Effect of metronidazole combined with autolytic debridement for the management of malignant wound malodor

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Abstract

Objective: To explore the effect of metronidazole combined with autolytic debridement for the management of malignant wound malodor.

Methods: Patients with malignant wounds who underwent dressing change at a wound outpatient clinic from September 2016 to February 2019 were randomized to an observation group (36 patients) or a control group (37 patients). The observation group was treated with metronidazole combined with debridement gel while the control group received wet dressing therapy combined with silver sulfadiazine. Malodor control was compared between the two groups from treatment initiation to days 3 and 12 after dressing change, and the social impact scale was used to compare stigma caused by malodor between the groups before and after treatment.

Results: The observation group had significantly superior malodor control on days 3 and 12 after dressing change compared with the control group. There was no difference in stigma between the two groups before treatment, but stigma in the observation group was significantly lower than that in the control group after treatment.

Conclusion: Metronidazole combined with autolytic debridement can effectively reduce the malodor of cancerous wounds while controlling infection, and alleviate patient stigma caused by malodor.

Keywords

Cancerous wound, metronidazole, autolytic debridement, malodor, malignant, dressing

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**Background**

Cancerous wounds differ from other chronic wounds in a number of ways. Given their specific pathogenesis, cancerous wounds have more complex manifestations, heal more slowly, and are more difficult to treat and manage.1 Extensive oozing, strong malodor, and intense pain are the main characteristics of cancerous wounds, all of which can seriously reduce the quality of life of patients with advanced malignant tumors.2,3 The proportion of patients with malodorous symptoms in this population has been reported as 10.4%, and these patients have been shown to be at risk of psychological disorders such as self-denial, anxiety, fear, insomnia, and social disorders.4 Metronidazole topical preparations are commonly used to clean wounds and can both deodorize and control infection.5 Wound debridement can reduce residual necrotic tissue and bacteria levels, leading to a reduction in malodor.6 Since mechanical debridement can frequently lead to pain and bleeding, autolytic debridement and biological enzyme debridement are preferred.7 The malodor associated with cancerous wounds is markedly different from that associated with chronic wound infection. The necrotic tissue of cancerous wounds is an ideal environment for bacterial growth which, when coupled with the typically low immunity of cancer patients, can lead to the proliferation of large numbers of anaerobic and aerobic bacteria. Anaerobic bacteria in particular produce decomposition products such as putrescine and cadaverine, which can cause a strong malodor.12 Cancerous wounds are typically treated over a long duration of time, which can affect the quality of life of patients to varying extents and result in a high economic burden. While palliative care of patients with cancer should be advocated throughout the entire treatment period, symptom management of cancerous wounds is increasingly attracting attention. In the present study, we evaluated the use of metronidazole combined with debridement gel in autolytic debridement management of malignant wound malodor to identify an effective and economical wound management strategy that can rapidly improve wound symptoms.

**Methods**

**Patients**

Patients with cancerous wounds who attended a wound clinic for dressing change from September 2016 to February 2019 at the tumor center of a major general hospital were eligible for inclusion. Other inclusion criteria were advanced malignant tumor with definite pathological diagnosis, skin metastases resulting from cancerous wounds, and a wound ulceration area of 2 x 3 cm to 25 x 30 cm and wound depth of 1 cm to 3 cm. Wound characteristics for inclusion were (1) irregular appearance, with new growth observed at the edge of the wound and new organisms detected on the edge of the wound; and (2) malodor, exudation, necrotic tissue, and oozing blood. Allergy to sulfadiazine was an exclusion criterion.

Eligible patients were randomized using the block method according to the order of time of treatment. The study protocol was approved by the Medical Ethics Committee of Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. It was deemed unnecessary to obtained informed consent from the study participants as both the observation group and the control group received routine standard of care for wound care and debridement.

**Wound management**

The same wound cleaning and dressing change protocol was used in the
observation group and the control group. For wound cleaning, 0.9% normal saline was used to wash the wound surfaces and saline cotton balls were used to wipe away necrotic tissues while avoiding exposed blood vessels and bleeding caused by friction. Disinfectant containing silver ions was used for more severe infections, and the wound was then washed with 0.9% normal saline. For wounds with secretions, swabs were taken for bacterial culture and systematic antibiotics prescribed as appropriate. The edges of the wound and surrounding skin were carefully observed during cleaning, and any signs of maceration dermatitis were immediately addressed.

For wound dressing after cleaning, an inner dressing was used in both the observation and control groups. In the control group, the wound base was evenly coated with debridement gel and covered with non-viscous sulfadiazine silver ion dressing (Urgo Medical, Paris, France). In the observation group, the wound base was evenly coated with metronidazole powder and debridement gel mixture (Coloplast, Humlebaek, Denmark) and then covered with petroleum jelly gauze to create a wet wound healing environment, reduce adhesion between the inner dressing and the wound, and prevent pain and bleeding when next changing the dressing. In both groups, sterile surgical cotton pads were used as the outer dressings, and were folded or cut to ensure complete wound coverage. Skin protectant spray was applied to the surrounding skin to form a transparent film that protected the skin from wound seepage, and the dressing was fixed with wide adhesive tape. An elastic bandage or abdominal band was used to fix wounds where adhesive tape was not appropriate. The frequency of dressing change was determined by the amount of exudate absorbed by the outer dressing.

Effectiveness evaluation

Assessment criteria. Wound malodor was evaluated using the Grocott Wound odor assessment as follows: 8  Level 0: malodor can be detected upon entering the patient’s room; Level 1: malodor can be detected at a one-arm’s-length distance from the patient; Level 2: malodor can be detected at less than one-arm’s-length distance from the patient; Level 3: malodor can be detected only at close proximity to the patient; Level 4: malodor can be detected only by the patient; and Level 5: no malodor detection. In our analysis, level 0–1 was classified as severe, level 2–3 as moderate, and level 4–5 as mild malodor severity. The Social Impact Scale (SIS) was used to evaluate stigma associated with wound malodor.[9] The SIS is widely used in patients with chronic diseases and includes 24 items within four dimensions, social exclusion, economic discrimination, inner sense of shame, and social isolation, evaluated using a Likert4 method where 1 point represents “strongly disagree”, 2 represents “disagree”, 3 represents “agree”, and 4 represents “strongly agree”. Total possible score ranged from 24 points to 96 points, with higher scores associated with a greater perceived social impact.

Evaluation methods. The wound condition was evaluated before each dressing change during a 14-day treatment period. Malodor assessment and SIS score were performed on days 3 and 12.

Statistical analysis. SPSS version 20.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Count data were described as percentages using a chi-square test and Fisher’s exact probability. A t-test of two independent samples was used for measurement data, and a rank sum test was used for rank data. Values of P<0.05 indicated statistical significance.
Results

Patient characteristics

There were 73 patients enrolled to this study (27 males and 46 females), including 36 patients in the observation group and 37 in the control group. Patients ranged in age from 18 to 82 years, with a median age of 50.7 years. Among the 73 patients, there were 35 cases of breast cancer, 17 of head and neck tumors, 15 of sarcomas, 4 of penile cancer, and 2 of skin metastasis of lung cancer. There were no significant differences in age, gender, tumor type, malodor assessment, wound area, and other basic clinical characteristics between the two groups prior to treatment (Table 1).

Comparison of evaluation indexes between two groups of patients

A statistically significant difference in the degree of malodor control was observed between the two groups on days 3 and 12 (P<0.05), as shown in Table 2 and Figure 1. There was no statistically significant difference in SIS score between the two groups prior to treatment. After treatment, the SIS score in the observation group was significantly lower than that in the control group (P<0.05), as shown in Table 3 and Figure 2.

Discussion

Malignant wounds are caused by the primary tumor or its infiltration of the skin, and are characterized by excessive oozing, malodor, infection, and pain. Wound management takes place alongside anti-tumor therapy, meaning that a long treatment time can be expected. Although silver ion dressings can control malodor with prolonged use, their use is limited by high costs. Previous researchers in China have used carbon filter pockets, carbon dressings,

| Clinical feature          | Observation group (n = 36) | Control group (n = 37) | Statistic | P-value |
|---------------------------|---------------------------|------------------------|-----------|---------|
| Gender                    |                           |                        | X² = 0.407| 0.524   |
| Males (n, %)              | 12 (33)                   | 15 (41)                |           |         |
| Females (n, %)            | 24 (67)                   | 22 (59)                |           |         |
| Age (years)               |                           |                        | X² = 1.330| 0.249   |
| <60                       | 25 (69)                   | 30 (81)                |           |         |
| ≥60                       | 11 (31)                   | 7 (19)                 |           |         |
| Tumor type                | None                      |                        |           | 0.753   |
| Breast cancer             | 18 (50)                   | 17 (46)                |           |         |
| Head-neck carcinoma       | 7 (19)                    | 10 (27)                |           |         |
| Sarcoma                   | 9 (25)                    | 6 (16)                 |           |         |
| Lung carcinoma            | 1 (3)                     | 1 (3)                  |           |         |
| Carcinoma of the penis    | 1 (3)                     | 3 (8)                  |           |         |
| Degree of malodor         |                           |                        | Z = 0.43  | 0.666   |
| Severe                    | 21 (58)                   | 19 (51)                |           |         |
| Moderate                  | 12 (33)                   | 16 (44)                |           |         |
| Mild                      | 3 (9)                     | 2 (5)                  |           |         |
| Wound area (cm²)          | 56.36 ± 17.40             | 61.05 ± 19.28          | t = 1.09  | 0.279   |

Note: Fisher’s exact probability method was used for the statistical analysis of tumor type, meaning that no statistical data were available.
Table 2. Comparison of malignant wound malodor between the treatment and control groups.

| Group       | N (cases) | Malodor control on day 3 | Malodor control on day 12 | Statistic | P-value |
|-------------|-----------|--------------------------|---------------------------|-----------|---------|
|             |           | Serious | Medium | Light | Serious | Medium | Light | Z     |          |         |
| Observation | 36        | 9       | 10     | 17    | 1       | 7      | 28    | 1.97  | 0.049    |         |
| Control     | 37        | 12      | 14     | 11    | 6       | 13     | 18    | 2.70  | 0.007    |         |

Figure 1. Evaluation of malodor control during dressing change on days 3 and 12 in the observation and control groups.

Table 3. Comparison of Social Impact Scale total score between the treatment and control groups before and after dressing change.

| Group       | N (cases) | Social Impact Scale total score |
|-------------|-----------|---------------------------------|
|             |           | Before dressing change | After dressing change |
| Observation | 36        | 72.56 ± 14.57           | 38.44 ± 9.34   |
| Control     | 37        | 73.89 ± 14.38           | 47.97 ± 10.11  |
| Statistic   |           | t = 0.394              | t = 4.179      |
| P-value     |           | 0.694                 | 0.000          |

Figure 2. Comparision of stigma using Social Impact Scale total scores before and after dressing change at the end of the 14-day treatment period between the observation and control groups.
and tea bags to absorb malodor in 11 patients with cancer wounds. Alternatively, air fresheners have been used to mask malodor. Some patients may also use traditional Chinese medicine therapy, which can maintain the cancer wound as a stable “necrotizing scab” with symptom control. However, these external approaches exert their effects through auxiliary means. The present study evaluated the use of metronidazole, which kills anaerobic bacteria and blocks the formation of fatty acids that help fight infection and reduce malodor. In parallel, hydrocolloid contained in the debridement gel was used to slowly remove necrotic tissue in the wound bed using endogenous enzymes in the body, resulting in autolytic debridement and reduction of residual necrotic tissue and bacterial growth. As shown in Table 2, wound malodor in patients with severe malodor prior to treatment was significantly improved on the third day after treatment initiation, indicating that malodor control could be rapidly achieved. Petroleum jelly gauze was applied externally to reduce dressing adhesion to the wound bed and prevent loss of moisture from hydrocolloid due to evaporation. Our approach may therefore effectively control malignant wound malodor in a cost-effective manner.

Given the difficulties associated with healing of malignant wounds, symptoms can reduce the quality of life of patients. In a survey of patients with cancerous wounds, malodor was the most significant and disruptive symptom reported. Furthermore, the results from a qualitative study indicated that wound malodor limited quality of life, and was described by patients as “strong,” “putrefying,” and “disgusting”. As shown in Table 3, malodor can have a stigmatizing effect in patients prior to treatment as they are unable to carry out normal social activities and can become isolated even from family members, who may be unable to provide necessary care because of an unbearable malodor. After dressing change, patients’ self-stigma decreased as the smell diminished or disappeared. The process of wound changing is objectively to improve wound symptoms, thus alleviating the patient’s self-stigma, the attention and timely support provided by medical staff may in itself have a beneficial effect. This effect can be increased using additional measures during dressing changing such as the use of soothing music, dark sheets to disguise bloodstains, appropriate communication, and patient feedback to adjust the treatment plan.

The present study had some limitations, including potential bias associated with cancer type and pathology, which we did not investigate. Furthermore, we did not assess quality of life measures other than stigma. Finally, wound malodor can result from other factors such as the present of local organic chemicals, and this was not considered in our study. Further studies are therefore needed to confirm our findings.

Summary
In the present study, metronidazole combined with debridement gel was used to treat malodor associated with malignant wounds, and was found to rapidly relieve the malodorous wound symptoms and alleviate the stigma among patients that results from malodor and social exclusion. Most malignant wounds are accompanied by disease progression, and death or poor treatment effects leading treatment discontinuation mean that wound outcomes are difficult to collect. Therefore, there has been insufficient clinical focus or research on malignant wounds and associated physical and social considerations to date. It is worth considering whether the wet healing theory is suitable for every stage of cancerous wound treatment, as wounds that develop a bacterial biofilm, for example, may be more appropriately treated with traditional dry
dressing debridement. Standard management of cancerous wounds should be considered in parallel with systemic anti-tumor treatment and the overall survival of patients, so that comprehensive, phased, and targeted wound management is adopted.

Declaration of conflicting interest
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