

INVESTIGATING ADVERSE EFFECTS OF COLD PLASMA IN TREATING SECOND AND THIRD DEGREE BURNS: A DESCRIPTIVE STUDY

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ABSTRACT

Objective: To describe the adverse effects of cold plasma therapy in treating burns. **Method:** A descriptive study was conducted, following 67 patients with second and third degree burns treated with cold plasma therapy for 10 seconds/cm². The patients were monitored for pain, burning sensation, and itching during and after the treatment. **Results:** The study showed a significant decrease in pain among the patients, from 28.4% to 7.5% after treatment. Out of 298 treatments, 56.9% of the patients did not report any pain, while 40.1% reported mild pain, and only 2% reported moderate pain. There were no cases of severe burning sensation, and the sensation reduced significantly after the treatment. The patients reported a decrease in itching sensation after the treatment, with 88.1% reporting no itching. Only 1 patient (0.3%) reported mild itching sensation. **Conclusion:** Cold plasma therapy is a safe and effective treatment for burns with minimal adverse effects. The adverse effects such as pain, burning sensation, and itching were mild and significantly reduced after the treatment.

Keywords: *Plasma, Cold plasma therapy, Burns, Adverse effects.*

I. INTRODUCTION

There are various treatment options available to expedite the healing process of burn wounds. In surgical settings, techniques such as bandage changes, debridement, skin

grafting, infection control, and plasma irradiation are commonly used [1]. Current research focuses on combining medications and treatment methods to promote faster healing of burn wounds [2].

Plasma is a mixture of ionized gas components comprising positive and negative charges in equilibrium and not combined with each other. Based on the temperature of formation, plasma is classified into hot and cold plasma. Cold plasma does not harm the surrounding healthy tissues but generates various reactions within the tissue. Unlike conventional methods that require high temperature or high concentration of chemicals such as ethylene oxide, ozone, and chlorine, cold plasma can also be used on heat and chemically sensitive surfaces [2], [3]. Clinical experiments have demonstrated the effectiveness of cold plasma treatment for infected wounds and even chronic wounds. In addition, there are many in-depth studies reporting the supportive effects of cold plasma on wound healing and keratinocyte proliferation, indicating that cold plasma is a new treatment method with great potential for medical applications [4], [5]. Since 2003, many clinical studies have been conducted to evaluate the safety and efficacy of cold plasma. With respect to safety, cold plasma does not affect skin moisture, does not cause irritation, and does not alter the stratum corneum or mucous membrane [6], [7].

To clarify any potential adverse effects of cold plasma irradiation in the treatment of

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burn wounds, we conducted a study with the aim of evaluating the safety and unintended effects of the PlasmaMed machine in the treatment of second and third degree burn wounds.

II. RESEARCH DESIGN AND METHODS

2.1. Objectives

A total of 67 patients with second and third degree burns were selected for the study. The selection criteria included patients aged 12 or above, with partial thickness burns of over 100cm², a total burn area of less than 20% of the body surface area, admission to the study within 72 hours of burn injury, and voluntary consent to participate. Exclusion criteria were systemic infection, diabetes, severe chronic internal diseases, pacemaker or defibrillator use, pregnant or lactating women, and patients who declined to participate in the study.

2.2. Methodology

This study is a prospective, descriptive, longitudinal observation of the treatment of second- and third-degree burns in each patient. Burns were treated with the standard burn care procedure and additional cold plasma treatment using a daily dose of 10 seconds/cm² on the studied burn area after cleaning the burn surface and covering it with 6 layers of gauze followed by a bandage.

Each patient was enrolled in the study and data were collected immediately after the first plasma treatment. The study was terminated when the burn area in the treatment had completely healed (histologically), when the patient had to be transferred to a different hospitals, or when the patient withdrew from the study.

2.3. Time and Location

The study was conducted at Hue Central Hospital and Cho Ray Hospital in Ho Chi Minh City, Vietnam. The study period lasted for 26 months, from July 2017 to September 2019.

2.4. Materials and monitored indicators:

The study used Cold Plasma generated by the PlasmaMed system manufactured and supplied by Plasma Technology Corporation, and operated according to the manufacturer's instructions [3].

The Cold Plasma treatment process: After caring for the burn wound according to standard burn treatment procedures, the cold plasma head is held about 2-5 mm away from the wound, while sweeping evenly over the surface of the wound for a total sweeping time of 10 seconds multiplied by the area of the treated wound (calculated in cm²). Repeat this process every 48 hours until the study burn area or affected area has epithelialized (healed).

Ask patients about sensations of heat, burning, and pain during and after the cold plasma treatment. Burning is rated on a scale of 1 to 4: 1. No burning, 2. Mild burning (easily tolerable), 3. Moderate burning (uncomfortable), 4. Severe burning (very uncomfortable). Pain is rated on a scale of 1 to 4: 1. No pain, 2. Mild pain (easily tolerable), 3. Moderate pain (uncomfortable), 4. Severe pain (very uncomfortable). Itching is rated on a scale of 1 to 4: 1. No itching, 2. Mild itching (easily tolerable), 3. Moderate itching (uncomfortable), 4. Severe itching (very uncomfortable).

Record any abnormal symptoms at the site and throughout the body during and after the cold plasma treatment. Any incidents and unusual developments are documented in detail on the monitoring form and research medical record. If the study area shows signs

and worsening progression of inflammation, necrosis, the plasma treatment will be temporarily stopped. Symptomatic treatment will be provided simultaneously.

2.5. Ethical issues

The cold plasma treatment has been safely conducted in some places around the world; the Plasma Med machine has been approved

by the Ministry of Health, with a certificate of registration for circulation of medical equipment products. The study was approved by the Hospital's Scientific Council before implementation.

2.6. Data analysis and management

The study used EPI-INFO 6.04 and SPSS 15.0 software to manage and analyze data.

III. RESULTS

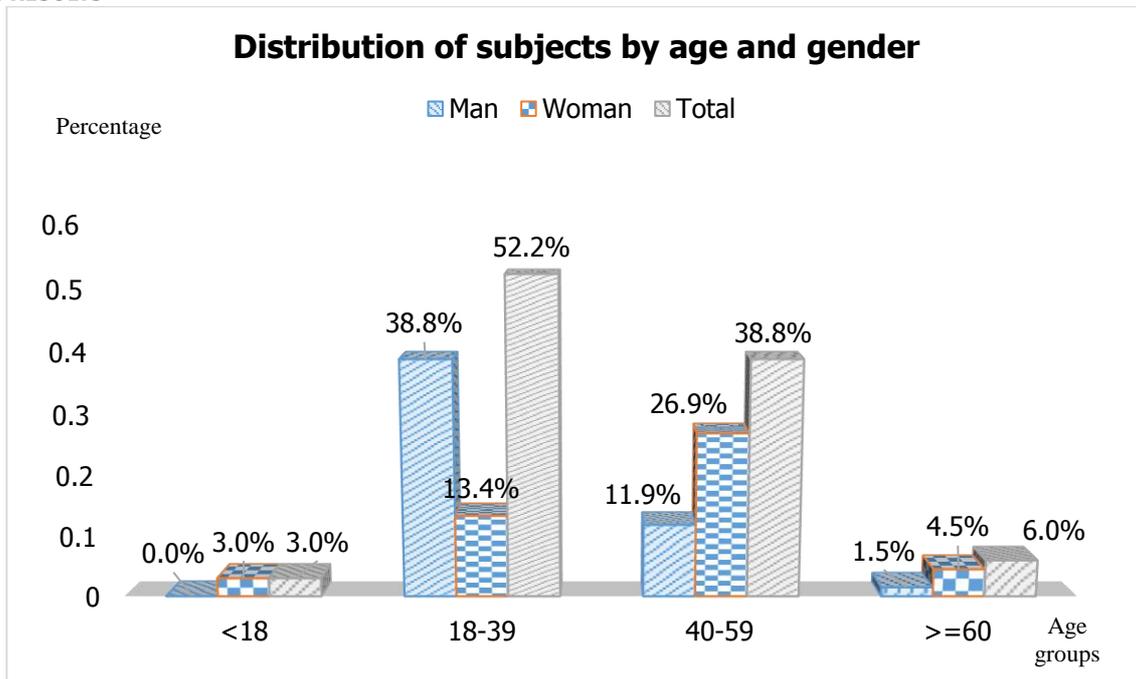


Chart 1. Distribution of study subjects by age and gender

The distribution of gender in the group of patients included in the study is fairly even, consisting of 35 men and 32 women. There are a total of 67 patients, with the affected areas and study being assigned to the same patient. Among the patients, the most concentrated age group is 18-39 years old, belonging to the main working age group that is susceptible to injuries during work and labor. Therefore, the sample size is appropriate and meets the requirements for a clinical study.

Table 1. Proportion of patients experiencing pain during treatment

Day	No	Mild	Moderate	Total
During treatment	19 (28.4%)	29 (43.3%)	19 (28.4%)	67 (100.0%)
D0	25 (37.3%)	30 (44.8%)	12 (17.9%)	67 (100.0%)
D2	30 (45.5%)	25 (37.9%)	11 (16.7%)	66 (100.0%)
D4	32 (50.8%)	27 (42.9%)	4 (6.3%)	63 (100.0%)
D6	22 (52.4%)	17 (40.5%)	3 (7.1%)	42 (100.0%)
D8	14 (58.3%)	9 (37.5%)	1 (4.2%)	24 (100.0%)
D10	6	8	1	15

Day	No	Mild	Moderate	Total
D12	0	4	2	6
D14	3	1	1	5
D16	1	1	1	3
D18	0	1	1	2
D20-D28	5	0	0	5
Total	138 (46.3%)	123 (41.3%)	37 (12.4%)	298 (100%)

Among 67 patients, none experienced severe pain during cold plasma irradiation, while 28.4% of patients reported mild pain at least once during irradiation, decreasing to 7.5% after irradiation. 28.4% of patients did not experience any pain during all irradiation sessions. The majority of patients experienced no or mild pain during cold plasma irradiation; out of a total of 298 irradiation sessions, 46.3% of sessions had no pain, 41.3% had mild pain, and only 12.4% had moderate pain.

Table 2. Pain incidence rates after cold plasma irradiation

Day	No	Mild	Moderate	Total
After treatment	22 (32.8%)	40 (59.7%)	5 (7.5%)	66 (100.0%)
D0	27 (40.3%)	39 (58.2%)	1 (1.5%)	67 (100.0%)
D2	34 (51.5%)	28 (42.4%)	4 (6.1%)	66 (100.0%)
D4	40 (63.5%)	23 (36.5%)	0	63 (100.0%)
D6	31 (73.8%)	10 (23.8%)	1 (2.4%)	42 (100.0%)
D8	17	7	0	24
D10	8	7	0	15
D12	3	3	0	6
D14	3	2	0	5
D16	1	2	0	3
D18	1	1	0	2
D20-D28	5	0	0	5
Total	170 (56.9%)	122 (40.1%)	6 (2.0%)	298 (100%)

Among 67 patients, no one experienced severe pain after exposure to cold plasma, and the proportion of patients who did not feel pain after cold plasma exposure increased to 32.8%. After 298 responses, most patients did not feel any pain (56.9%), 40.1% felt mild pain, and only 2% felt moderate pain.

Table 3. The proportion of patients experiencing a burning sensation during cold plasma irradiation

Day	No	Mild	Moderate	Total
During treatment	1 (1.5%)	33 (49.3%)	33 (49.3%)	67 (100.0%)
D0	9 (13.4%)	34 (50.7%)	24 (35.8%)	67 (100.0%)
D2	20 (30.3%)	24 (36.4%)	22 (33.3%)	66 (100.0%)
D4	24 (38.1%)	27 (42.9%)	12 (19.0%)	63 (100.0%)
D6	20 (47.6%)	15 (35.7%)	7 (16.7%)	42 (100.0%)
D8	13	6	5	24
D10	7	8	0	15
D12	0	5	1	6
D14	3	1	1	5
D16	1	1	1	3

Day	No	Mild	Moderate	Total
D18	0	1	1	2
D20-D28	5	0	0	5
Total	102 (34.2%)	122 (40.1%)	74 (24.8%)	298 (100%)

Among 67 patients, there was no case of severe burning sensation during cold plasma irradiation. The percentage of patients who did not feel any burning sensation increased to 32.8% after irradiation. Among a total of 298 responses, the majority did not feel any burning sensation (56.9%), 40.1% felt mild burning sensation, and only 2% felt moderate burning sensation. This could be explained by the gentle pressure exerted by the ArgonMed gas flow (which is a consumable material of the machine) on the surface of the burn, causing a mild burning sensation in patients.

Table 4. Incidence of burning sensation in patients during cold plasma irradiation

Day	No	Mild	Moderate	Total
After treatment	7 (10.4%)	51 (76.1%)	9 (13.4%)	66 (100.0%)
D0	16 (23.9%)	47 (70.1%)	4 (6.0%)	67 (100.0%)
D2	24 (36.9%)	36 (55.4%)	5 (7.7%)	66 (100.0%)
D4	34 (54.0%)	28 (44.4%)	1 (1.6%)	63 (100.0%)
D6	28 (66.7%)	14 (33.3%)	0	42 (100.0%)
D8	14	9	1	24
D10	9	5	1	15
D12	4	2	0	6
D14	3	2	0	5
D16	2	1	0	3
D18	1	1	0	2
D20-D28	5	0	0	5
Total	140 (47.0%)	145 (48.7%)	12 (4.0%)	298 (100%)

There were no cases of severe itching after cold plasma irradiation among the 67 patients. 13.4% of the patients reported mild itching at least once during the treatment. 10.4% of the patients did not experience any itching during any of the irradiations. After the treatment, the percentage of patients reporting moderate itching significantly decreased to 4%, while most of the responses were either no itching or mild itching.

Table 5. The incidence of patients experiencing itching during cold plasma irradiation

Day	No	Mild	Moderate	Total
During treatment	58 (86.6%)	8 (11.9%)	1 (1.5%)	67 (100.0%)
D0	66 (98.5%)	1 (1.5%)	0	67 (100.0%)
D2	66 (100.0%)	0	0	66 (100.0%)
D4	62 (98.4%)	1 (1.6%)	0	63 (100.0%)
D6	37 (88.1%)	5 (11.9%)	0	42 (100.0%)
D8	20	4	0	24
D10	13	1	1	15
D12	4	2	0	6
D14	3	2	0	5
D16	2	1	0	3
D18	1	1	0	2
D20-D28	5	0	0	5
Total	279 (93.6%)	18 (6.0%)	1 (0.3%)	298 (100%)

No patient experienced severe itching during cold plasma treatment, 1.5% of patients had a moderate itching sensation at least once during cold plasma treatment, and up to 86.6% of patients did not experience itching during cold plasma treatment in all sessions. Among a total of 298 treatment sessions with feedback, 93.6% reported no itching sensation during treatment, 6% had a mild itching sensation, and only 1 reported a moderate itching sensation (0.3%). Therefore, the use of cold plasma treatment is unlikely to cause significant itching sensation for patients during treatment.

Table 6. Proportion of patients experiencing itching after cold plasma treatment

Day	No	Mild	Moderate	Total
After treatment	59 (88.1%)	6 (9.0%)	2 (3.0%)	66 (100.0%)
D0	65 (97.0%)	2 (3.0%)	0	67 (100.0%)
D2	66 (100.0%)	0	0	66 (100.0%)
D4	62 (98.4%)	1 (1.6%)	0	63 (100.0%)
D6	38 (90.5%)	3 (7.1%)	1 (2.4%)	42 (100.0%)
D8	21	1	2	24
D10	13	1	1	15
D12	4	2	0	6
D14	3	2	0	5
D16	2	1	0	3
D18	1	1	0	2
D20-D28	5	0	0	5
Total	280 (94.0%)	14 (4.7%)	4 (1.3%)	298 (100%)

No patient experienced severe itching after cold plasma irradiation, 3.0% of patients had a moderate itching sensation at least once after cold plasma irradiation. As many as 88.1% of patients did not have itching after cold plasma irradiation in all irradiation sessions. Most patients did not experience itching during treatment, only a few days at the beginning had itching sensation. Therefore, after studying 298 irradiation sessions, we found that this method is very safe to use.

IV. DISCUSSION

Chart 1 shows the age and gender distribution of a random sample of 67 individuals. The total number of men is 35 (52.2%) and the total number of women is 32 (47.8%). The majority of the study subjects were aged 18-39 (52.2%), followed by those aged 40-59 (38.8%), with the smallest number belonging to those over 60 (6.0%). In terms of gender distribution, there were more men than women, but the difference was not significant. Based on these data, it

can be concluded that the age group of 18-39 accounts for the largest proportion of the study sample. This result is consistent with many studies on the incidence of burns in Vietnam, including the study by Do Hoang Tung [8].

The study results showed that none of the 67 patients experienced severe pain during cold plasma irradiation. 28.4% of patients had at least mild pain during cold plasma irradiation, and this rate decreased to 7.5% after irradiation. This indicates the pain-

reducing effect of cold plasma irradiation. Additionally, 28.4% of patients did not experience pain during cold plasma irradiation at all. When compared with the study by Fetykov et al. (2009), which was conducted on 48 patients with diabetic foot ulcers using a low-temperature plasma source, the results of the present study also showed pain reduction and improved wound healing after cold plasma irradiation [9]. The rate of patients experiencing pain during cold plasma irradiation in this study was relatively low, with only 12.4% of irradiations causing patients to experience mild pain. Most patients did not experience pain or only experienced mild pain during cold plasma irradiation; out of a total of 298 irradiations, 46.3% did not cause pain, and 41.3% caused mild pain. After irradiation, based on a total of 298 responses, the majority did not experience pain (56.9%), 40.1% experienced mild pain, and only 2% experienced moderate pain.

The study on the adverse effects of burning and itching during and after cold plasma irradiation showed that none of the 67 patients experienced severe burning during irradiation. However, 49.3% of patients experienced mild itching during cold plasma irradiation at least once. During plasma irradiation, the ArgonMed air flow blows onto the surface of the burn, causing a slight pressure sensation that can cause mild itching in the patient [10]. Out of 298 plasma irradiation time, 34.2% had no tingling sensation, 40.1% had mild tingling, and 24.8% had moderate tingling. After cold plasma irradiation, no patients experienced severe tingling, and only 13.4% of patients felt moderate tingling at least once. This indicates a significant reduction in tingling sensation after cold plasma irradiation. None

of the patients experienced severe itching during cold plasma irradiation, and only 1.5% of patients felt moderate itching at least once. However, safety studies have shown that cold plasma does not harm healthy cells at treatment doses and does not damage skin structures in *in vivo* and *ex vivo* studies by authors Pompl et al. and Daeschlein et al. [10]. Therefore, using cold plasma has many benefits in treating burns, including reducing treatment time, significantly reducing the amount of bacteria cultured on the skin, without causing pain or tingling as with other methods.

Among 298 cold plasma irradiation time, 86.6% of patients did not experience any itching during the treatment. This rate significantly improved after the end of the treatment, with 88.1% of patients reporting no itching sensation. Only 3.0% of patients reported mild itching sensation after cold plasma irradiation, and no patients experienced severe itching. With a total of 298 time, there was only one report of mild itching sensation (0.3%). Therefore, it can be concluded that this method is very safe and causes little discomfort for patients during the treatment. Isbary (2010) studied the effectiveness of argon cold plasma treatment in 150 patients with chronic infected wounds and found that this technique was safe and painless, reducing the amount of bacteria in the wound and promoting wound healing. Both studies demonstrated the efficacy and safety of cold plasma in the treatment of patients. However, these studies were limited to examining very few unwanted effects, such as itching during treatment for second and third degree burns. More studies are needed to better evaluate the effects and safety of this method in the treatment of other diseases [4].

Therefore, our study results indicate that the cold plasma therapy is a safe method for treating superficial second and third degree burns. No serious adverse events were recorded during the study. Common adverse events such as mild to moderate pain, stinging, and itching were reported. Pain during plasma treatment was present in 71.6% of cases, but decreased to 27.2% after treatment. In particular, mild pain decreased significantly from 28.4% during treatment to 7.5% after treatment. The results of this study are consistent with previous international studies. Cold plasma does not harm healthy cells during treatment, and very little damage is detected if skin cells are exposed for too long. Short treatment time significantly reduces the amount of bacteria on the skin, without causing any damage to the skin structure in in vivo and ex vivo studies by Pompl et al. [10].

V. CONCLUSIONS

The study results demonstrate that cold plasma irradiation is a safe method for treating non-severe second and third-degree burns. No serious adverse events were recorded during the study. The most common adverse events were mild to moderate pain, burning, and itching at the site of treatment, which quickly decreased after cold plasma irradiation. Short treatment and irradiation times did not cause any harm to the skin structure, and the incidence of unwanted effects was minimal. Therefore, the cold plasma irradiation method should be widely applied in clinical settings.

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