

1. INTRODUCTION

Peripheral arterial disease (PAD) in the diabetic foot compromises distal tissue oxygenation, impairing wound healing and increasing amputations risk. Nitric oxide (NO) deficiency is a recognised contributor to endothelial dysfunction, diminished angiogenesis and chronic wound hypoxia in this population. **Exogenous NO delivery** has demonstrated vasodilatory, pro-angiogenic and antimicrobial properties in preclinical and early clinical studies. This case series aimed to evaluate the effect of topical NO therapy on wound healing time in diabetic foot ulcers (DFUs)complicated by PAD and distal tissue hypoxia.

2. METHOD

Five consecutive patients with diabetic foot ulcer and confirmed PAD (ABI < 0,7) , absent distal pulses were treated with topical NO releasing therapy as an adjunct to standard wound care. All patients presented with clinical and transcutaneous oximetry (TcPO2) < 30 mm Hg evidence of distal tissue hypoxia. Ulcer were classified using the SIMBAD score. Wound area reduction, time to complete healing and adverse events were recorded.

3. RESULTS

Mean patient age was 69,6 years, with a mean diabetes duration 30 years. Baseline mean ulcer area was 3.1 cm2 The ulcers were treated according to the standard of care, but showed no satisfactory improvement after 4 weeks. Following adjunctive topical NO therapy, 5 patients achieved complete wound closure within a mean of 36 days. , representing a greater reduction in wound area compared with the expected healing trajectory under standard care alone.. No treatment related adverse event were observed.

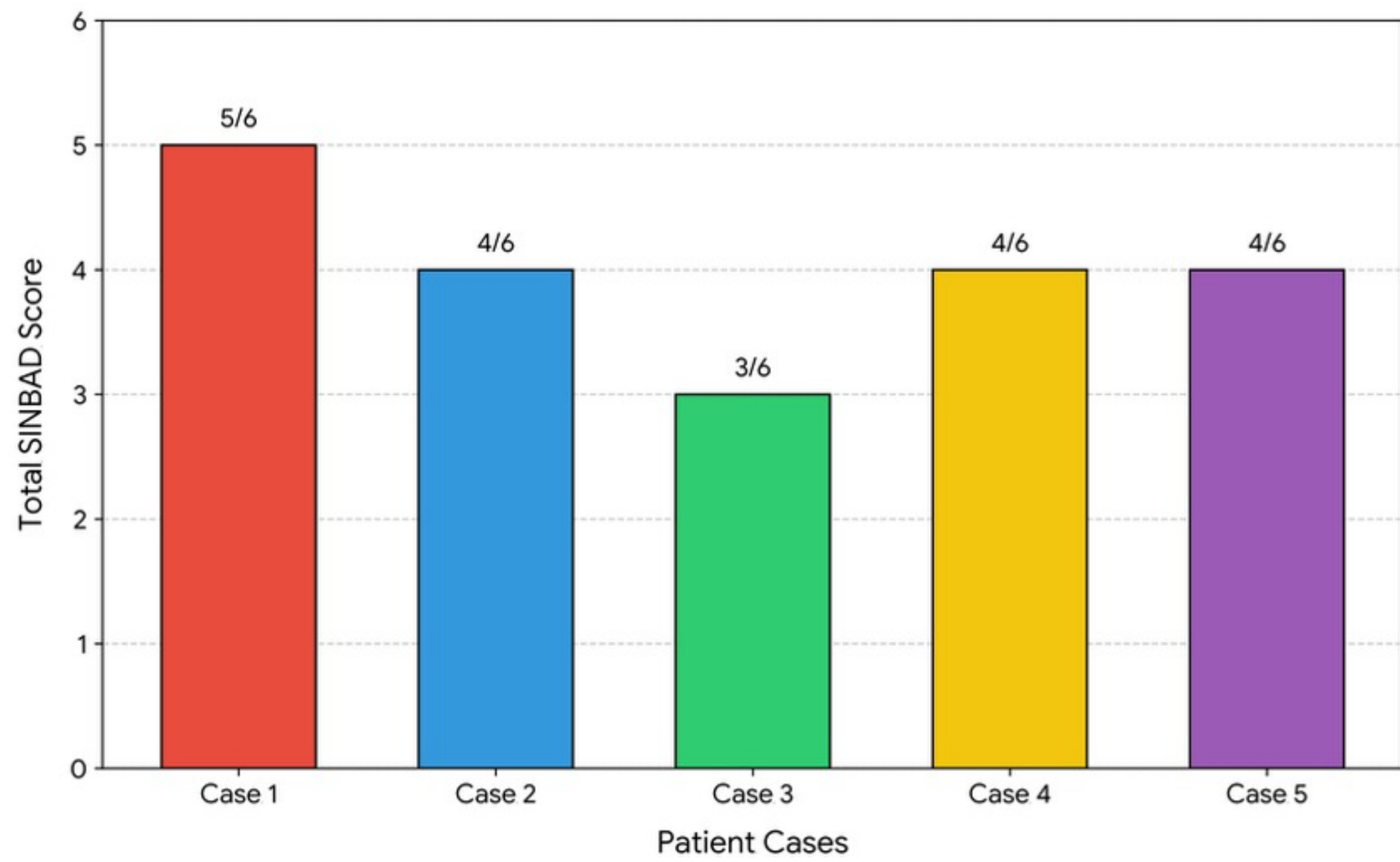
Baseline Characteristics	Patients (N=5)
Mean Age	69.6 years
HTA	4 (80%)
DM	5 (100%)
DL	4 (80%)
Heart Disease	4 (80%)
CKD	3 (60%)
CLI	5 (100%)
HTA: Hypertension, DM: Diabetes Mellitus, DL: Dislypemia, CKD: Chronic Kidney Disease, CLI: Critical Limb Ischaemia	

Ulcer characteristics	Patients (N=5)
Mean ulcer area (cm²)	3,10 ± 0,59
Mean tcPO2 (mmHg)	14,40 ± 10,22
Mean time of healing (days)	39,0 ± 3,16

SINBAD SCORE

Patient	Site (S)	Ischemia (I)	Neuropathy (N)	Bacterial Infection (B)	Area (A)	Depth (D)	Total SINBAD Score
Case 1	Hindfoot (1)	Present (1)	Present (1)	Absent (0)	≥ 1 cm² (1)	Deep (1)	5/6 (S ₁ I ₁ N ₁ B ₀ A ₁ D ₁)
Case 2	Hindfoot (1)	Present (1)	Present (1)	Absent (0)	≥ 1 cm² (1)	Superficial (0)	4/6 (S ₁ I ₁ N ₁ B ₀ A ₁ D ₀)
Case 3	Forefoot (0)	Present (1)	Present (1)	Absent (0)	≥ 1 cm² (1)	Superficial (0)	3/6 (S ₀ I ₁ N ₁ B ₀ A ₁ D ₀)
Case 4	Hindfoot (1)	Present (1)	Present (1)	Absent (0)	≥ 1 cm² (1)	Superficial (0)	4/6 (S ₁ I ₁ N ₁ B ₀ A ₁ D ₀)
Case 5	Hindfoot (1)	Present (1)	Absent (0)	Absent (0)	≥ 1 cm² (1)	Deep (1)	4/6 (S ₁ I ₁ N ₀ B ₀ A ₁ D ₀)

SINBAD SCORE



4 CASE REPORTS



5. CONCLUSION

Topical NO therapy may enhance wound healing in ischaemic diabetic foot ulcers associated with distal tissue hypoxia. By targeting local NO deficiency at the wound site, this approach may represent a complementary therapeutic strategy for PAD-related DFUs.