




Cold Plasmamed Beam as a Supporting Treatment of Soft Tissue Injuries in Severe Covid-19 Patients: A Preliminary Report

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Background: Cold plasma has many characteristics that allow for effective wound healing. Due to its efficacy, we have applied it in treating patients with severe Covid-19 who have soft tissue skin lesions and diseases including burns, pressure ulcers, shingles, and contact or atopic dermatitis. This study aims to assess the general characteristics of Covid-19 patients with soft tissue lesions and to conduct a fundamental evaluation of the efficacy of cold plasmamed beams in treating soft tissue wounds in patients with severe Covid-19.

Methods: This prospective study was conducted on 20 severe Covid-19 patients with soft tissue lesions at the Intensive Care Center for Covid-19 of Hue Central Hospital in Ho Chi Minh City from September 25 to November 11, 2021. These patients were performed cold plasma irradiation at any stage of wound progression, including new injuries and chronic wounds.

Results: Among 915 severe Covid-19 patients treated at our center, 20 patients had soft tissue lesions. Grade I, II, and III pressure ulcers accounted for 70% of the 20 cases of soft tissue lesions and 1.53% of the total patients at the time of the survey. Pressure ulcers were present in only 0.55% of patients (5/915 patients). Eleven out of 20 patients (55.0%) had lesions before admission, and 9 (45.0%) had lesions that appeared after admission. After 14 days of treatment, 14/20 patients had complete epithelialization (70%), and in 18/20 patients, wound exudation had ceased. The wounds became painless; after 3 weeks, the rashes had completely disappeared.

Conclusion: The study emphasizes that irradiation with cold plasma contributes to the wound healing process.

Keywords: cold plasma, COVID-19, pressure ulcers, dermatology, intensive care unit

Introduction

Cold plasma is a mixture of many components: charge carriers (ions, electrons), free radicals and active substances, electromagnetic fields, temperature, visible light, and ultraviolet rays. The synergistic effect of these components lead to a wide variety of plasma applications.¹⁻³ Plasma has been used in medicine for many years; it is used in the sterilization of surfaces of implanted materials, sterilization of medical instruments, and in wound treatment.^{4,5} Cold plasma's sterilization applications include: i) rapid killing of bacteria, including multidrug-resistant bacteria; ii) killing of fungi; and iii) inhibiting the growth of viruses.⁶

When cold plasma is applied to the human body during wound treatment, it does not affect the water content of skin, cause irritation, or change the stratum corneum, and it is safe for mucous membranes.^{7,8} In terms of efficacy, cold plasma has demonstrated significant effects in dermatological treatments such as the treatment of acne, fungal infections, and psoriasis.^{9,10}

Cold plasma is a new technology that many countries are interested in researching and applying in various medical specialties, including wound treatment, dentistry, dermatology, and hemostasis. Germany has the fastest growing industry; they have many brands of cold plasma generators. The United States, Israel, Russia, and Japan have also introduced products for medical applications and had many successes. There are widely evaluated reports in prestigious medical journals.^{11,12}

The PlasmaMed cold plasma generator is based on the principle of sliding arc plasma and is manufactured within the framework of the subject of cold plasma beams with high application value in dermatology.¹³ Moreover, PlasmaMed

received patent protection for a cold jet plasma generator for application in biomedicine; it was issued by the National Office of Intellectual Property, Ministry of Science and Technology, on September 29, 2015.

The application of cold plasma produced by PlasmaMed Vietnam Joint Stock Company has many qualities that facilitate effective treatment in the wound healing process. Due to its efficacy, we have applied this technology in patients with severe Covid-19 infection who have soft tissue skin lesions and diseases such as burns, pressure ulcers, shingles, and contact and atopic dermatitis. The introduction of this technology in the treatment of severe Covid-19 patients has had many positive effects, and is a pioneering step for the leadership team, and the doctors and nurses at Hue Central Hospital. This study aimed to assess the general characteristics of patients with severe Covid-19 having soft tissue lesions and to fundamentally evaluate the efficacy of cold plasmamed beam technology in treating soft tissue wounds in patients with severe Covid-19.

Materials and Methods

Study Population

A descriptive cross-sectional study including 915 severe Covid-19 patients was conducted from September 25, 2021, to October 10, 2021, at the Intensive Care Center for Covid-19 Patients, Hue Central Hospital, Ho Chi Minh City.

The inclusion criteria were as follows: (1) All cases of soft tissue damage, skin damage of any origin in patients with severe Covid-19 infection, including contact dermatitis, burns, pressure ulcers, shingles, atopic dermatitis; and (2) Pressure ulcers stage I, II, and III (according to the 1989 National Pressure Ulcer Advisory Panel Staging System). Patients were excluded if they had i) acute myocardial infarction, with severe coagulopathy, and were being treated with extracorporeal membrane oxygenation (ECMO); in these patients we were unable to intervene with cold plasma irradiation; ii) pressure ulcers stage IV; these were treated according to the 2016 National Pressure Ulcer Advisory Panel Staging System.¹⁴

Technical Procedure

Twenty patients fulfilled inclusion criteria were performed with cold plasma irradiation at any stage of wound progression, including new injuries and chronic wounds.

Plasma irradiation is performed by opening the wound dressing, cleaning the wound with sodium chloride 0.9%, removing the necrotic tissue, then irradiating the wound with a dose of 10s/cm². The cold plasma jet is kept at a distance of 2–5 mm from the wound and is moved back and forth, sweeping evenly over the wound surface for 10s multiplied by the treated wound area (cm²). This procedure is repeated every 24 h until the wound is healed.

Effects of Cold Plasma

It has bactericidal, analgesic, and anti-inflammatory properties; skin surface collagen regeneration occurs, along with rapid healing, and minor scarring.^{15,16}

Data Analysis

Medical records were prepared so that the history of soft tissue lesions and diseases in patients with severe Covid-19 infection could be examined. Daily wound assessment and care were conducted. The disease progression was monitored during care; information was recorded, and data was collected.

Data were analyzed using SPSS 16.0 (IBM, Chicago, IL, USA). All descriptive data were presented as means and standard deviations (SDs) or percentages.

Results

Baseline Characteristics

Table 1 presents the gender and age distribution of Covid-19 patients with soft tissue lesions. The prevalence of lesions was higher in females aged >51 years and was more evenly spread in males aged >31 years. **Table 2** shows that the main causes were pressure ulcers, lying for an extended period, limited movement in patients with severe Covid-19, and diseases with severe underlying medical conditions such as older age, weakness, exhaustion, and confusion, which accounted for 70% of

Table 1 Gender and Age Distribution

Age Group	Males (n,%)	Female (n,%)
1–30	0 (0.0%)	0 (0.0%)
31–50	5 (50.0%)	0 (0.0%)
51–70	3 (30.0%)	6 (60.0%)
≥ 70	2 (20.0%)	4 (40.0%)

Table 2 The Causes of Soft Tissue Lesion

Causes of Soft Tissue Lesion	N (%)
Pressure ulcers	14 (70.0%)
Gases	1 (5.0%)
Contact ulcers	3 (15.0%)
Varicella zoster virus infection	1 (5.0%)
Other causes	1 (5.0%)
Total	20 (100%)

cases (14/20 cases). Table 3 shows that 55% of soft tissue lesions in patients with severe Covid-19 were detected at the lower level hospital (before admission), while only 45% were detected after admission at the Intensive Care Unit (ICU).

Clinical Features

Table 4 shows that patients with severe Covid-19 and severe underlying diseases had the highest number of necrotizing ulcer lesions (70%), followed by contact dermatitis (15%), and the remaining atopic dermatitis, burns, and shingles at 5%. Soft

Table 3 The Onset of Soft Tissue Lesion

Lesion Onset	N (%)
Before admission	11 (55.0%)
After admission	09 (45.0%)
Total	20 (100%)

Table 4 Type of Soft Tissue Lesion

Type Lesion	N (%)
Necrotic ulcers	14 (70.0%)
Burns	1 (5.0%)
Atopic dermatitis	1 (5.0%)
Contact dermatitis	3 (15.0%)
Shingles	1 (5.0%)
Total	20 (100%)

Table 5 Locations of Soft Tissue Lesions

Location of Lesion	N (%)
Regions of back and buttocks, sacrum, and coccyx	12 (60.0%)
Anal margin	1 (5.0%)
The chest and abdomen	3 (15.0%)
Mixed locations	4 (20.0%)
Total	20 (100%)

Table 6 Combined Treatment

Combined Treatment	N (%)
Changed the bandage after saline wash, UrgoClean patch, Vliwasorb	15 (75.0%)
Only applied Cicabio cream, potassium permanganate	5 (25.0%)
Total	20 (100%)

Table 7 Treatment Results of Soft Tissue Wound

Treatment Response	Day of Treatment (Days)				
	< 5	5 - < 10	10 - < 15	15 - < 20	≥ 20
Complete epithelialization	2 (10.0%)	4 (20.0%)	8 (40.0%)	4 (20.0%)	2 (10.0%)
The wound is still exudating	14 (70.0%)	10 (50.0%)	5 (25.0%)	2 (10.0%)	0 (0.0%)
The wound is painless and rash free	18 (90.0%)	16 (80.0%)	10 (50.0%)	6 (30.0%)	0 (0.0%)

tissue lesions occur mainly on the back, buttocks, sacrum, and coccyx (60%) and are expressed due to serious and critical diseases, older age, weakness, confusion, lying for an extended period and prolonged pressure ulcers (Table 5).

Treatment results for Soft Tissue Wounds Using the Cold Plasmed Beam as Supporting Treatment

Before plasma irradiation, we changed the bandages, washed the lesions with saline to remove the necrotic plaque, then irradiated them to achieve the optimal effect.

After finishing, we continued to apply a moist patch and compress the wound (in 15/20 cases; 75%). In the remaining 5/20 patients (25%) wounds were only washed with potassium permanganate, and Cicabio cream was applied Tables 6 and 7 showed that after 2 weeks of cold plasma irradiation treatment, 14/20 patients had complete epithelialization. A total of 18/20 patients had no wound exudation; the remaining two cases had ulcerated sacra with little fluid in the bandages, while the other patients were completely dry. The wound sites were painless and after 3 weeks the rashes had completely disappeared.

Discussion

General Characteristics

The gender and age distribution of the survey group was the same for males and female. Initially, the results showed that the prevalence of serious comorbidities such as diabetes, liver failure, heart failure, hypertension, stroke, and obesity was much higher in younger males than in females. This situation was related to nutritional factors, preventive treatment, or

daily eating habits that affect and increase the risk of comorbidities in males; therefore, when infected with Covid-19, it might become more severe in males than in females, and pathologies such as soft tissue damage would appear earlier. Conversely, soft tissue damage developed at the age of 50 and older in females; this age group is possibly frailer and more exhausted, with limited mobility.

With respect to the cause, the present study found that pressure was the most common cause, responsible for 70% of all lesions, which is understandable, as it was difficult to take care of these immobile patients with serious underlying diseases. This is a challenge for doctors in high care centers, not just in the ICU. We help patients with posture changes, massage, and nourishment, and provide good general care. Preliminary results show that in 45 days, there were 915 patients with severe Covid-19 infection, while only 14 had pressure lesions. This is 1.53% of the total number of patients at the time of the survey. Of these patients, 9/14 (64.28%) were transferred to the hospital with pressure ulcers, while only 5/14 (35.71%) developed lesions during treatment at the center. The rate of soft tissue damage in the total number of patients receiving treatment at the time of the survey was 2.18% (20/915 patients), and patients developing pressure ulcers during the time at the center had a very low rate, 0.55% (5/915 patients). This shows that the process of caring, changing posture, nurturing, and especially preventing soft tissue damage in patients with severe Covid-19 infection at the center is excellent.

Clinical Characteristics

Regarding the pathology of lesions detected in the survey, grade I, II, and III necrotic ulcers were the most common, occurring in 14/20 patients (70%), 11 of whom had lesions before being transferred to the hospital. During treatment at the center, only 9 cases were detected, and 5 patients had pressure ulcers. Other patients developed lesions from shingles and contact dermatitis, as analyzed above. In our patients, contact dermatitis is typical with symptoms of itching, erythema, vesicles, bullae, and swelling. The shingles rash was characterized by vesicular vesicles growing along the nerve, with burning, stinging, and painful sensations.

The localized susceptibility caused by SARS-CoV-2 manifestations may be the potentiating factor that allows reactivation of latent viral infections. These events could be explained by a local susceptibility of previously damaged skin which underpins concepts like the Wolf isotopic response or/equal to Koebner phenomena type V. The Koebner phenomenon is the appearance of skin lesions over the site of injury, forming a linear line with exposure or irritation. The vesicular lesions of Covid are small vesicular lesions that are often scattered and unrelated to the site of injury, contact, and this lesion usually resolves spontaneously after 10 days.

Although patients came to us with comorbidities and severe pneumonia caused by Covid-19 infection, the incidence was low.

Results of Supportive Treatment of Soft Tissue Injuries with a Cold Plasmed Beam

On May 31, 2016, the Ministry of Health's Department of Medical Equipment and Construction issued a Certificate of Registration for the PlasmaMed cold jet plasma generator manufactured by the Corporation, allowing for the circulation of this medical equipment in Vietnam. Plasma technology was produced based on research, to evaluate its safety and efficacy in the treatment of 36 patients at 3 major hospitals (15 patients at Hue Central Hospital, 15 patients at Ho Chi Minh City University Hospital of Medicine and Pharmacy and 6 patients at Cho Ray Hospital) in 2016. In 2017, the initial clinical trial study conducted at Hue Central Hospital demonstrated the safety and efficacy of the PlasmaMed cold plasma generator manufactured by Plasma Technology Joint Stock Company.

Before plasma irradiation, we treated ulcer lesions with Imipenem antibiotic and albumin infusion. The wound was cleaned with saline, and the dressing was changed daily with Vaseline gauze. We applied potassium permanganate and topical Cicabio cream (copper, zinc, and hyaluronic acid). Lesions healed with granulomatous tissue formation, gradual epithelialization, and connective tissue regeneration. With contact dermatitis, we limit the exposure to risk factors for aggravating the disease and keep the patient's skin clean. The patient applied topical Povidone-iodine 10% and Cicabio cream. Lesions progress from reducing redness, vesicle collapse, vesicles, and pruritus. With atopic dermatitis, the patient was treated with antihistamine and Cicabio cream. Lesions reduce redness and blisters. In burn lesions, we administrated with Imipenem antibiotic, pain relief, and Cicabio cream. Lesions improved with dry, reduced exudation,

collapsed blisters, and the patient's skin was epithelialized. In Zona, patients ministered with Acyclovir, pain-relief, vitamin B-3, and topical Povidone Iodine 10%. Lesions reduced redness and collapsed blisters.

After screening, for 15/20 patients (75%), we continued to apply a moist patch and compress the wound; the remaining 5 cases (25%) were treated with only potassium permanganate and Cicabio cream.

Some report has approved the benefit of other topical creams, for example, the combination of Magistral Prescription (Silver Nitrate and Peru Balsam).¹⁷ However, Balsam of Peru, originating from the trunk of an El Salvadoran tree, is a known contact allergen and may cause 9.6% of contact dermatitis. Due to the limited supply caused by the pandemic, we only had Cicabio cream containing copper, zinc, and hyaluronic acid. These ingredients help disinfect local skin lesions, retain moisture, and promote granulation tissue proliferation.¹⁸

After 14 days of cold plasma irradiation during the survey period, there were 14/20 patients with complete epithelialization (70%). After two weeks, in 18/20 patient's exudation from the wound had ceased. The remaining two cases had ulcers in the sacrum with little fluid in the dressing. However, all patients' injuries were eventually completely dry. Wounds became painless, and rashes had completely disappeared after three weeks. Previously, when cold plasmamed irradiation was not applied, these lesions took longer to epithelialize or ulcerated even further with more exudation. With the use of this method, the wound was quickly epithelialized and the rash cleared, while exudation of the ulcers was limited.

Thus, treatment with plasmamed irradiation supports effective wound healing, as seen in the study conducted by Chou.¹ Friedman reviewed current achievements and new trends in dermatological cold plasma research, discussed fundamental concepts of plasma physics and plasma engineering, and described important areas of plasma engineering clinical research. Laboratory plasma studies provide a comprehensive understanding of this exciting emerging technology's nature, current applications, and future promise.²

Heinlin demonstrated that plasmas influence biochemical processes and offer new possibilities for the selective application of customized medically active substances. In dermatology, new possibilities are emerging for wound healing, tissue regeneration, treatment of skin infections, and probably many more diseases. The first clinical trials showed the efficacy and tolerability of plasma in treating chronic wounds.^{8,12} Besides this, the use of plasma gasification technology was shown to circumvent medical waste in a post-Covid-19 scenario.¹¹

Conclusion

This study demonstrates that irradiation with cold plasma contributes to the wound healing process. The care of critically ill patients is vitally important in the prevention of unfortunate complications, and at the same time, for the minimization of soft tissue damage caused by lying down for an extended period, pressure, not being able to exercise, etc. Every health worker should be aware of this to coordinate scientifically and professionally to help with the early recovery of patients and reduce the mortality rate, especially in those with severe Covid-19 infections.

We will continue to apply PlasmaMed beam irradiation as supportive treatment for the healing of soft tissue wounds and diseases in the ICU.

Ethics Approval and Consent to Participate

This study has been reviewed by the Ethics Committee of Hue Central Hospital; all procedures performed in studies involving human participants were conducted according to the ethical standards of the institutional research committee and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for Publication

Written consent form was obtained from all participants after explaining the study's aims.

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Disclosure

The authors declare that they have no competing interests.

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