



Combination of Polyhexamethylene Biguanide and Cadexomer Iodine in Healing Chronic Venous Leg Ulcers: A Case Report

¹Asmat Burhan, ²Septian Mixrova Sebayang

Faculty of Health Sciences, Universitas of Harapan Bangsa

Email: ¹asmatburhan@uhb.ac.id, ²septiansebayang@uhb.ac.id

Abstrak

Chronic Venous Leg Ulcers (CVLUs) are vascular diseases and require complex wound care from a patient, wound, health personnel and dressing factors. Cadexomer Iodine (CI) and Polyhexamethylene Biguanide (PHMB) are antimicrobial and broad-spectrum wound washing fluids. The uncontrolled infection will complicate wound healing due to bacteria or plankton from the biofilm stage to infection, which causes a long healing time. Purpose: to determine the effectiveness of the combination of Polyhexamethylene biguanide and Cadexomer Iodine on venous leg ulcer wound healing. Methods: This study is a case study using CVLUs as a sample, with pre-test and post-test designs, patients with CVLUs received topical antimicrobial CI and PHMB interventions on wounds for 7 weeks. The sample in this study used one sample with a pre-post treatment design for seven days.. The instrument uses the Bates Jensen Wound Assessment Tool. Results: The combination of CI and PHMB was shown to improve the healing of CVLUs by controlling bacterial infection in wounds. In the 2nd week, the wound was 26cm x 15cm, the slough was reduced, and the red base wound increased. In the 3rd week, the wound was stage 4, and the granulation increase was 75%. In the 7th treatment, the wound size scale increased 7cmx4cm, the wound became stage 2, and a significant increase in epithelialization was 75%. Conclusion: The combination of PHMB and CI has been shown to control infection at the biofilm stage to critical colonization, reduce odour and significantly control infection, and increase granulation and epithelialization in CVLUs.

Keywords: *Chronic leg ulcers, wound healing, infection control*

INTRODUCTION

The infection has a high risk of inhibiting the healing of CVLUs caused by biofilm or plankton, which causes the wound to be difficult to heal, enlargement of wound scale and pain in the wound area and increased exudate (Green et al. 2014; Pugliese 2016). The prevalence of VLUs increases every year with an average of women and at the age of 65 years from 0.5% new cases of 1000 people in 2010 to 1 new case every year 1000 people in 2014 and continues to increase between 0.8% and 2.2 % VLU for everyone who has difficulty healing VLUs (Berenguer Pérez et al. 2019). The prognostic factors for VLUs are most problems with blood vessels, age, gender, infection, ulcer area and duration of ulcers. Vena Leg ulcers in patients with a diagnosis of wound infection 74.7% of wound peeling and expansion of <1.3 be $>10\text{cm}^2$ (Jenkins et al. 2019)

Amputated VLUs patients had 20.4% infection and 7.7% with wound complications (Jupiter 2020). VLU wound healing through a complex process of wound washing, control of wound infection and exudate to improve the wound healing process and prevent amputation in VLUs patients (Atkin et al. 2019). Wound washing using PHMB antiseptic does not only wash but also gently removes dead tissue, necrotic slough and biofilm (Shahram et al. n.d.). PHMB showed a significant improvement in controlling bacteria in the biofilm stage, contamination, colonization, reducing pain more effectively caused by bacterial metabolism, increasing chronic wound healing and

eliminating methicillin-resistant *Staphylococcus aureus* (Dyck and Gerber 2016). Wound washing with irrigation using 0.04% PHMB can prevent the management of surgical site infection, and acute wound healing is significantly increased by 97.0% using PHMB in the longitudinal cohort study (Dissemond et al. 2016). PHMB also reduced bacteria to log 10 with the highest average of 4.81% (Schwarzer 2019).

Biofilm is always present on the surface of acute or chronic wounds, and biofilm colonizes within 2-4 hours, mechanical disruption and biofilm formation take 24 hours, and enhancement of biofilm colony evolution takes 2-4 days (Malic et al. 2011). Biofilms are often found in chronic Venous Leg Ulcer wounds, which are very difficult to heal and have implications for delayed healing because the granulation tissue growth tissue is damaged due to biofilm activity (Azevedo et al. 2020).

Biofilm can evolve within 2-4 days, so antimicrobials that can last 3x24 hours are needed. Cadexomer iodine can last up to 2x24 hours on the wound surface, reducing biofilm and exudate, which often causes maceration, so that wound healing is delayed and determines the duration of treatment (Gueltzow et al. 2018). Biofilm can evolve within 2-4 days, so antimicrobials that can last 3x24 hours are needed. Cadexomer iodine can last up to 2x24 hours on the wound surface, reducing biofilm and exudate (Sweere et al. 2020).

From the explanation above, the writer wants to know whether there is an effect of the combination of

Polyhexamethylene biguanide and Cadexomer Iodine relaxation on increasing venous leg ulcer wound opening in the categories of wound size, infection, and wound healing time. The author conducted research at the Luke Hospital in Bangkalan.

METHODOLOGY

This study is a case study using samples of patients with chronic venous leg ulcers, with pre-test - post-test designs, CVLUs patients receiving topical antimicrobial cadexomer iodine intervention and wound washing using Polyhexamethylene Biguade on the wound surface for 7 weeks in 14 treatments. The sample in this study was one person with a pre-post treatment design at the Lukas Hospital in Bangkalan. Assessment of wound healing results using the Bates Jensen Wound Assessment Tool instrument 13 items that have been validated and reliable with 1 item including size, depth, wound edges, undermining, type of necrotic tissue, amount of necrotic tissue, type of exudate, amount of exudate, colour around the wound, , granulation and epithelialization. By healing category: Heal 1-12 Score, Regeneration 13-60 Score and Degeneration >60 Score (Bates-Jensen et al. 2019).

CASE REPORT

A 47-year-old woman came with a wound on her right leg that appeared 3 months ago. He has been hospitalized previously with a leukocyte value of 17,289sel/ul, and the patient's blood sugar is 190. The patient has been diagnosed with type 2 diabetes mellitus for 5 years, with the patient's blood sugar being uncontrolled due to

not routine control and taking medication. Patients come to independent nursing practice with vital signs in normal condition. At the time of the assessment using the first BJWAT, we obtained a score of 56 with the wound condition, two areas of leg wounds measuring 2x2cm and the second wound 7x5cm, the depth of the wound were Stage 3, the edges of the wound did not merge with the wound bed, there was a cave connecting one wound to the second wound area of 4cm. There is an odour in the wound, necrotic tissue, and sticky. Hard sought with an amount of 100% of the wound bed, the type of exudate released is purulent with a large amount of exudate, the skin around the wound is dark red with signs of erythema, swollen left leg by palpation for pitting oedema less than <4mm around the wound, slough 100%, a lot of exudates, wound, there is no hardening of the tissue edge of the wound, there is no granulation tissue and epithelialization. Examination of the ABI in the patient got a value of 0.8 mmHg, and there was a problem in the venous system.

RESULT



Figure 1. Assesment

Wound condition BJWAT score 56, and there is infection with leukocytes 17,289 cells/ul, slough 100% exudate, a lot of odour, erythema, oedema with pitting <4mm around the wound, stage 3 wound depth, ABI 0.8 mmHg, no tissue, Hb 8g/dl, Normal Albumin.



Figure 2. Application Combination Polyhexamethylene Biguanide and Cadexomer Iodine

In the second week, we washed the wound using PHMB and Conservative Sharp Wound Debridement (CSWD) to remove all necrotic tissue, reached slough and the red wound base, and the wound data became one with wound size 26cmx15cm, no undermining, 50% slough, there is still an odour, a lot of exudates, the edges of the wound look partially fused with the granulation wound bed 25%, there is no epithelialization, and the APBI is 0.7 mmHg.



Figure 3. Wound Healing Process

In the fourth week, the wound size decreased to 24x11cm, and the depth became stage 3. A small portion of the wound area has a stage 4 of 15%, and there is still a biofilm, there is no odour, the edges of the wound and the surface begin to merge and a significant increase in granulation of 85% and growth epithelium by 25%.



Figure 4. Process Epitelization

In the seventh week, Hb 11 g/dl, leukocytes 12,649 cells/ul, BJWAT score 22, wound size also increased to 7cmx 4cm, 75% significant epithelial increase with 75% granulation.

DISCUSSION

Infection control in the healing of CVs wounds is very important. Comprehensive treatment should be implemented to improve outcomes and prevent amputation of the foot (Hinchliffe et al. 2019). The main goal of treatment is to wash the wound properly and control infection from biofilm, contamination and colonization to improve the wound healing process (Tate, Price, and Harding 2018). Wound healing is very complex due to internal factors of smooth venous blood vessels, and angiogenesis, while external infection control, dressings and good clinical care according to standard operating

procedures (Guest, Fuller, and Vowden 2018). The things that underlie wound care are biofilm control that can inhibit the process of granulation growth and epithelialization, excessive exudate causes maceration caused by bacterial metabolism, plasma leakage in veins causing edema in the extremities (Metcalf, Parsons, and Bowler 2016; Roy et al. 2020; Settipalli et al. 2019).

Cadexomer Iodine (CI) is an antimicrobial that is applied to the wound surface to control and kill infections caused by bacteria or plankton that can last 2x 24 hours on the wound surface. (Fitzgerald et al. 2017; Skog et al. 1983). The odour in the wound was identified as a bacterial infection caused by metabolism. Besides being able to control CI infection, it can also control bioburden and exudate in the wound so that the wound healing process is not disturbed (Norman et al. 2018). There are many techniques for controlling infection in CVLUs that can be used by nursing professionals.

Polyhexamethylene Biguanide (PHMB) is a liquid for washing wounds properly and correctly, irrigation using PHMB is cleaner and removes bacteria, and compression techniques on the wound surface CVLUs are more effective in removing biofilm (Bain et al. 2020). Mechanical debridement with PHMB using gauze to remove and remove bioburden and slough in chronic wounds (Sams-Dodd and Sams-Dodd 2020). Proper washing of the wound will facilitate further management so that it can improve the healing process (Worsley et al. 2019)

CVLU wound healing also includes autolytic debridement using zinc cream to remove necrotic or sloughy tissue by combining Alginate to support angiogenesis and growth of granulation to epithelialization (Phillips et al. 2020; Sanaei and Tahmasebpour 2021). Foam for absorption of excess exudate so as to prevent maceration and widening of the wound surface (Ousey et al. 2019). The overall performance of the combination of PHMB and Cadexomer Iodine was shown to function as infection control in the biofilm, contamination, and colonization stages, and we observed a decrease in bioburden, infection and a significant increase in granulation and epithelialization as well as a decrease in exudate.

Wound healing CVLUs are difficult to heal and often recur. Complex management must be given from infection control from the inflammatory stage to wound closure (Xia et al. 2020). Bioburden needs to be removed to increase the epithelialization process and good venous circulation to prevent plasma leakage so as to prevent oedema in the lower extremities, which can cause complications in CVLUs wound healing due to ischemia (Mayandi et al. 2020; Sermsathanasawadi et al. 2020). The healing process of CVLUs requires complex management of wound factors, patients, health workers and selection of dressings to control wound infection so as to improve healing outcomes (Jones 2019).

The researcher's assumption is that combining Polyhexamethylene Biguanide and Cadexomer Iodine in

Chronic Venous Leg Ulcers (CVLUs) can control infection at the biofilm stage; contamination and colonization can even reduce odor. Healing time is faster in increasing granulation and epithelialization. This combination is also an alternative to mechanical debridement as a non-invasive procedure and can be done by nursing.

CONCLUSION

We observed that wound care combined with Polyhexamethylene Biguanide and Cadexomer Iodine in Chronic Venous Leg Ulcers (CVLUs) improves the wound healing process by reducing the biofilm on the wound surface and controlling the infection. In addition, it reduces odor and is an option as a mechanical debridement to improve the granulation and epithelialization process in Chronic Venous Leg Ulcers (CVLUs).

REFERENCES

- Atkin, Leanne, Zofia Bućko, Elena Conde Montero, Keith Cutting, Christine Moffatt, Astrid Probst, Marco Romanelli, Gregory S. Schultz, and William Tettelbach. 2019. "Implementing TIMERS: The Race against Hard-to-Heal Wounds." *Journal of Wound Care* 28(Sup3a):S1–50. doi: 10.12968/jowc.2019.28.Sup3a.S1.
- Azevedo, Maria-Manuel, Carmen Lisboa, Luís Cobrado, Cidália Pina-Vaz, and Acácio Rodrigues. 2020. "Hard-to-Heal Wounds, Biofilm and Wound Healing: An Intricate Interrelationship." *British Journal of Nursing* 29(5):S6–13. doi: 10.12968/bjon.2020.29.5.S6.
- Bain, Michael A., George J. Koullias, Keith Morse, Santana Wendling, and Michael L. Sabolinski. 2020. "Type I Collagen Matrix plus Polyhexamethylene Biguanide Antimicrobial for the Treatment of Cutaneous Wounds." *Journal of Comparative Effectiveness Research* 9(10):691–703. doi: 10.2217/cer-2020-0058.
- Bates-Jensen, Barbara M., Heather E. McCreath, Deniz Harputlu, and Anabel Patlan. 2019. "Reliability of the Bates-Jensen Wound Assessment Tool for Pressure Injury Assessment: The Pressure Ulcer Detection Study." *Wound Repair and Regeneration* 27(4):386–95. doi: 10.1111/wrr.12714.
- Berenguer Pérez, Miriam, Pablo López-Casanova, Raquel Sarabia Lavín, Héctor González de la Torre, and José Verdú-Soriano. 2019. "Epidemiology of Venous Leg Ulcers in Primary Health Care: Incidence and Prevalence in a Health Centre—A Time Series Study (2010-2014)." *International Wound Journal* 16(1):256–65. doi: 10.1111/iwj.13026.
- Dissemond, Joachim, Bernd Assenheimer, Anke Bültemann, Veronika Gerber, Silvia Gretener, Elisabeth

- Kohler-von Siebenthal, Sonja Koller, Knut Kröger, Peter Kurz, Severin Läuchli, Christian Münter, Eva-Maria Panfil, Sebastian Probst, Kerstin Protz, Gunnar Riepe, Robert Strohal, Jürg Traber, and Hugo Partsch. 2016. "Compression Therapy in Patients with Venous Leg Ulcers: Compression in Leg Ulcers." *JDDG: Journal Der Deutschen Dermatologischen Gesellschaft* 14(11):1072–87. doi: 10.1111/ddg.13091.
- Dyck, Rebecca, and Stephanie Gerber. 2016. "The Effectiveness of Topical Polyhexamethylene Biguanide (PHMB) Agents for the Treatment of Chronic Wounds: A Systematic Review." *Advanced Wound Healing Surgical Technology InternationalXXIX* 45–51(29):7.
- Fitzgerald, Daniel J., Paul J. Renick, Emma C. Forrest, Shannon P. Tetens, David N. Earnest, Jillian McMillan, Brett M. Kiedaisch, Lei Shi, and Eric D. Roche. 2017. "Cadexomer Iodine Provides Superior Efficacy against Bacterial Wound Biofilms in Vitro and in Vivo: Cadexomer Iodine Biofilm Efficacy." *Wound Repair and Regeneration* 25(1):13–24. doi: 10.1111/wrr.12497.
- Green, J., R. Jester, R. McKinley, and A. Pooler. 2014. "The Impact of Chronic Venous Leg Ulcers: A Systematic Review." *Journal of Wound Care* 23(12):601–12. doi: 10.12968/jowc.2014.23.12.601.
- Gueltzow, Maria, Poroshat Khalilpour, Katharina Kolbe, and York Zoellner. 2018. "Budget Impact of Antimicrobial Wound Dressings in the Treatment of Venous Leg Ulcers in the German Outpatient Care Sector: A Budget Impact Analysis." *Journal of Market Access & Health Policy* 6(1):1527654. doi: 10.1080/20016689.2018.1527654.
- Guest, Julian F., Graham W. Fuller, and Peter Vowden. 2018. "Venous Leg Ulcer Management in Clinical Practice in the UK: Costs and Outcomes: Health Economic Impact of VLU in the UK." *International Wound Journal* 15(1):29–37. doi: 10.1111/iwj.12814.
- Hinchliffe, Robert J., Rachael O. Forsythe, Jan Apelqvist, Ed J. Boyko, Robert Fitridge, Joon Pio Hong, Konstantinos Katsanos, Joseph L. Mills, Sigrid Nikol, Jim Reekers, Maarit Venermo, R. Eugene Zierler, and Nicolaas C. Schaper. 2019. "Guidelines of the International Writing Group on the Diabetic Foot on Diagnosis." *Wileyonlinelibrary Journal* 12. doi: 10.1002/dmrr.3276.
- Jenkins, David A., Sundus Mohamed, Joanne K. Taylor, Niels Peek, and Sabine N. van der Veer. 2019. "Potential Prognostic

- Factors for Delayed Healing of Common, Non-traumatic Skin Ulcers: A Scoping Review.” *International Wound Journal* 16(3):800–812. doi: 10.1111/iwj.13100.
- Jones, Menna Lloyd. 2019. “Wound Care. What Is New in Best Practice: Addressing the Complexities in the Management of Venous Leg Ulcers. Part 1.” *British Journal of Healthcare Assistants* 13(10):6.
- Jupiter, Daniel C. 2020. “Transmetatarsal and Minor Amputation Versus Major Leg Amputation: 30-Day Readmissions, Reamputations, and Complications.” 7.
- Malic, S., K. E. Hill, R. Playle, D. W. Thomas, and D. W. Williams. 2011. “*In Vitro* Interaction of Chronic Wound Bacteria in Biofilms.” *Journal of Wound Care* 20(12):569–77. doi: 10.12968/jowc.2011.20.12.569.
- Mayandi, Venkatesh, Alvin Chua Wen Choong, Chetna Dhand, Fui Ping Lim, Thet Tun Aung, Harini Sriram, Neeraj Dwivedi, Mercy Halleluyah Periyah, Sreepathy Sridhar, Mobashar Hussain Urf Turabe Fazil, Eunice Tze Leng Goh, Gorka Orive, Roger W. Beurman, Timothy Mark Sebastian Barkham, Xian Jun Loh, Zhao-Xun Liang, Veluchamy Amutha Barathi, Seeram Ramakrishna, Si Jack Chong, Navin Kumar Verma, and Rajamani Lakshminarayanan. 2020. “Multifunctional Antimicrobial Nanofiber Dressings Containing ϵ -Polylysine for the Eradication of Bacterial Bioburden and Promotion of Wound Healing in Critically Colonized Wounds.” *ACS Applied Materials & Interfaces* 12(14):15989–5. doi: 10.1021/acsami.9b21683.
- Metcalf, Daniel G., David Parsons, and Philip G. Bowler. 2016. “Clinical Safety and Effectiveness Evaluation of a New Antimicrobial Wound Dressing Designed to Manage Exudate, Infection and Biofilm.” 11.
- Norman, Gill, Maggie J. Westby, Amber D. Rithalia, Nikki Stubbs, Marta O. Soares, and Jo C. Dumville. 2018. “Dressings and Topical Agents for Treating Venous Leg Ulcers” edited by Cochrane Wounds Group. *Cochrane Database of Systematic Reviews*. doi: 10.1002/14651858.CD012583.pub2.
- Ousey, Karen, Angela Walker, Jacalyn Brace, Franck Duteille, Astrid Probst, Maria Hughes, Cathy Milne, and Windy Cole. 2019. “A Multipurpose Dressing: A Clinical Review of the Absorption, Debridement and Healing Properties of Aquacel Foam.” *Journal of Wound Care* 28(Sup9a):S1–23. doi: 10.12968/jowc.2019.28.Sup9a.S1.

- Phillips, Ceri J., Ioan Humphreys, Dan Thayer, Muhammad Elmessary, Huw Collins, Chris Roberts, Gurudutt Naik, and Keith Harding. 2020. "Cost of Managing Patients with Venous Leg Ulcers." *International Wound Journal* 17(4):1074–82. doi: 10.1111/iwj.13366.
- Pugliese, Douglas J. 2016. "Infection in Venous Leg Ulcers: Considerations for Optimal Management in the Elderly." *Drugs & Aging* 33(2):87–96. doi: 10.1007/s40266-016-0343-8.
- Roy, Sashwati, Suman Santra, Amitava Das, Sriteja Dixith, Mithun Sinha, Subhadip Ghatak, Nandini Ghosh, Pradipta Banerjee, Savita Khanna, Shomita Mathew-Steiner, Piya Das Ghatak, Britani N. Blackstone, Heather M. Powell, Valerie K. Bergdall, Daniel J. Wozniak, and Chandan K. Sen. 2020. "Staphylococcus Aureus Biofilm Infection Compromises Wound Healing by Causing Deficiencies in Granulation Tissue Collagen." *Annals of Surgery* 271(6):1174–85. doi: 10.1097/SLA.000000000000053.
- Sams-Dodd, Jeanette, and Frank Sams-Dodd. 2020. "Micropore Particle Technology Promotes Wound Healing, Whereas Polyhexamethylene Biguanide Causes Tissue Degeneration: A Case Report." 32(3):6.
- Sanaei, Leila, and Maryam Tahmasebpoor. 2021. "Physical Appearance and Arsenate Removal Efficiency of Fe(III)-Modified Clinoptilolite Beads Affected by Alginate-Wet-Granulation Process Parameters." *Materials Chemistry and Physics* 259:124009. doi: 10.1016/j.matchemphys.2020.124009.
- Schwarzer, Saskia. 2019. "The Efficacy of Topical Agents Used in Wounds for Managing Chronic Biofilm Infections: A Systematic Review." *Journal of Infection* 80(3):261–70. doi: <https://doi.org/10.1016/j.jinf.2019.12.017>.
- Sermsathanasawadi, Nuttawut, Jarunee Jieamprasertbun, Kanin Pruekprasert, Khamin Chinsakchai, Chumpol Wongwanit, Chanean Ruangsetakit, and Pramook Mutirangura. 2020. "Factors That Influence Venous Leg Ulcer Healing and Recurrence Rate after Endovenous Radiofrequency Ablation of Incompetent Saphenous Vein." *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 8(3):452–57. doi: 10.1016/j.jvsv.2019.11.003.
- Settipalli, Sarala, P. Sandeep, AY Lakshmi, and V. Sivakumar. 2019. "Vascular Access Related Complications with Ipsilateral Upper Limb Oedema In Hemodialysis." *Indian Journal of Vascular and Endovascular Surgery* 6(2):10.

- Shahram, Paydar, Ziaeiian Bijan, Dehghanian Amirreza, Heidarpour Mohsen, Alavi Moghadam Roshanak, Dalfardi Behnam, and Hallaj Karladani Abbas. n.d. "A Comparison of the Effects of Topical Prolavacid Solution (a Polyhexamethylene Biguanide-Based Wound Cleanser) and Medihoney Ointment in a Rat Model of Cutaneous Wound." 6.
- Skog, E., B. Arnesjo, T. Troeng, J. E. Gjores, L. Bergljung, J. Gundersen, T. Hallbook, Y. Hessman, L. Hillstrom, T. Mansson, U. Eilard, B. Ekloff, G. Plate, and L. Norgren. 1983. "A Randomized Trial Comparing Cadexomer Iodine and Standard Treatment in the Out-Patient Management of Chronic Venous Ulcers." *British Journal of Dermatology* 109(1):77–83. doi: 10.1111/j.1365-2133.1983.tb03995.x.
- Sweere, Johanna M., Heather Ishak, Vivekananda Sunkari, Michelle S. Bach, Robert Manasherob, Koshika Yadava, Shannon M. Ruppert, Chandan K. Sen, Swathi Balaji, Sundeep G. Keswani, Patrick R. Secor, and Paul L. Bollyky. 2020. "The Immune Response to Chronic *Pseudomonas Aeruginosa* Wound Infection in Immunocompetent Mice." *Advances in Wound Care* 9(2):35–47. doi: 10.1089/wound.2019.1039.
- Tate, Sophia, Annie Price, and Keith Harding. 2018. "Dressings for Venous Leg Ulcers." 7.
- Worsley, Anna, Kristin Vassileva, Janice Tsui, Wenhui Song, and Liam Good. 2019. "Polyhexamethylene Biguanide:Polyurethane Blend Nanofibrous Membranes for Wound Infection Control." *Polymers* 11(5):915. doi: 10.3390/polym11050915.
- Xia, Guixue, Dongqing Zhai, Yue Sun, Lin Hou, Xiaofan Guo, Lixia Wang, Zhijian Li, and Feng Wang. 2020. "Preparation of a Novel Asymmetric Wettable Chitosan-Based Sponge and Its Role in Promoting Chronic Wound Healing." *Carbohydrate Polymers* 227:115296. doi: 10.1016/j.carbpol.2019.115296.