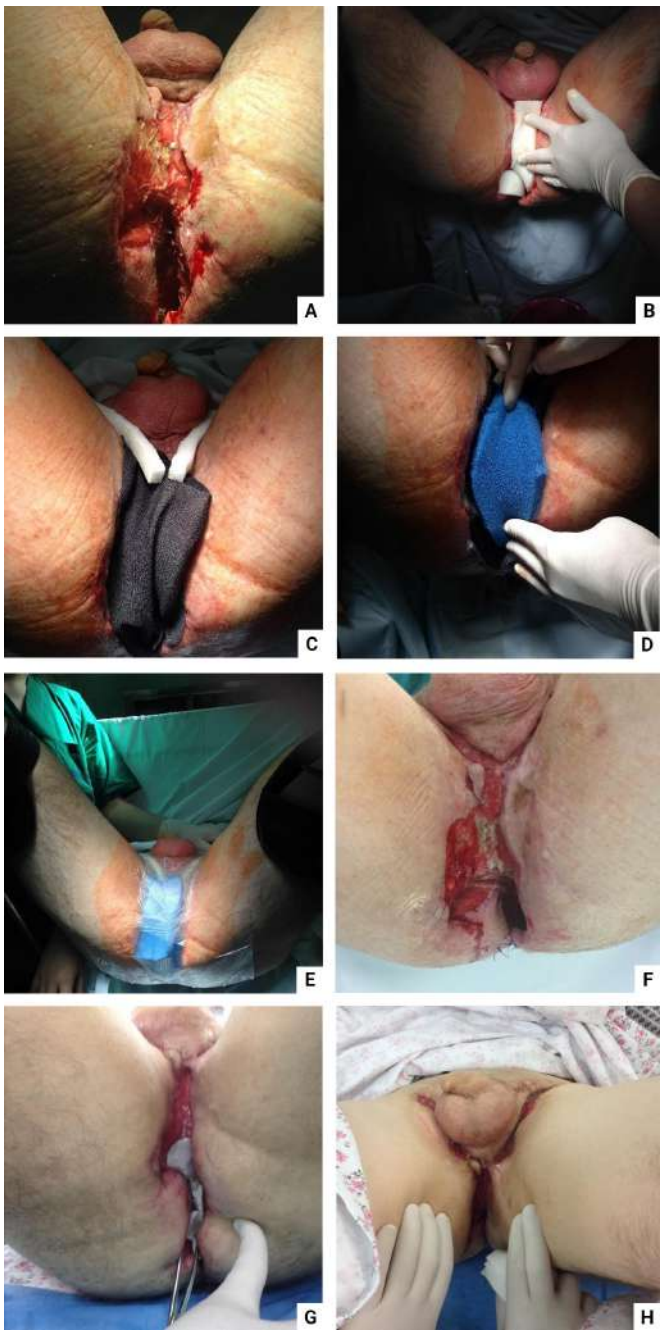

Figure 1. Patient 1 — Crohn's disease, a deep, infected wound of the perineum after rectal amputation

sponge; SERB SA). The first studies indicate a significantly lower rate of surgical site infection.[2] The gentamicin-collagen sponge has been used as a topical antibiotic for many years. Its usefulness has been confirmed in many areas of surgery, such as: colorectal surgery, orthopedics and traumatology, cardiac surgery, and neurosurgery.[10–12]

Scientific research has negated the use of topical antibiotics, except for the gentamicin-collagen sponge (as Garamycin® sponge).[3, 13–17]

The gentamicin-collagen sponge is a sterile implant that contains gentamicin sulfate, an aminoglycoside antibiotic with a broad spectrum of activity (gram-negative and gram-positive bacteria). High local concentrations may persist for several days. The Garamycin implant in the form of a sponge is used to ensure a high concentration of gentamicin at the site of implantation, thereby eliminating local inflammation or preventing its formation. The gentamicin-collagen sponge is especially useful in patients at high risk of wound infection. The following microorganisms are sensitive to this antibiotic (MIC <1 μg/ml): *Pseudomonas aeruginosa*, *Proteus spp.*, including *Proteus vulgaris* and *Proteus mirabilis*, *Escherichia coli*, bacteria of the *Klebsiella-Enterobacter-Serratia* group, *Streptococcus spp.*, *Salmonella spp.*, *Shigella spp.*. The minimal activity of gentamicin on *Streptococcus faecalis* has been demonstrated, while the majority of anaerobic bacteria (*Clostridium, Bacteroides*) and coryneform bacteria (*Corynebacterium*) are resistant.

In vitro, studies have shown that gentamicin is eight times more potent at pH 7.5 than at pH 5.5. Bacterial resistance related to inactivating gentamicin develops slowly and gradually. Cross-resistance with other aminoglycoside antibiotics is possible. The combination of gentamicin and antibiotics from the penicillin or cephalosporin group, administrated systemically, shows a synergistic bactericidal effect against some strains of bacteria. The analysis of exudates showed that high local concentrations of the antibiotic in the tissues, ranging from 300 to 9000 mg/l, are achieved within 1 to 2 hours. These concentrations are many times higher than the bactericidal concentrations of gentamicin. High concentrations in the exudate may persist for 3 to 4 days after surgery.

In addition, gentamicin in combination with a collagen carrier-sponge has a hemostatic effect (this function is performed by the collagen).[18]

Gentamicin Sulfate is a water-soluble antibiotic. Even a brief soaking of the gentamicin-collagen sponge prior to its insertion into the patient's tissues results in a significant loss of gentamicin, which may be clinically significant, reducing the effectiveness and increasing the risk of wound infection. The results of two multicentre clinical trials conducted with the use of the gentamicin-collagen sponge in colorectal and cardiac surgery, published in 2010, did not confirm the clinical effectiveness of the product. This may have been caused by soaking the sponge prior to its insertion into the tissues, thus washing away the gentamicin from the product.[19–21] However, a meta-analysis from 2015, which included 1,685 patients, showed a significant reduction in postoperative wound infection.[22]

The serum concentration of gentamicin during the use of the product is safe. No serious side effects were observed during the use of up to 7 implants (10 × 10 × 0.5 cm or 5 × 20 × 0.5 cm). Local redness, itching, and increased discharge from the wound may occur during the application of the product, caused by the resorption of collagen. Side effects resulting from the neurotoxicity and nephrotoxicity of gentamicin may occur. Particular attention should be paid to patients with an impaired renal function.[23]

The combination of negative pressure therapy with antibacterial dressings seems to be a clinically promising direction in the treatment of difficult wounds.

Table I
PATIENTS WITH DIFFICULT WOUNDS IN THE COURSE OF CROHN'S DISEASE, TREATED WITH THE USE OF THE GENTAMICIN-COLLAGEN SPONGE COMBINED WITH NPWT

	Disease	Treatment duration	Number of surgical interventions	Wound assessment prior to treatment initiation	Treatment result
Patient 1	Crohn's disease, a deep, infected wound of the perineum after rectal amputation (Fig. 1)	2 cycles 2 weeks 3 months break, & 3 weeks	1st cycle: 2 wound debridements in general anesthesia, 5 times NPWT dressing with the gentamicin-collagen sponge 2nd cycle: one wound debridement in general anesthesia, 6 times NPWT dressing, of which the gentamicin-collagen sponge in the first two applications	Extensive, infected wound, after numerous attempts at surgical interventions and systemic antibiotic therapies	Healing of a deep perineal wound, elimination of inflammation, exudation, and infection, healing by granulation and epithelialization, assessed by the patient as satisfactory. Termination of treatment
Patient 2	Crohn's disease, stoma complicated with skin and soft tissue infection (pyoderma gangrenosum)	4 weeks	2 surgeries in general anesthesia, 4 NPWT cycles, of which the first two without the gentamicin-collagen sponge (slow healing progression), and the following 2 with the gentamicin-collagen sponge (rapid healing progression), cleaning of the wound	Extensive necrotic and purulent skin lesions, deep infected pockets, no healing progression (steroid therapy), ineffective antibiotic therapy, standard dressings	Healing of the wound with its almost complete primary closure, without the need for reconstructive techniques or transplants
Patient 3	Crohn's disease, perianal fistula — deep "pockets" in the gluteal region	9 days	1 surgery (debridement of fistula) in general anesthesia with simultaneous NPWT and the application of the gentamicin-collagen sponge into the pockets, 3 NPWT changes, each with the gentamicin-collagen sponge	Extensive subcutaneous canals after excision of a fistula with abscesses, pronounced inflammation, local skin and subcutaneous tissue infection	Healing of the extensive complex anal fistula (stage healing), the described stage allowed for the conversion of an infected complex fistula into a simple fistula, treated with redon drainage followed by successful biological treatment

There are also studies confirming the effectiveness of combining negative pressure therapy with the gentamicin-collagen sponge. In one of them, in 40 patients who received NPWT with the sponge, a measurable acceleration of wound healing, thus a shortened hospitalization period, was demonstrated.[24–28]

CASE REPORT

Table I presents three cases of patients with difficult wounds in the course of Crohn's disease, treated with the use of the gentamicin-collagen sponge combined with NPWT at the Department of General Surgery, Endocrinology, and Gastroenterological Oncology in Poznan.

In the three cases reported above, the Hartmann Vivano system with a constant negative pressure of 125 mmHg was used to treat wounds in the abdominal cavity and perineal area. Dressings were changed every 2–4 days, details are shown in (Tab. I).

The gentamicin-collagen sponge, cut to the appropriate size, was placed directly on the wound. The sponge was then covered with an intermediate layer, i.e. a permeable dressing preventing the sponge from adhering directly to the wound. The next step was to apply a polyurethane sponge adjusted to the size of the wound. To seal the system and reduce the risk of leaks, stoma paste was applied around it. The system was attached with a standard adhesive foil, and the port (pad) was located at the lowest point by gravity to prevent the accumulation of potential secretion under the foil and unsealing of the dressing. The suction was set to a continuous mode at the negative pressure of 125 mmHg Wound debridements and the first applications of vacuum dressings were performed in the operating room under general anesthesia. Subsequent dressing changes were performed without the need for general anesthesia in the treatment room every third day or as needed. Initially, the size of the polyurethane sponge was directly adapted to the size of the wound. As the healing of the wound progressed, the size of the polyurethane sponge applied was reduced to fit the size of the wound. The sponge was secured with several single sutures to the edge of the wound, passively drawing the edges of the wound together, and gradually reducing its size.

The gentamicin-collagen sponge can be safely used in sensitive areas, with exposed muscles, nerves, and vessels. It is therefore an additional intermediate layer between the wound and the polyurethane sponge.

SUMMARY

Combining negative pressure therapy with an additional drug seems to be a good prognosis for the future and may extend its list of indications.

The presented cases demonstrate that gentamicin-collagen sponge combined with NPWT is a feasible therapeutic option for difficult wounds, including Crohn's disease.

Further comparative and randomized studies are necessary to provide an unambiguous assessment of the effectiveness of using NPWT in combination with the gentamicin-collagen sponge for difficult wounds.

ACKNOWLEDGEMENTS

This Manuscript was not supported by any funding.

REFERENCES

[1] E. Zimlichman, D. Henderson, O. Tamir, C. Franz, P. Song, C. K. Yamin, C. Keohane, C. R. Denham, and D. W. Bates, "Health care–associated infections: a meta-analysis of costs and financial impact on the us health care system," *JAMA internal medicine*, vol. 173, no. 22, pp. 2039–2046, 2013.

[2] S. S. Sawant and B. Dattatray, "Is local gentamycine useful with vac (vaccume assisted closure in wound healing??)," *International Journal of Science and Research*.

[3] H. Knaepler, "Local application of gentamicin-containing collagen implant in the prophylaxis and treatment of surgical site infection in orthopaedic surgery," *International journal of surgery*, vol. 10, pp. S15–S20, 2012.

[4] R. E. Horch, "Incisional negative pressure wound therapy for high-risk wounds," *Journal of Wound Care*, vol. 24, no. Sup4b, pp. 21–28, 2015.

[5] C. Willy, A. Agarwal, C. A. Andersen, G. D. Santis, A. Gabriel, O. Grauhan, O. M. Guerra, B. A. Lipsky, M. B. Malas, L. L. Mathiesen *et al.*, "Closed incision negative pressure therapy: international multidisciplinary consensus recommendations," *International wound journal*, vol. 14, no. 2, pp. 385–398, 2017.

[6] M. J. Morykwas, L. C. Argenta, E. I. Shelton-Brown, and W. McGuirt, "Vacuum-assisted closure: A new method for wound control and treatment," *Annals of Plastic Surgery*, vol. 38, no. 6, p. 553–562, 1997.

[7] A. Hussain, K. Singh, and M. Singh, "Cost effectiveness of vacuum-assisted closure and its modifications: a review," *International Scholarly Research Notices*, vol. 2013, 2013.

[8] M. Sopata, A. Jawień, B. Mrozikiewicz-Rakowska, Z. Augusewicz, M. Bakowska, I. Samson, M. Gabriel, T. Grzela, T. Karpiński, I. Kuberka *et al.*, "Wytyczne postępowania miejscowego w ranach niezakażonych, zagrożonych infekcją oraz zakażonych–przegląd dostępnych substancji przeciwdrobnoustrojowych stosowanych w leczeniu ran. zalecenia polskiego towarzystwa leczenia ran," *Leczenie Ran*, vol. 17, no. 1, pp. 1–21, 2020.

[9] A. Bobkiewicz and T. Banasiewicz, "Wykorzystanie terapii podciśnieniowej w chirurgii," *Chirurgia po Dyplomie*, vol. 02, 2020.

[10] Ö. Friberg, R. Svedjeholm, B. Söderquist, H. Granfeldt, T. Vikerfors, and J. Källman, "Local gentamicin reduces sternal wound infections after cardiac surgery: a randomized controlled trial," *The Annals of thoracic surgery*, vol. 79, no. 1, pp. 153–161, 2005.

[11] A. De Bruin, M. Gosselink, E. Van der Harst, and H. Rutten, "Local application of gentamicin collagen implants in the prophylaxis of surgical site infections following gastrointestinal surgery: a review of clinical experience," *Techniques in coloproctology*, vol. 14, pp. 301–310, 2010.

[12] M. Kowalewski, W. Pawliszak, K. Zaborowska, E. P. Navarese, K. A. Szwed, M. E. Kowalkowska, J. Kowalewski, A. Borkowska, and L. Anisimowicz, "Gentamicin-collagen sponge reduces the risk of sternal wound infections after heart surgery: meta-analysis," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 149, no. 6, pp. 1631–1640, 2015.

[13] E. C. for Disease Prevention and Control, "Surveillance of antimicrobial resistance in europe–annual report of the european antimicrobial resistance surveillance network (ears-net) 2017," *ECDC: Surveillance Report*, 2018.

[14] A. Kramer, J. Dissemond, S. Kim, C. Willy, D. Mayer, R. Papke, F. Tuchmann, and O. Assadian, "Consensus on wound antisepsis: update 2018," *Skin Pharmacology and Physiology*, vol. 31, no. 1, pp. 28–58, 2018.

[15] C. Acton, S. Berret, and P. Beldon, "Best practice statement: the use of topical antiseptic/antimicrobial agents in wound management. second edition." [Online]. Available: http://www.wounds-uk.com/pdf/content_9969.pdf.

[16] "Prevention and management of wound infection." [Online]. Available: https://www.who.int/publications-detail-redirect/prevention-and-management-of-wound-infection

[17] A. Kramer, J. Dissemond, S. Kim, C. Willy, D. Mayer, R. Papke, F. Tuchmann, and O. Assadian, "Consensus on wound antisepsis: update 2018," *Skin Pharmacology and Physiology*, vol. 31, no. 1, pp. 28–58, 2018.

[18] I. Yetim, O. Özkan, A. Dervişoglu, K. Erzurumlu, and E. Canbolant, "Effect of local gentamicin application on healing and wound infection in patients with modified radical mastectomy: a prospective randomized study," *Journal of International Medical Research*, vol. 38, no. 4, pp. 1442–1447, 2010.

[19] E. Bennett-Guerrero, T. N. Pappas, W. A. Koltun, J. W. Fleshman, M. Lin, J. Garg, D. B. Mark, J. E. Marcet, F. H. Remzi, V. V. George *et al.*, "Gentamicin–collagen sponge for infection prophylaxis in colorectal surgery," *New England Journal of Medicine*, vol. 363, no. 11, pp. 1038–1049, 2010.

[20] E. Bennett-Guerrero, T. B. Ferguson, M. Lin, J. Garg, D. B. Mark, V. A. Scavo, N. Kouchoukos, J. B. Richardson, R. L. Pridgen, G. Corey *et al.*, "Effect of an implantable gentamicin-collagen sponge on sternal wound infections following cardiac surgery: a randomized trial," *Jama*, vol. 304, no. 7, pp. 755–762, 2010.

[21] G. Godbole, V. Pai, S. Kolvekar, and A. P. Wilson, "Use of gentamicin–collagen sponges in closure of sternal wounds in cardiothoracic surgery to reduce wound infections," *Interactive cardiovascular and thoracic surgery*, vol. 14, no. 4, pp. 390–394, 2012.

[22] Y.-F. Lv, J. Wang, F. Dong, and D.-H. Yang, "Meta-analysis of local gentamicin for prophylaxis of surgical site infections in colorectal surgery," *International journal of colorectal disease*, vol. 31, pp. 393–402, 2016.

[23] "Charakterystyka produktu leczniczego." [Online]. Available: http://chpl.com.pl/data_files/2012-07-16_20120704_garamycin_gabka_chpl-urclean.pdf

[24] A. Kramer, J. Dissemond, S. Kim, C. Willy, D. Mayer, R. Papke, F. Tuchmann, and O. Assadian, "Consensus on wound antisepsis: update 2018," *Skin Pharmacology and Physiology*, vol. 31, no. 1, pp. 28–58, 2018.

[25] D. A. Back, C. Scheuermann-Poley, and C. Willy, "Recommendations on negative pressure wound therapy with instillation and antimicrobial solutions–when, where and how to use: what does the evidence show?" *International wound journal*, vol. 10, no. s1, pp. 32–42, 2013.

[26] T. E. Serena, O. Jalodi, L. Serena, K. Patel, and M. Mynti, "Evaluation of the combination of a biofilm-disrupting agent and negative pressure wound therapy: a case series," *Journal of Wound Care*, vol. 30, no. 1, pp. 9–14, 2021.

[27] M. S. Timmers, N. Graafland, A. T. Bernards, R. G. Nelissen, J. T. Van Dissel, and G. N. Jukema, "Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis," *Wound Repair and Regeneration*, vol. 17, no. 2, pp. 278–286, 2009.

[28] A. H. Zhao, C. H. R. Kwok, A. Jacques, L. Stopher, J. A. Hockley, M. W. Garbowski, and S. J. Jansen, "Gentamicin-containing collagen implant may reduce surgical site infections after open infrainguinal arterial revascularization," *Annals of vascular surgery*, vol. 78, pp. 84–92, 2022.