The Treatment of Skin Ulcers Due to Hemoglobinopathies

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Background

Hemoglobinopathies and hemolytic anemia due to genetic defects such as sickle cell disease, thalassemia syndromes, and other hemolytic diseases are often associated with leg ulcers.(1,2,3) These diseases have in common abnormal hemoglobin chains resulting in abnormal oxygen carrying capacity and red blood cell deformation and adhesion, This causes shortened cell survival, red blood cell rigidity, reduced red cell deformation to get through the microcirculation, increased hemolysis of the cells, anemia, ineffective erythropoiesis, oxidative damage, an associated significant nitric oxide deficiency due to decreased production and consumption by the increased free serum hemoglobin, and a chronic hypercoagulable state due to endothelial abnormalities and abnormal coagulation proteins.(4,5,6,7,8) Increased red blood cell lysis results in high levels of free hemoglobin in the serum. Free hemoglobin binds to and inactivates nitric oxide significantly contributing to the hypercoagulable state and endothelial damage. (9,10) These conditions can lead to tissue ischemia and ulcer development.

The most common location for ulcers in patients with hemoglobinopathies is the lower extremity. (11) Five percent of patients with sickle cell disease over age 10 have a history of a sickle cell ulcer and 75% of patients over age 30 had a history of a sickle cell ulcer.(12,13) Up to 22% of thalassemia patients have had a leg ulcer. (5)

Because the underlying etiology is a genetic abnormality, current therapies have generally proven inadequate. Most of the abnormal conditions in patients with hemoglobinopathy skin ulcers have a basis in nitric oxide deficiency. Treatments to restore nitric oxide have shown promise because of the ability of nitric oxide to restore red blood cell deformability, reduce red blood cell lysis, reverse endothelial abnormalities, improve the hypercoagulation state, and result in microcirculation improvement (14,15)

A device that generates nitric oxide out of the air and delivers it to the wound bed in a gaseous and plasma energy stream has been developed. The technology significantly increases the half-life of the nitric oxide molecule so it can be delivered to the wound surface and still be effective and can carry the nitric oxide molecule up to 3 centimeters through intact skin or other tissue. This allows the nitric oxide to penetrate into the tissue to have its effects of dilating blood vessels, restoring endothelial cell function, reducing blood cell and platelet adhesiveness, and reducing the ROS and inflammatory reaction. The nitric oxide delivered in this manner is highly antimicrobial killing all organisms. This is the preferable way to deliver the nitric oxide so that systemic effects can be avoided in these patients. (16,17) In an effort to find a more effective treatment for patients with skin ulcers due to hemoglobinopathies, a series of patients with these ulcers were treated with nitric oxide/plasma energy gas therapy.

Methods

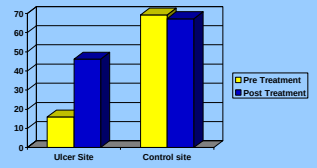
After IRB approval of the protocol 4 patients with lower extremity ulcers due to hemoglobinopathies were chosen to be treated with the nitric oxide/plasma energy gas therapy. After signing the approved consent form, the patients' ulcers were treated with nitric oxide/plasma energy gas therapy for 6 minutes once per week. Between treatments the wounds were covered with a non-adherent, absorbative dressing which was changed once per week. One patient consented to have the $TcPO_2$ of the ulcer site and a distant site measured before and after therapy to evaluate the indirect measure of nitric oxide effectiveness.

Results

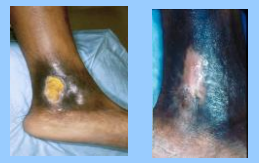
The $TcPO_2$ measurement showed significant reduced levels at the wound site compared to the control site on the thigh prior to therapy with the nitric oxide/plasma energy gas. Following one treatment the $TcPO_2$ at the wound site was significantly elevated yet the control site on the thigh was unchanged. (see graph above) This finding reflected the effect of the therapy on the microcirculation at the ulcer site and the fact that there was no systemic effect. The average healing rate of the patients was 10 weeks. No complications or adverse events were recorded.

Conclusion

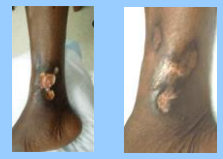
Because of these promising results treating skin ulcers due to hemoglobinopathies with nitric oxide/plasma energy gas, we recommend further trials with this therapy to define its role in the treatment of these very difficult to heal skin ulcers.



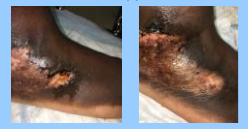
TcPO2 at ulcer site and control site when treated with Nitric Oxide/Plasma Energy Gas showing marked improvement



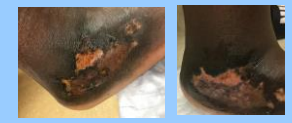
Sickle Cell Ulcer Healed After 8 Weeks NO/Plasma Therapy



Sickle Cell Ulcer Healed After 12 Weeks of NO/Plasma Therapy



Sickle Cell Ulcer Healed After 14 Weeks NO/Plasma Therapy



Sickle Cell Ulcer Healed After 5 Weeks of NO/Plasma Therapy

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