

## Effects of immunonutrition in patients with chronic wounds: a case series



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**Abstract:** Chronic wounds have been well known to negatively impact on a patients quality of life (QoL). Chronic wounds and illnesses such as diabetes mellitus are chronic inflammatory states and are associated with increased energy expenditure and catabolism of lean body mass. This causes a decline in nutritional status, which in turn prevents wound healing. Studies have demonstrated that incorporating immunonutrition into standard of care can reduce inflammatory biomarkers and increase serum albumin levels in critically ill patients. This study aims to demonstrate the effect of supplementing standard wound care with immunonutrition (NeoMune enteral formula, Thai Otsuka Pharmaceuticals Co. Ltd, Thailand) on the serum albumin and wound healing of patients with chronic wounds. This study had shown a modest increase in our patients' serum albumin levels over the 14 days of consuming the protein-based supplement. A majority of them also showed reduction in wound size in addition to a healthier looking wound base.

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Chronic wounds, be it diabetic foot ulcers (DFU), venous leg ulcers (VLU), pressure ulcers (PU), or non-healing surgical wounds are well known to negatively impact on a patients quality of life (QoL). There is an increased rate of hospitalisations, disability, mortality, treatment cost and a negative psychosocial impact. Chronic hard-to-heal wounds and illnesses such as diabetes mellitus are chronic inflammatory states and associated with increased energy expenditure and catabolism of lean body mass. This causes a decline in ones nutritional status, which in turn prevents wound healing.

The European Pressure Ulcer Advisory Panel (EPUAP), National Pressure Injury Advisory Panel (NPIAP) and Pan Pacific Pressure Injury Alliance (PPPIA) (2019) guidelines for the prevention and treatment of PUs suggests 30–35kcal/kg/day calorie intake and 1.2–1.5g/kg/day protein intake in adults with PUs who are malnourished or at risk of malnutrition. They also recommend high calorie, high protein, arginine, zinc, antioxidant oral supplements to the usual diet if nutritional requirements cannot be achieved by normal dietary intake.

Studies have demonstrated that

incorporating immunonutrition in to standard of care can reduce inflammatory biomarkers and increase serum albumin levels in critically ill patients. (Chuntrasakul et al, 1998; Wischmeyer, 2019)

### Aims

This study aims to demonstrate the effect of supplementing standard wound care with immunonutrition (NeoMune enteral formula, Thai Otsuka Pharmaceuticals Co. Ltd, Thailand) on the serum albumin and wound healing of patients with chronic wounds.

### Methods

#### Study design

Patients were recruited who presented to the Wound Care Unit, Kuala Lumpur Hospital, Malaysia (WCUHKL) as outpatients with chronic wounds (lasting more than three months).

This study conformed to the guidelines set out in the Declaration of Helsinki for Ethical Principles for Medical Research involving Human Subjects and was approved by the Kuala Lumpur Hospital Review Board (local institution board). The study objectives and potential risks involved were explained to the patient in detail.

**Table 1: Albumin levels and wound size while on protein enteral formula**

Patient	Age	Sex	Weight (kg)	Albumin (n 35-55g/l)		Wound size (cm <sup>2</sup> )	
				Day 0	Day 14	Day 0	Day 14
1	71	F	68	37	37	52.0	38.5
2	53	M	71	37	40	18.0	15.2
3	44	F	64	32	37	162.5	143.0
4	51	F	52	27	28	44.0	29.6
5	66	M	51	35	36	6.0	4.5
6	51	M	62	33	30	14.0	10.5
7	82	F	37	26	32	5.0	2.6
8	48	M	70	22	30	1,5	1,0
9	67	M	110	31	31	28.0	20.0
10	70	M	72	33	35	42.0	42.0

### Case 1. Chronic venous ulcer

- A 71-year-old Chinese lady
- Underlying diabetes mellitus
- Presented with a chronic non healing venous leg ulcer that she had for over 13 years.

**Day 0** 8.0 x 6.5cm



**Day 14** 7.0 x 5.5cm



Informed consent and permission to use wound photographs and case details for publication/ research purposes were obtained.

### Methodology

Patients were supplemented with a high energy protein enteral formula; NeoMune (Thai Otsuka Pharmaceuticals Co. Ltd, Thailand). The formula, 60g mixed with 210ml water, was taken twice daily for 14 days. The patients were observed by their family members while taking the formula.

In addition to the enteral formula, patient were given standard of care by the WCUHKL staff that involves wound assessment, wound bed preparation, debridement and application of wound dressings, appropriate to

wound aetiology.

The patients selected were existing patients who have been under the care of the Wound Care Unit HKL. The initial patient selection was random, and proceeded to measurement of serum albumin levels. The patients with lower levels of serum albumin were then selected to be part of this study.

### Data collection

Blood samples were taken from patients on day 0 and day 14 while on enteral formula to measure and compare serum albumin levels. Photographs of the wound and measurements of wound size using a ruler and length and width were also documented during the same time period.

## Case 2. Chronic non-healing postoperative wound

- A 53-year-old Malay gentleman
- Medical history of diabetes mellitus and ischaemic heart disease
- He underwent a wound debridement for an infected wound on the dorsum of his right foot 5 years ago and is still coming for regular dressing changes since then

Day 0 4.5 x 4.0cm



Day 14 4.0 x 3.8cm



## Case 3. Chronic Venous Ulcer

- A 44-year-old Malay lady
- Poorly controlled diabetes mellitus and chronic kidney disease stage 4
- A chronic venous ulcer with a history of multiple superimposed bacterial infections

Day 0 13.0 x 12.5cm



Day 14 13.0cm x 11.0cm



### Potential source of bias

Selection bias will be present in this pilot study as the participants were selected only from the pool of patients with chronic wounds at the Wound Care Unit, Kuala Lumpur Hospital and therefore may not represent the wider population.

### Results

We recruited 10 patients with chronic wounds, that had been present more than three months. There was a modest increase in their serum albumin levels –9% to 36% over the 14 days of consuming the protein-based supplement. The patients' results are shown in

## Case 4. Diabetic foot ulcer

- A 51-year-old Indian lady with underlying
- She had diabetes mellitus and hypertension and a history of Ray amputation right 1st toe (recovered) and developed an abscess on the sole of her foot where she had a diabetic ulcer
- Despite surgical drainage and multiple debridements she now has a chronic non-healing wound

**Day 0** 8.0 x 5.5cm



**Day 14** 8.0 x 3.7cm



## Case 5. Diabetic foot ulcer

- A 66-year-old Malay gentleman, Underlying DM and hypertension.
- Developed Charcot foot with diabetic foot ulcers and has been self medicating with traditional medications and dressings before he presented to our clinic for regular dressing.

**Day 0** 3.0 x 2.0cm



**Day 14** 3.0 x 1.5cm



## Case 6. Diabetic foot ulcer

- 51-year-old Indian gentleman
- A (healed) chronic venous ulcer over the left medial malleolus and a non-healing wound post Ray amputation of 1st toe.

**Day 0** 4.0 x 3.5cm



**Day 14** 3.5 x 3.0cm



## Case 7. Post Ray Amputation of 2nd toe for wet gangrene

- A 82-year-old Chinese lady with uncontrolled diabetes mellitus
- Post Ray amputation (two weeks) he presented with persistent exudate from a wound on the left 2nd toe presented with

**Day 0** 2.5 x 2.0cm



**Day 14** 2.0 x 1.3cm



## Case 8. Diabetic foot ulcer with wet gangrene, refused amputation

- A 48-year-old Indian gentleman with underlying diabetes mellitus
- Presented with an infected diabetic foot ulcer at the base of his 1st toe which had a connection with the 1st web space. He also had wet gangrene of his 4th toe but refused amputation.

**Day 0** 1.5 x 1.0cm



**Day 14** 1.0 x 1.0cm



## Case 9 Diabetic foot ulcer

- A 67-year-old man
- Underlying diabetes mellitus and hypertension had a non-healing DFU on his left 1st toe.

**Day 0** 3.5 x 8.0cm



**Day 14** 2.5 x 8.0cm



**Table 1.** The majority of patients also showed reduction in wound size with total surface area reduction ranging from 12.6% to 48.0% (measured in length and width) in addition to a healthier looking wound base. All patients have tolerated the formula well. No adverse effects were observed during the two weeks study.

**Cases 1-10** show the individual patients.

## Discussion

When managing patients with chronic wounds, one will need to consider other factors contributing to why a patient's wound is non-healing despite standard wound care. Patients with chronic wounds are in a chronic inflammatory state. Most of these patients also have underlying chronic illness which puts them in a pro-inflammatory state. This, in turn, makes them highly catabolic.

Nutrition is often an overlooked component of wound healing. International (EPUAP, NPUAP, PPIIA, 2019) and national wound care guidelines (Ministry of Health, 2014) have highlighted the fact that nutrition does play a vital role in the wound healing process, in particular, high calorie dietary supplementation and protein (EPUAP/NPIAP/ PPIIA, 2019. Gomes, 2018. Posthauer, 2015).

Multiple studies have suggested how important certain micronutrients are in immune modulation and wound healing which includes the study by Alexander, J. W., & Supp, D. M. in 2014 whereby they have concluded that arginine and the omega-3 long chain polyunsaturated fatty acids can have major effects on wound healing and wound infection.

## Conclusion

In addition of standard wound care, patients

with chronic wounds also benefit from supplemental immunonutrition. NeoMune enteral formula has shown a modest increase in our patients' serum albumin over 14 days. The formula was well tolerated from all our patients and there were no reported side effects. Further studies observing the impact on supplemental immunonutrition on ones serum albumin levels and rate of wound healing over a longer period of time should be conducted.

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### Case 10. Chronic venous leg ulcer

- A 70-year-old Indian man with
- Presented with chronic venous insufficiency and a non-healing venous ulcer for more than 10 years.

**Day 0** 6.0 x 7.0cm



**Day 14** 6.0 x 7.0cm

