

CASE STUDY

OZONE REGIONAL NON-INVASIVE (ORNI) THERAPY IN COMBINATION WITH NURSING MANAGEMENT OF DIABETIC FOOT ULCER CARE: A CASE STUDY

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ABSTRACT

Diabetic Foot Ulcer (DFU) patients must be treated properly in less than 30 days to prevent the infection spread to the bone. Prolonged treatment can lead to less opportunity to recovery and a higher risk for amputation. Ozone therapy has a clearer clinical effect, that is, the wound healing process, which can be seen from the decreased length of hospital stay. This study aimed to analyse the effectiveness of ozone regional non-invasive (ORNi) therapy in combination with nursing care to manage diabetic foot ulcer car. The result showd a significant improvements in three cases after treating with ORNi in combination with standard nursing treatment. There was no sign of infection and granulation, while epithelization processes were running optimal and exudate production was controlled. ORNi therapy as an adjunct to standard nursing care has shown a significant improvement on DFU's healing process. The average growth rate of granulation and epithelization during 15 days of treatment was up to 22%. It is recommended to design more research with a larger sample regarding the use of ozone therapy as an adjunct to nursing treatment in wound care.

Keywords: Diabetic foot ulcer; ozone therapy



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INTRODUCTION

The number of diabetic patients in Indonesia is predicted to increase every year. International Diabetes Federation (IDF) estimated that there were 10.7 million diabetic patients in the adult population (20-79 years old) in 2019, and it is estimated to increase by 11% and 11.8% in 2030 and 2045 respectively. Diabetes is one of the non-contagious chronic diseases in Indonesia, which was predicted that there were 2% of Indonesians diagnosed with diabetes (Riskesdas, 2018). 1 of 16 adult Indonesians had a risk of acquired diabetes (IDF, 2019). Indonesia becomes the 2nd highest country of diabetes cases in the Western Pacific and the 7th highest country with the most diabetes cases in the world (IDF, 2019). DFU (Diabetic Foot Ulcer) is one of the diabetes complications with a global prevalence of 6.3% and the prevalence in North America, Asia, Europe, Africa, and Oceania was 13%, 5.5%, 5.1%, 7.2%, and 3.0% respectively (Zhang, et al., 2017). Complications of DFU are amputation caused by gangrene and infection. The incidence of DFU in men was higher (4.5%) than women

(3.5%) and was higher in type 2 Diabetes Mellitus/T2DM (6.4%) than type 1 Diabetes Mellitus/T1DM (5.5%) (Zhang, et al., 2017).

Every 30 seconds, an amputation occurs in diabetic patients and 85% of them are preceded by diabetic foot wounds that develop complications of gangrene and infection (IDF, 2019). Diabetic foot problems, especially wounds, are still a very big problem. Most of the diabetic patients who came to RSCM (Cipto Mangunkusumo Hospital – one of the national referral centers for government hospitals located in Central Jakarta) have diabetic foot problems (111 patients in 2010-2011). The mortality rate was 16% and the amputation rate was 25% (Sitompul et al., 2014). A retrospective cohort study in RSCM found 70 patients with PTA (Percutaneous Transluminal Angioplasty) and 43 of them acquired DM and arterial peripheral disease. Of these 43 patients, 30.2% had gangrene, 30.2% had an ischemic ulcer, and 39.5% had no lesions (Hasan, 2013). IDF predicted that by 2040 there will

be 642 million diabetics with more than 25% having the risk of DFU (IDF, 2019).

The risk factor for foot amputation starts from problems in diabetic patients. It is caused by DPN (*Diabetic Peripheral Neuropathy*), *Peripheral Arterial Disease* (PAD), *Charcoat Neuro-Osteoarthropathy* (CNO), *Diabetic Foot Ulcer*, and infection including gangrene. Risk factors for amputation are increased in diabetic patients with poor glycemic control, DPN with LOPS (*Lost of Protective Sensation*), smokers, foot deformities, pre-ulcer conditions (e.g., callus, corn), PAD with previous foot ulcer, previous amputation, visual impairment, and patients with dialysis (American Diabetes Association, 2018).

DFU, also known as neuropathic ulcer, is caused by damage to the nerve structure of the lower extremities leading to disturbances in sensory, motoric, and autonomic neuropathy. DFU can also occur due to disorders or peripheral vascular disease and decreased immunity due to hyperglycemia conditions (Smeltzer, Bare, and Hinkle., 2010). Patients diagnosed with DFU should be properly treated within 30 days to maximize the recovery potential and to decrease the risk of tissue and bone infection as a cause of amputation (Baranoski., 2012). Most of DFU infections are caused by polymicrobial and anaerobe negative gram bacterial (cocci), named staphylococcus and streptococcus. An ulcer that is not accompanied by a sign of tissue and bone infection does not require antibiotic therapy (American Diabetes Association, 2020).

Ozone therapy is one of the therapeutic modalities to accelerate wound healing. It has a clearer clinical effect, significantly affects the wound healing process, and increases lipid peroxidation and antioxidant protection index. The success of therapy can be seen from the decreased length of the patient's hospital stay (Rosul & Patskan, 2016). A Randomized Control Trial (RCT) study about the efficacy of comprehensive ozone therapy in DFU healing was conducted in 200 DFU patients, where in the intervention group, the healing process was found faster than the control group as evidenced by the size of the wound (wound closure) and the incidence of amputation (Izadi et al., 2019). The action mechanism of ozone therapy in DFU has an impact on increasing antioxidant capacity, pathogen inactivation, modulation of growth factors from inside, and immune system activation (Wen & Chen, 2020). In another study comparing ozone therapy with standard treatment (using antibiotics), it showed that the number of wounds healed with ozone therapy was 70% and with standard treatment was 63%; the size reduction with ozone therapy was 34.66 cm² and with standard treatment was 14.12 cm²; and the length of stay with ozone therapy was 26 days and with standard care was 34 days, without side effects (Wang et al., 2015).

There are ways to use ozone therapy for DFU treatment: (1) 200 ml NaCl ozonized using ozone machines UM 80 (concentration: 1000-1300mcg/l) and given by intravenous; (2) for regional therapy (application on the wound surface) using ozone dissolved in 0.9% NaCl solution and seabuckthorn oil ozonated at a concentration of 4000 mcg/l (Rosul & Patskan, 2016). Another study using non-invasive ozone with 20-50 ml concentration was a bag for 30 minutes per day for 20 days with an ozone humazonpromedic machine (Zhang et al., 2014). This study aims to evaluate and report DFU patients using ozone regional non-invasive (ORNi) therapy.

METHOD

This case study was conducted from November to December 2020. Three DFU patients were treated with ORNi therapy which was given every 3 times a week (not every day) combined with standard care in MOIST Care (nursing care healing center in Jakarta). These 3 patients have similar characteristic which is the wound bed is mostly granulating tissue in which its healing is in the proliferation phase (granulating and epithelization). The evaluation of this study was measured by the wound size and other wound characteristics using BWAT (Bates-Jensen Assessment Tools) scoring system (Bates-Jensen, 2001). BWAT evaluates wound bed, wound size, undermining cavity, wound edge, exudates, periwound skin, signs of infection, and tissue type.

RESULT Case 1 Assessment

Mr. I, 63 years old, a Muslim, a diploma graduate, and a retired civil servant. He lives with his wife; his children are already married and live separately with him. He has been diagnosed with DM in the past 5 years. He came to MOIST Care after amputation surgery in one of the hospitals in Bogor. He said that the surgery was 2 weeks ago. When he came to MOIST Care, his wound was still wet and had not healed yet. Before amputation, he had gangrene and infection. After surgery, he took care of the wound at home by himself and was helped by his wife and children. After one week, the wound became dry (necrotic tissue) and he still had edema. His family came to MOIST Care to have wound care. After 6 treatments (3 times a week), the wound bed got better (autolytic debridement work): there was granulation tissue - from 100% necrotic tissue became 90% granulating tissue. Since he came, he already had medication from a physician in which Gliquidone 30 mg, Metformin 500 mg, Acarbose 50 mg, Asamtranexamat 500 mg, Cefadroxil 500 mg (during 1 week treatment in MOIST Care, he was not continuing medication, except for glucose control). Assessment on December 21st, 2020 (the 17th visitation), he was compos mentis, E4M6V5; Blood Pressure (BP): 120/70; Temperature (T): 36.7°C; SpO2: 98%; Heart Rate (HR): 93 beats per minute (bpm); Respiratory Rate (RR): 20 breaths per minute (bpm); blood glucose: 287 gr/dl. He said his feet were more comfortable if he put a pillow under them when he sleeps. The dressing strike through after 2 days. Physical assessment: Height: 165 cm, Weight: 55 kg, BMI: 20.2 kg/m² (normal). Palpation: dorsalis pedis and posterior tibial palpable, warm extremity periphery, no cyanotic and no claudication or rest pain (specific characteristics of PAD), no need to check ABI (Ankle Brachial Index). Foot pain sometimes appears when he does activities with a score pain of 3-5. MMSE (Mini Mental State Examination) score: 30 (normal). Mobility: walking without help. Activity and rest: he can sleep without awakening. Muscle power: 4 = 75%, he can move his joints actively and against pressure. Positive LOPS (Lost of Protective sensation) Wound scoring using BWAT: 40 (1st wound) and 38 (2nd wound). Blood glucose is uncontrolled with a rate of 200 gr/dl. The patient reported that sometimes the wound gets wet after he went to the toilet.

Case 2 Assessment

Mrs. T, 57 years old, a Muslimah, a married-woman with 5 children, a senior high school graduate, a housewife, and living in Jakarta. She came to MOIST Care on November 12th, 2020, with DFU in the past 2 weeks. It started with chapped and blistered feet. She had a history of foot amputation (2nd and 3rd digital) in 2016. Her medication was from a physician: amlodipine 1x1, metformin 2x1. Assessment on December 21st, 2020, (30th visitation):

compos mentis, E4M6V5; BP: 130/90; T: 36.6°C; SpO2: 99%; HR: 89 bpm; RR: 20 bpm; blood glucose: 277 gr/dl. Height: 160 cm, Weigth: 50 kg, BMI 19,5 kg/m² (normal). Palpation: dorsalis pedis and posterior tibial palpable, warm extremity periphery, no cyanotic and no claudication or rest pain (specific characteristics of PAD), no need to check ABI (Ankle Brachial Index). Foot pain sometimes appears when she does activities with a score pain of 3-5. MMSE score: 30 (normal). Mobility: walking without help. Activity and rest: she can sleep without awakening. Muscle power: 4 = 75%, she can move her joints actively and against pressure. Positive LOPS wound scoring using BWAT: 48 (1st wound) and 46 (2nd wound). Blood glucose is uncontrolled with a rate of 190 gr/dl. The patient reported that sometimes she did not attend the care on schedule due to no one taking her for the treatment.

Case 3 Assessment

Mrs. E, 58 years old, a Muslimah, a married-woman with 3 children, a diploma graduate, and a teacher who lives in Jakarta. Her first visit to MOIST Care was on December 5th, 2020, with DFU in the past 2 weeks with symptoms of foot blisters after traveling. The wound was watery and was taken care of by her husband using NaCl 0.9 % gauze. She had her amputation on digital 2, 3, and 4 in one of the hospitals in Jakarta in 2016. Her medication was given by a physician: Amlodipin 1x1 and metformin 1x1. Assessment on December 21st, 2020, (8th visitation): compos mentis, E4M6V5; BP: 120/70; T: 36.5°C; SpO2: 98%; HR: 90 bpm; RR: 19 bpm; blood glucose: 279 gr/dl. Height: 150 cm, weigth: 40 kg, BMI 17.7 kg/m² (underweight). Palpation: dorsalis pedis and posterior tibial palpable, warm extremity periphery, no sign of cyanotic, and no claudication or rest pain (specific characteristics of PAD), no need to check ABI (Ankle Brachial Index). MMSE score: 30 (normal). Mobility: activities with wheelchairs. Activity and rest: she can sleep and sometimes get awakened. Muscle power: 3 = 50%, she can move her joints actively and against pressure. Positive LOPS wound scoring using BWAT: 31. Blood glucose is uncontrolled with its rate of 210 gr/dl.

Nursing Diagnoses

Based on the assessment results, the nursing diagnoses are similar in cases 1, 2, and 3, which are (1) impaired skin integrity related to alterations in skin integrity, (2) risk for infection related to alterations in skin integrity and insufficient knowledge to avoid exposure to pathogens, (3) risk for unstable blood glucose level related to ineffective dietary intake and inadequate blood glucose monitoring. Based on those problems and nursing diagnoses, a nursing care plan and outcome criteria are arranged, including the use of ORNi in combination with standard treatment in MOIST Care.

Outcome Criteria

Outcome criteria in nursing care are given based on the nursing diagnosis. The first nursing diagnosis outcome criteria are (1) the occurrence of the wound healing process (granulation and epithelization); (2) controlled exudate (moisture balance); (3) controlled germ colonization (controlled biofilm). The second nursing diagnosis outcome criteria are: (1) increased knowledge related to infection control; (2) enhanced immunity; (3) no signs of local or systemic infection; (4) no complaint of pain, warmth, or fever on the wound; and (5) normal limits of whole blood count (laboratory results). The criteria for the third nursing diagnosis include (1) normal blood glucose limits; (2) normal HbA1C count; (3) prevented acute and chronic complications; and (4) increased knowledge about blood glucose control.

Nursing Intervention

Nursing intervention plan includes independent and collaborative practices that were given based on the nursing diagnosis and outcome criteria. The first nursing diagnosed interventions are: (1) monitor wound development such as wound bed, exudate, wound edge, and periwound skin (2) wound debridement of necrotic tissues and biofilm; (3) dressing selection and application; (4) offloading techniques to reduce pressure; (5) use adjunct therapy to promote wound healing (such as hydrotherapy, HBTO, VAC, ozone, electrical stimulation); (6) health education related to nutrition and multivitamins that support wound healing (i.e., micro-macronutrient, antioxidant); and (7) collaborative intervention (e.g., surgical debridement for necrotic tissue). The second nursing diagnostic interventions are: (1) monitor for signs of local infection and systemic; (2) infection control management with identification of signs of infection; (3) do handwashing properly before and after treatment; (4) maintain septic and aseptic techniques; (5) wound management prior to preventing infection; (6) wound cleansing using adequate antiseptic; (7) use antimicrobial dressing with occlusive or semi-occlusive techniques; (8) give antibiotic oral therapy (collaborative intervention) as indicated. The third nursing diagnosed interventions are: (1) monitor blood glucose and HbA1C; (2) assess patients' knowledge related to DM management; (3) educate patients and family about hyperglycemic management (medication, nutrition, physical activitiy, and positive habits or lifestyle and stress management); (4) motivate to do passive or active physical activities regularly; and (5) collaborative intervention including controlling regular blood glucose, ketone, blood gas analyze control, and medication to control blood glucose.

Implementation

Nursing implementation in these cases is similar, which was given 3 times a week. These case studies give results as follows:

1. Wound cleansing (standard care)

When patients came to change the dressing, the wound was washed first before doing the assessment. Wound cleansing was done by soaking technique with ozonized mineral water for 5 minutes. The wound and feet were cleaned using antiseptic soap and then the wound was rinsed and dried. Before the ORNi, the wound was evaluated for its improvement.

2. Ozone regional non-invasive (ORNi) therapy (combination of adjunct therapy)

After cleaning and evaluating the wound, ORNi therapy was given for 15 minutes on the wound surface area, covered by a plastic bag (bagging system). The ozone device used is UVC3000 type, with a density of 800mg/H. Picture 1 shows the application of ORNi therapy for case 1 and 2 wounds.



Picture1. ORNi-therapy covered with a plastic bag

3. Mechanical debridement and massage therapy of the wound edge (standard care)

After using the ORNi, mechanical debridement was done to clean the biofilm on the wound surface. While massaging the wound edge, the wound was cleaned again using polyhexamethylene biguanide (PHMB) solution (compress). Massaging the wound edge is meant to reduce the epibole (*rolled under the epithel*) and to promote epithelization.

4. Dressing selection and application (standard care)

The next implementation is covering the wound with a dressing (semi-occlusive technique). The dressing selected should be able to prevent infection, maintain moisture, absorb exudate, and promote granulation tissue. In the 1st and 2nd cases, antimicrobial ointment and serum were used, calcium alginate as primary dressing, and gauze as a secondary dressing. As for the 3rd case, antimicrobial salf and serum were used as primary dressing, and foam was used as a secondary dressing

5. Education (standard care)

During the treatment, the patients and their families were given health education related to infection control and blood glucose control, for example, what should do with the wound at home and how to control infection and blood glucose at home. The patients and family were also informed about the next schedule to change the dressing, knowledge about physical activities which can be done at home, fulfillment of nutritional needs, and how to do stress management at home.

6. Collaborative (standard care)

Collaborative implementation for these patients to promote wound healing is glucose control and infection control as needed. During the 15 days of treatment, there were no signs of infection, and the oral antibiotics were discontinued.

Evaluation

There was significant improvement in cases 1, 2, and 3 after treatment with ORNi as a combination of standard care. Total treatments for both cases 1 and 2 are 7 times (3 times a week of dressing change) and for case 3 as much as 5 times (2 times a week of dressing change) for a total of 15 days of treatment. Case 1 evaluation using the BWAT scoring system was seen from 40 to 27 (1st wound) and from 38 to 24 (2nd wound).

Table 1. Wound regeneration process of cases 1, 2,and 3



Case 2 evaluations using the BWAT scoring system are from 48 to 34 (1st wound) and from 46 to 31 (2nd wound). Case 3 evaluation using the BWAT scoring system was from 31 to 15 (regeneration). There were no signs of infection found, good granulation and epithelization process, and controlled exudate amount. Table 1 describes the wound regeneration process.

DISCUSSION

The wound healing processes involve inflammation, proliferation with healing time less than 21 days (in acute wounds), and maturation process up to two years. In a chronic wound, which is difficult or fails to heal certainly takes a longer time to heal or closed. (Baranoski S., 2012). Factors that affect wound healing that should be considered include oxygenation, excess bioburden (e.g., germs, foreign bodies) in wounds, history of smoking, nutritional status, comorbidities (e.g., DM, CKD), obesity, drugs used, age, immunosuppressants, stress factors, cellular abilities, or malignancy. Overcoming and controlling complication factors can accelerate the healing of the wound (Doughty & Sparks, 2016). The patients (cases 1, 2, and 3) had chronic wounds with the same factors affecting the wound, which are DM and age over 50. The characteristics of the wound generally have the similar condition, that is, the wound bed which is mostly granulation tissue (>75%), with the same goal to stimulate the granulation and epithelization process. This case study using ozone therapy is to promote or stimulate the granulation and epithelization process. Ozone therapy is one of the management recommended for treating DFU.

The standard management recommendations for DFU are (1) offloading techniques; (2) necrotic tissue debridement; (3) dressing selection; (4) adjunct (e.g., using growth factors, stem cell, oxygen therapy HBOT, vacuum assisted closure (VAC), energy-based therapies) (Eleftheriadou et al., 2020). The International Working Group and the Diabetic Foot (IWGDF) guidelines also recommend management for DFU including: (1) debris necrotic tissue, callus as indicated; (2) use appropriate dressing based on exudate level, effectiveness and efficiency; (3) do not use antimicrobial dressing as a single goal (promote wound healing); (4) consider using a sucrose-octasulfate dressing as an adjunct treatment; (5) consider using systemic oxygen hyperbaric therapy; (6) topical oxygen therapy as an adjunct intervention is not recommended; (7) consider using VAC (in post DFU surgery; (8) not recommended using VAC in DFU non post surgery; (9) consider using placenta-derived products as an adjunct treatment; (10) not recommended to use platelet gel growth factors, biologically engineered products, or ozone alone; (11) consider using platelet gel growth factors, biologically engineered products, or ozone as adjunct therapy; (12) do not use agents that alter the physical environment, for example, through electrical stimulation alone; (13) do not use interventions that aim to correct nutrition (supplementation, additional vitamins) to accelerate wound healing (Rayman et al., 2020). Number 11th recommendation is one of the basic considerations for ORNi therapy as an adjunct therapy combination to the standard of DFU care. Ozone therapy will not be given alone but in conjunction with standard care. The basic standard treatments for DFU are cleansing, debridement, massage, using a specific dressing to cover the wound, education, and collaborative intervention.

Ozone therapy has shown increased expression of VEGF (Vascular endothelial Growth Factor) significantly, TGF- β (Transforming growth factor- β), and PDGF (Platelet-Derived Growth Factor) and has shown a significant reduction of wound size (J. Zhang et al., 2014). It can be seen in cases 1, 2, and 3 in this case study, which experienced a significant change in wound size during a total of 15 days of treatment with a variation frequency of the dressing changing. Cases 1 and 2 changed the dressing 3 times a week (7 changes in total) and case 3 changed the dressing 2 times a week (5 changes in total). In addition, the exudate amount was controlled, there was no malodour and no purulent exudate. This case study applied the BWAT scoring system to evaluate wound regeneration, where the higher score indicates degeneration and the lower score indicates the regeneration process of the wound. There are 13 questions in BWAT format - each question scores 1 to 5, with the total highest score of 65 and the total lowest score of 13 (Bates-Jensen, 2001). The BWAT score of case 1: the 1st wound decreased by 20%, the 2nd wound decreased by 21.5%. BWAT score of case 2: the 1st wound decreased by 21.5% and the 2nd wound decreased by 23.1%. BWAT score of case 3 shows a decrease of 24.6 %. Thus, it can be seen that average wound repair using ORNi therapy as an adjunct treatment in DFU patients has decreased the BWAT score by 22% for 15 days of treatment.

There is a difference in the frequency of dressing changes between cases 1, 2 and case 3. This is related to the size of the wound and the exudate amount of the wound. The size and exudate number of wounds in cases 1 and 2 are bigger and higher than the wound in case 3. Dressing change frequencies of wounds 1 and 2 were 3 times a week (7 times in 15 days of treatment) and case 3 was only 2 times a week (5 times in 15 days of treatment). The frequency of dressing changes with modern dressing depends on the presence or absence of infection and the amount of exudate. Wound infection is the process of bacteria's invasion into a wound by proliferating microorganisms to a level that involves the host (patient) response both locally and systemically (International Wound Infection Institute/IWII, 2016). Not all chronic wounds are considered infected - this depends on the number or level of germs in the wound (bioburden) which can be categorized as contaminated, colonized, critical colonization, or infection (International Wound Infection Institute/IWII, 2016). Cases 1 and 2 had signs of local infection before treatment with ORNi, which means that the wound is critically colonized. Case 3 did not have the sign of local infection, yet she had biofilm before ORNi therapy, which means that case 3 is colonized. After 15 days of treatment, all cases became contaminated wounds only. The use of dressings containing antimicrobials is one way to treat germs in the wounds at the level of colonization by infection. Meanwhile, at the level of contamination, adequate washing and the use of absorbent dressings are sufficient. Exudate is the fluid that comes out due to leakage of blood vessels containing molecules and cells including electrolytes, nutrients (glucose), proteins (cytokines), inflammatory mediators, matrix metalloproteinases (MMPs), growth factors, various cells (leukocytes, macrophages, neutrophils, and platelet), and microorganisms (Cutting 2004; White and Cutting 2006 in Barret, 2015). Factors that influence the exudate amount are the prolonged wound healing process, the autolysis debridement process, the infection process (increased and uncontrolled germ proliferation), the presence of foreign bodies, edema, systemic disorders (e.g., renal failure, heart failure), wound location, drugs used (diuretics) and inappropriate dressings usage (WUWHS, 2007). In addition, the size of the wound will also be affecting: the wider the wound, the more the exudates are (WUWHS, 2007). Using absorbent dressing can retain moisture. If the wound is accompanied by a sign of infection, it can be combined with an antimicrobial dressing. This condition requires special knowledge and skills of health workers who perform wound care (Vowden et al., 2015). The limitation of this study is that there was no laboratory data to support the number of microbes before and after the treatment. The treatment

evaluation is only on clinical signs of infection (local and systemic).

CONCLUSION AND RECOMMENDATION

The conclusion from the results of this case study suggests that ORNi, as an adjunct therapy to nursing standard care, shows significant progress in wound healing. It can be seen from the speed in the process of proliferation and epithelization during 15 days of treatment with an average growth of up to 22%. The selected cases have similar characteristics: the wound bed was >75% of granulating tissue, DFU, no signs of PAD, aged over 50 years, and patients with LOPS. This case study evaluation used the BWAT scoring system to standardize the assessment of the wound tools. The recommendation from this study is that further studies with different designs and larger sample sizes are needed. Evaluation can be more specific to the wound size, the exudate amount, the level of microorganisms in the wound, and how long the treatment could be safe to use on the wound surface.

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