



Review Article

Disrupting the Racial and Ethnic Disparity in Diabetes: New Treatments and Solutions

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Abstract

In the United States, diabetes is the leading risk factor for non-traumatic lower extremity amputation in adults. Minorities with diabetes have significantly higher rates of diabetic complications, including amputation and death. These higher rates are due to differences in practice patterns, routine preventative care, education, and access to efficacious and affordable treatments. Efforts to address these inequities can assist in reducing the rates of disparate care and the highly morbid consequences of longstanding and poorly managed diabetes.

Many diabetic therapies are cost prohibitive and vary in efficacy. Emerging and novel treatments, including those derived from botanicals, have shown promise to expedite healing, contributing to a better quality of life, reduced healthcare costs, reduced hospitalizations, and a lowering of the risk and necessity of limb amputation in these at-risk populations.

Keywords: Racial Disparity in Diabetes; Diabetic Foot Ulcer; Diabetic Treatment; Inula Viscosa AGS RIED; New Diabetes treatment

Introduction

In the United States (US), diabetes affects over 38 million people and is the leading risk factor for non-traumatic lower extremity amputation in adults, resulting in approximately 150,000 amputations per year [1]. Of those with diabetes, minorities have a much higher disease burden than the general population, which results in considerably higher rates of diabetic complications and [2] mortality, and a disproportionately higher risk, up to 9 times, for amputation [3,4]. According to the Centers for Disease Control and Prevention (CDC), affected minority populations include African Americans, Asian Americans, Hispanics, and American

Indians/Alaska Natives [5]. A “diabetes belt” has been identified to exist in the Southeast US, and includes 15 states, including large sections of Alabama, Georgia, Kentucky, Louisiana, Mississippi, South Carolina, Tennessee, and West Virginia [6]. Outside of this “diabetes belt,” there are also many counties and areas across the US, including in New York, Florida, and Texas, that have been identified as “diabetic clusters,” and include higher concentrations of the local population that have diabetes and are more susceptible to diabetes and the resulting complications [7,8]. Many of these clusters are located in lower-income and minority areas. Preventing amputations has proven challenging for clinicians who treat patients in minority communities due to several factors. According to a recent report, 50,000 New York State residents, which have been identified as part of a diabetic cluster, have lost their limbs or feet to diabetes-related amputations since 2009. Results of the analysis

indicate that early clinical intervention and self-management education programs to address diabetic complications drastically reduces amputation rates. In 3 of the boroughs in New York City, Bronx, Queens, and Manhattan, which can be considered areas of diabetic clusters, amputation rates from 2009-2020 increased up to 103%, more than double the National average [9].

Compared to areas not considered to be in the “diabetes belt,” or part of a “diabetic cluster,” there are several factors that contribute to the higher prevalence of diabetes that lead to significant downstream implications such as the development of diabetic foot ulcers (DFUs) and amputations. These include cigarette smoking, dyslipidemia, obesity, physical inactivity, insulin resistance, high blood pressure, inadequate glycemic control [10], preventative care nonadherence, and lack of comprehensive insurance coverage, among others.

In addition, Peripheral Artery Disease (PAD) is considered a major risk factor for morbidity and mortality [11], and studies have shown an increased prevalence of PAD in lower-income areas [11]. Nearly 100,000 major leg amputations are performed every year in the US. Of these, over half are attributable to a combination of diabetes and PAD [4,12,13]. For patients with diabetes and PAD, especially in minority communities where there is a significant higher risk of amputation and poor survival, preventative care and care coordination are critical to avoid progression to Chronic Limb-Threatening Ischemia (CLTI), ulceration, amputation, and death. Integrating routine diabetic foot care and examinations and leveraging inexpensive tests, including hemoglobin A1c testing, and non-invasive vascular assessments have been shown to help limit amputation [14-16].

Inequities in healthcare outcomes exist when there are variations in the distribution of resources based on the geographic location of a population that contributes to the lack of opportunity and leads to the unavoidable differences in health outcomes. Recent community-based efforts to improve access to care, affordability, peer practices, community education, and adherence to treatment plans have been a focus of clinicians and patient advocacy groups alike [17]. The development of DFUs is a highly morbid consequence of longstanding and poorly managed diabetes. Of those patients with diabetes, close to 35% will develop a DFU in their lifetime, with 20% of those resulting in a lower-extremity amputation, either below or above the ankle, or both [18]. Additionally, 10% will die within 1 year of their DFU diagnosis [19,20]. Differences in practice patterns and insurance directives have been shown to contribute to unequal outcomes in minority populations [3,21-24]. For example, patients with DFUs that lack health insurance are less likely to undergo revascularization or wound debridement and more likely to have an amputation than those with private insurance [12,17,25]. These higher rates of amputation and increased mortality are much larger in low income

and minority communities [26]. Since 2014, the incidence of lower-extremity amputation among these communities is growing, with some areas showing a 50% increase [27-29]. The combined effects of the socioeconomic differences, limited accessibility to proper healthcare, the disparities in levels of care and amputation rates by race and ethnicity cannot be and should not be ignored [30,31].

Emerging Botanical Based Treatments

Most commercially available treatments address only one component of a DFU at a time, such as inflammation, resulting in a significantly higher cost with little or no guarantee of success. Other treatments concentrate on addressing tissue bacterial loads while others promote improved vascularization.

Emerging, and novel botanical therapies that are safe, effective and low-cost could be a solution in overcoming gaps in care and providing alternatives to conventional treatments in this at-risk population (Figure 1). A botanical-based supercharged hydrogel, LAVIOR Diabetic Wound Gel (LAVIOR Pharma Inc., Miami, Florida), was developed to address many barriers to wound healing including inflammation, bacteria, vascularization, and hypoxia to support expedited wound healing. The product has been approved for reimbursement by Medicare -Part B and endorsed by the American Diabetes Association’s Better Choices For Life Program that provide consumers a simple way to identify products and services that are suitable for people with diabetes or at-risk for diabetes. National retail chains, such as Walmart, have also made this affordable over-the-counter treatment available, allowing easy access to this patient population in need of care, especially those with no insurance or those with high deductibles.

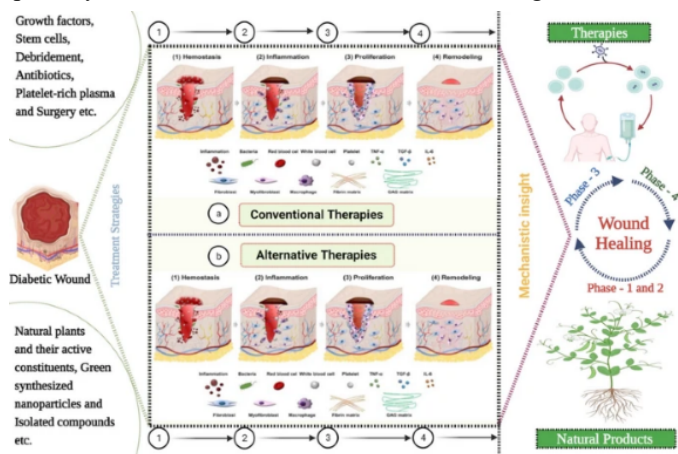


Figure 1: Reference: Yadav, J.P., Singh, A.K., Grishina, M. *et al.* Insights into the mechanisms of diabetic wounds: pathophysiology, molecular targets, and treatment strategies through conventional and alternative therapies. *Inflammopharmacol* (2024). Reprinted with permission.

Many diabetic foot ulcers therapies can be cost prohibitive and vary in efficacy. One area of concentration and research has been identifying natural, non-synthetic treatment options, including those derived from botanicals. These well-researched botanicals, including *Inula Viscosa* and *Inula Viscosa* AGS RIED (Figure 2) are flowering plants native to the Middle East.



Figure 2: *Inula Viscosa* AGS RIED.

Inula viscosa (compositae) is known in traditional medicine for a large range of biological activities including antipyretic, anti-bacterial and antifungal activity [32]. It has been used to treat diabetes, bronchitis, diarrhea, rheumatism, and injuries, among other ailments. *Inula Viscosa* has been shown to elicit several responses in the body, including antimicrobial, antioxidant, antiulcerogenic, anthelmintic, and complications resulting from diabetes [33-38]. After over a decade of research, a new species of *Inula Viscosa*, AGS-RIED, has been incorporated into an Over the Counter (OTC) supercharged wound hydrogel (LAVIOR Diabetic Wound Gel®, LAVIOR Pharma Inc., Miami, FL) yielding a wide array of sesquiterpenoids, especially Sesquiterpene Lactones (SLs) [39-44]. SLs and have been shown to exhibit antimicrobial, antitumor, anti-inflammatory, antifungal, and antimalarial activity

[40]. LAVIOR's Diabetic Wound Gel specializes in addressing chronic wounds mired in the prolonged inflammatory stage, impeding proper healing. The gel is designed to be a vasodilator by encouraging oxygen to the wound. With their advanced technology, patient case reports have illustrated expedited healing, contributing to a better quality of life, reduced healthcare costs, reduced hospitalizations, and a lowering of the risk and necessity of limb amputation [45].

Case Reports

Herein the authors present two patient case reports reviewing the successful treatment with a supercharged hydrogel. Both patients had significant comorbidities and diabetes-related complications and were facing amputation. The patients have given consent for the use of their photos in this manuscript.

Patient 1 - History and Presentation:

A 46-year-old Haitian American male with a history of AIDS, sickle cell anemia, blood glucose abnormalities, chronic pain syndrome, deep vein thrombosis (DVT), and deficiency of nutrients. Patient presented with a 4 cm x 3 cm chronic medial malleolus ulcer (venous ulcer) with 100% fibrotic tissue and severe pain (Figure 3).

Prior Treatments: The patient did not receive any prior treatment before seeing the clinician.

Treatment Algorithm

The wound bed was rinsed with normal saline and the supercharged wound hydrogel was applied to entire wound surface and covered with a nonadherent dressing, 4x4 gauze and wrapped with Kling. Patients were instructed to apply the wound gel 2x/week with nonadherent dressing as daily changes causes maceration.



Figure 3: Treatment and healing progression of 46-year-old Haitian American male with a history of AIDS, sickle cell anemia, blood glucose abnormalities, chronic pain syndrome, Deep Vein Thrombosis (DVT), and deficiency of nutrients with Lavior Diabetic Wound Gel.

Results

After 7 days of treatment, the wound size reduced to 3 cm x 3 cm and there was 100% granulation, no pain on palpation, no drainage, and no sign of local infection. After 51 days of treatment with the hydrogel, the wound had 98% closure. After 3 months from initial treatment, the wound had complete closure.

Patient 2 - History and Presentation:

History: A 46-year-old Haitian American female with a history of diabetes and obesity who presented with a dry distal gangrenous 4th digit with necrotic changes, local edema, and erythema (Figure 4).

Prior Treatments: Previous treatment included Augmentin 500mg p.o every 12h x 10 days and Bactroban dressing on daily basis with no improvement.

Treatment Algorithm

The wound bed was rinsed with normal saline and the supercharged wound hydrogel was applied to entire wound surface and covered with a nonadherent dressing, 4x4 gauze and wrapped with Kling. Patients were instructed to apply the wound gel 2x/week with nonadherent dressing as daily changes causes maceration.



Initial presentation:
Distal fourth digit gangrenous necrotic changes, with local edema and erythema.



After 40 days of Treatment:
Medial digital maceration, stopped the hydrogel for 1 week. Then applied Betadine. Then returned to Lavior.



After 70 days of treatment:
The distal eschar detached, and a healed digit was noted.



Appearance - Day 100
Completely healed. Note the nail has grown back.

Figure 4: Treatment and healing progression of 46-year-old Haitian American female with a history of diabetes and obesity who presented with a dry distal gangrenous 4th digit with necrotic changes, local edema, and erythema with Lavior Diabetic Wound Gel.

Results

By day 70 the distal digit was covered with new epithelium. By day 100 it was noted that a new toenail had completely grown back.

Discussion

Preventive care practices such as foot examinations and annual foot screenings have been shown to prevent or delay the incidence and progression of diabetes related complications. Examples of initiatives that have resulted in positive outcomes include easily accessible community-based peer education, diabetic conscious nutritional based programs, and other outreach to promote screening, prevention, and routine care. The success of self-management peer-peer education programs using granted federal funds that have been implemented, such as those overseen by Health People, a New York City based non-profit, in homeless

shelters in Bronx, New York, resulted in a 45% reduction in emergency room visits for diabetes-related causes over a 6-month period [8]. According to Chris Norwood, Executive Director of Health People, implementation of these peer-to-peer leadership programs, developed and evaluated at Stanford, has shown to rapidly increase awareness and interest in self-care among the low income and minority community, leading to a low-cost initiative that can have an immediate impact on the diabetic population in these diabetic cluster communities. Additionally, access to cost-effective DFU treatments in marginalized communities is of paramount importance.

Successful chronic wound management in low-income communities and minorities is not without challenges. Limited or lack of insurance coverage for advanced therapies, high out of pocket cost, inability to afford home health nursing care and lack of compliance with treatment due to work schedules are just some

obstacles encountered in this patient population. Patient access to inexpensive yet effective OTC wound treatments such as LAVIOR Diabetic Wound Gel helps to overcome these existing healthcare disparities.

Early clinical interventions promoting diabetes management and prevention, while increasing access to cost effective and efficacious treatments will support a reduction in diabetic-related amputations. LAVIOR Pharma has recently initiated the development of a healthcare-focused consortium consisting of local and state government officials, clinicians, and healthcare executives from across the country to address diabetic related disparity issues. The goal of this collaborative community is to help to develop patient education initiatives while promoting effective emerging and novel therapies, such as botanical-based supercharged hydrogel's that elicit multimodal healing actions and are showing promise in addressing the underlying causes of wound chronicity.

Limitations

The sample size represented in this case series makes it difficult to draw sound conclusions about the effects of novel botanical therapeutics. Further head-to-head randomized control, double-blinded trials are in development to reinforce and support the use of comprehensive and cost-effective botanical-based products highlighted here as a solution to overcoming healthcare disparities.

Conclusions

The combined effects of the socioeconomic differences, limited accessibility to proper healthcare, the disparities in levels of care and amputation rates by race and ethnicity cannot be underestimated and should not be ignored. There is a need to ensure health equity in all patients with diabetes. By addressing the significant gaps between patient outcomes in lower-income and minority communities, stakeholders can prevent or delay the incidence and progression of diabetes related complications. The adoption and incorporation of preventative care initiatives and the access to safe, efficacious, and affordable treatments should result in a positive impact on diabetic prevalence, complications, cost, amputation rates, and the quality of life in these marginalized populations.

Conflict Of Interest

Windy Cole, DPM, Imaze Marian Davis, and Sung-Ho Steve Bae, DPM, serve on the Scientific Executive Advisory Board of LAVIOR Pharma Inc., Peter Hurwitz serves on the Board of Directors for LAVIOR Pharma Inc. Chris Norwood has no conflicts to report.

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