

Foot care education and platelet derived growth factor on wound healing in foot ulcers among adults

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ABSTRACT

Aim: The aim of the study was to evaluate the combined efficacy of foot care education and recombinant human platelet-derived growth factor (rhPDGF) on the wound healing in foot ulcers among adults with type 2 diabetes (T2D). **Subjects and Methods:** A randomized control trial and a factorial design were used in this study in a 500-bedded private teaching hospital with four major surgical units in 2013. A sample size of 50 adults with T2D was selected in each of the three groups; the combined intervention (foot education and rhPDGF), the medication intervention (rhPDGF), and the control group (CG) (Betadine gel). A standard clinical practice guideline was adopted for the three groups at baseline, 15th day, and 30th day. A modified Bates-Jensen wound assessment tool was used to assess the wound healing. **Results:** Combined efficacy of foot care education and rhPDGF resulted in complete closure of wound with a mean time of 15.91 days compared to the medication intervention (rhPDGF) and the CG in foot ulcers. There was better wound healing characteristics among adults with T2D exposed to the foot care education and rhPDGF compared to the use of rhPDGF and Betadine. **Conclusion:** Combined efficacy of foot care education with PDGF improved the total wound healing and ensured better wound characteristics in lower extremity foot ulcers among adults with T2D.

Key words: Betadine, diabetes, foot care clinical practice guidelines, foot care education, foot ulcer, platelet derived growth factor, wound healing

INTRODUCTION

Adults with type 2 diabetes (T2D) have increased body fat and insulin resistance and has been associated to younger age, high body mass index (BMI), and waist circumference leading to complications such as retinopathy, nephropathy, neuropathy, angiopathy, cerebrovascular, and peripheral vascular disease.^[1] Adults with T2D have a 25% risk of developing foot ulcers and an 85% risk of lower-extremity

amputation.^[2] Foot ulcers are caused by injury due to impaired sensation, vision, ineffective circulation, infections, biochemical changes, and limited joint mobility.^[3] Age, gender (male), depression, alcohol,^[4,5] ethnicity,^[6] education, duration more than 10 years, high BMI, poor glycemic control,^[7] peripheral neuropathy, abnormal structure of foot, peripheral arterial disease, smoking, previous ulcer or

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amputation cause foot problems and impair wound healing.

Wound healing is controlled by growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor, and basic fibroblast growth factor.^[8,9] Standard medications used for foot ulcers delay healing and cause further complications. Recombinant human PDGF (rhPDGF-BB) initiates healing after its release from platelet aggregating.^[10] Becaplermin gel (100 µg/g) is used for treating foot ulcers extending to the subcutaneous tissue with adequate blood supply among adults with T2D.^[11,12] Foot care clinical practice guidelines are used for wound care. There are very few studies on the combined efficacy of foot care education and rhPDGF in improving wound healing among adults with T2D. This study was conducted to assess the efficacy of foot care education and topical rhPDGF in wound healing in Grade 1 and 2 foot ulcers among adults with T2D in India.

SUBJECTS AND METHODS

A randomized control trial was used to assess the combined efficacy of foot care education and PDGF on wound healing in lower extremity foot ulcers among adults with T2D. A factorial design with three clusters, the combined intervention (foot care education and rhPDGF/becaplermin gel), the medication

intervention (use of PDGF/becaplermin gel), and the control group (CG) (use of Betadine gel 1%/povidone-iodine) was used. Wound healing was assessed with modified Bates-Jensen wound assessment tool (WAT) at baseline, 15th day, and 30th day for all the groups using repeated measures.

This study was conducted at a selected 500-bedded private teaching hospital with four major surgical units. At the time of the study, 200 adults with foot ulcers and T2D were registered in the inpatient surgical unit.

The sample size was determined to achieve a small population effect size at power of 90% and delta value of 0.7 at two-sided 0.05 level of significance.^[13] The total sample size was estimated was 50 adults with T2D in the combined intervention group (CIG), 50 adults in the medication intervention group (MIG), and 50 adults in the CG. Cluster randomization was used to select the adults with T2D and lower extremity foot ulcers registered in this diabetes clinic between March and April 2013. This involves randomly assigning clusters of adults with T2D to the three intervention groups through a computer generated numbers across three measurements (baseline, day 15, and day 30) [Figure 1].

Inclusion criteria

Adults aged > 18 years and above diagnosed with T2D with Grade 1 and 2 foot ulcers, presence of dorsal or

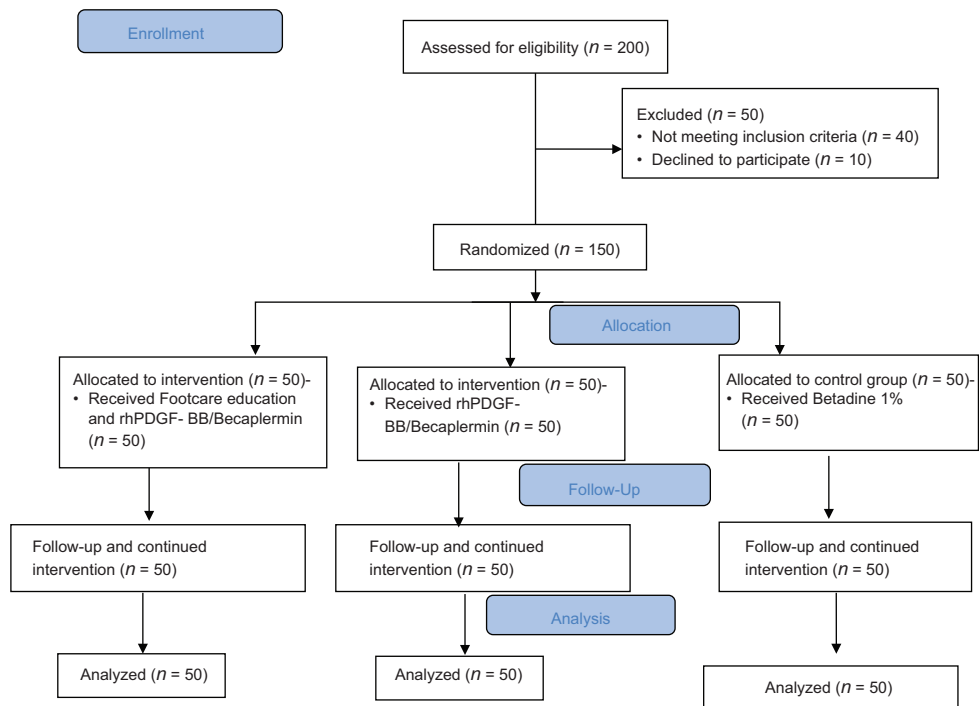


Figure 1: Consort flow diagram

posterior tibial pulse, ankle-brachial blood pressure index >0.70, and those who speak local Kannada and Konkani were included in the sample.

Exclusion criteria

Adults who had an ankle brachial pressure index of >0.71, electrical/chemical/radiation burns, venous sufficiency, uncontrolled infection, cellulitis, osteomyelitis, concomitant diseases (cancer, rheumatic, or vascular collagen disease), chronic renal insufficiency, uncontrolled hyperglycemia, amputation, cognitive, sensory impairments, hypersensitivity to PDGF and Betadine, and those on immunosuppressives were excluded.

The modified Bates–Jensen WAT was used in this study, which has 13 items with five graded options depending on the wound characteristics and total of 65 score.^[14,15] The WAT consist of wound size, depth, edges, undermining, necrotic tissue type, necrotic tissue amount, exudate type, exudate amount, skin color surrounding wound, peripheral tissue edema and induration, granulation tissue, epithelialization. Scores range from 1 to 5, and higher the score, the more severe is the wound status. Wound status continuum is scored from 1 (healthy tissue) to 13 (wound regeneration) up to a score of 60 (wound degeneration). The inter-rater reliability of the WAT was 0.85.^[16] In this study, the reliability test of the WAT was done among 30 adults with foot ulcers using inter-rater reliability. The tool was found to be appropriate, valid, and reliable ($r = 0.88$).

Ethical approval was obtained from the Institutional Hospital Board (FMHC/IG/1/2013). The eligibility criteria were confirmed, and informed consent was obtained from the adults with T2D before enrollment in the study. The study protocol, data collection procedure, and the ethical guidelines were explained to the adults with T2D. These adults were examined and admitted for treatment under the surgical consultant and medical specialist. Preassessment of wound was done at baseline, and post assessment of wound on day 15 and day 30. The three groups (intervention, medication, and control) were provided standard medical care of appropriate antibiotics based on blood culture and sensitivity report, prescribed hypoglycemic agents (insulin/oral form), and wound care protocol (aseptic surgical wound dressing technique). The wound size and depth was measured before selecting the dose of rhPDGF length (cm) × width (cm)/4. Intended dose was 8 µg/cm² ulcer per day with an average body weight of 40 kg.

Adults with T2D in the CIG or Group 1 were delivered foot care education and topical application of rhPDGF. Adults with T2D in the MIG (MIG or Group 2) received topical application of rhPDGF gel. Adults with T2D in the CG or Group 3 were treated with local application of Betadine gel 1% (povidone-iodine). The MIG consisted of twice a day application of rhPDGF/becaplermin gel (0.01%) based a universal wound care protocol. Antibiotics, insulin, and wound care protocols was a standard clinical protocol for 30 days. For the CG, wound cleansing was done twice a day with normal saline and Betadine (1%), a broad spectrum antiseptic, a nongrowth factor resulting from the combination of molecular iodine and polyvinylpyrrolidone.

The CIG received foot care education 3 times during the study. They were provided foot care education on day 2 (direct face-to-face interactive foot care education), on day 10 (reinforcement of foot care education), and on day 20 (motivation to follow foot care education). Topical application of rhPDGF was administered twice daily using wound care clinical practice protocol. Foot care education was delivered by the registered nurse on total nonweight-bearing (use of crutches and wheelchair) and pressure off-loading (use of splints, plaster of Paris casts with plantar ulcers), use of specialized footwear (microcirculation), prevention of infection and complications, and good foot care practices. Ongoing monitoring for signs of blood glucose, infection, pressure off-loading, and nonweight bearing were conducted on a daily basis and maintained in the patient log book.

Multivariate test (General Linear) repeated measures using IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp with last variable as repeated measure was used to evaluate changes in the dependent variables (wound healing at baseline, 15, and 30 days) across the three groups (CIG, MIG, and CG). This test was used to compare between groups by accounting to variation and adjust comparisons between groups for imbalance in important prognostic variables between these groups.^[17]

RESULTS

Demographic and clinical variables

Nearly half percent of the adults with T2D had history of foot ulcers in the CIG (46%) and the CG (46%) compared to those in the MIG (40%) [Table 1]. One-third percent of the adults with T2D had glycated hemoglobin more than 7.6% in the CIG (52%) compared to the MIG (48%) and the CG (50%).

Post-test wound healing status at 15 and 30 days was higher among adults with T2D in the CIG compared

Table 1: Demographic and clinical characteristics among the combined intervention, medication, and control groups (n=150)

Characteristics	Footcare/PDGF (n=50)		PDGF (n=50)		Betadine (n=50)	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Age (years)						
25-45	5	10	15	30	23	46
46-65	30	60	20	40	19	38
>66	15	30	15	30	8	16
Gender						
Male	28	56	34	68	29	58
Female	22	44	16	32	21	42
Education						
Primary	18	36	18	36	15	30
Secondary	17	34	17	34	20	40
Graduate	15	30	15	30	15	30
Employment						
Unemployed	26	52	33	66	24	48
Employed	24	48	17	34	26	52
Marital status						
Married	35	70	37	74	30	60
Single	15	30	13	26	20	40
Income (IRS)						
<10,000	23	46	19	38	29	58
10,001-15,000	17	34	21	42	9	18
>15,001	10	20	10	20	12	24
Duration of DM						
1-5	12	24	8	16	6	12
6-10	19	38	26	52	38	76
>11	19	38	16	32	6	12
History of foot ulcers						
Yes	23	46	20	40	23	46
No	27	54	30	60	27	54
Present foot ulcer (months)						
2	21	42	30	60	22	44
>2	29	58	20	40	28	56
Cause of foot ulcer						
Neuropathy	25	50	25	50	22	44
Arterial	16	32	14	28	20	40
Infection	9	18	11	22	8	16
HbA1c (%)						
<6.5	9	18	6	12	3	6
6.6-7.5	26	52	24	48	25	50
>7.6	15	30	20	40	22	44
BMI (kg/m ²)						
Normal	17	34	17	34	16	32
Mild	15	30	15	30	21	42
Moderate	14	28	14	28	10	20
Severe	4	8	4	8	3	6

PDGF: Platelet-derived growth factor; BMI: Body mass index; DM: Diabetes mellitus; HbA1c: Glycated hemoglobin

to the MIG and CG [Figure 2]. Post-test wound healing status at 15 and 30 days was higher among adults with T2D in the CIG [Figure 3] compared to the MIG at day 15 and 30 [Figure 4] and CG [Figure 5].

Multivariate test

Factor 1 shows the differences among all the wound healing characteristic variables in foot ulcers across

the three measurements (day 1, 15, and 30) among adults with T2D in the CIG, MIG, and CG [Table 2]. There is a significant difference among adults with T2D provided foot care education and rhPDGF in the CIG ($n = 50$), MIG ($n = 50$), and CG ($n = 50$). Among the adults with T2D exposed to foot care education and rhPDGF in the CIG, MIG, and CG ($n = 150$), if compared, between the baseline, 15, and 30 days,

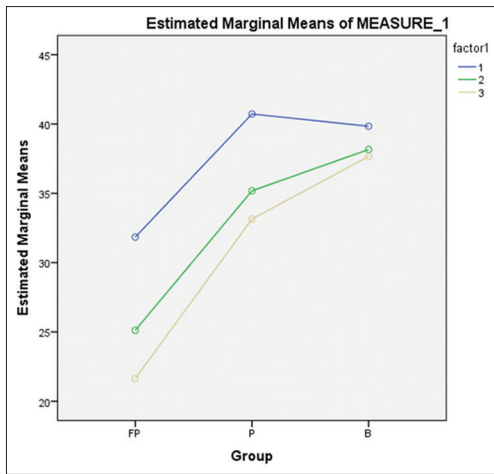


Figure 2: Posttest wound healing status among the three intervention groups across three measurements at baseline, 15 days, and 30 days

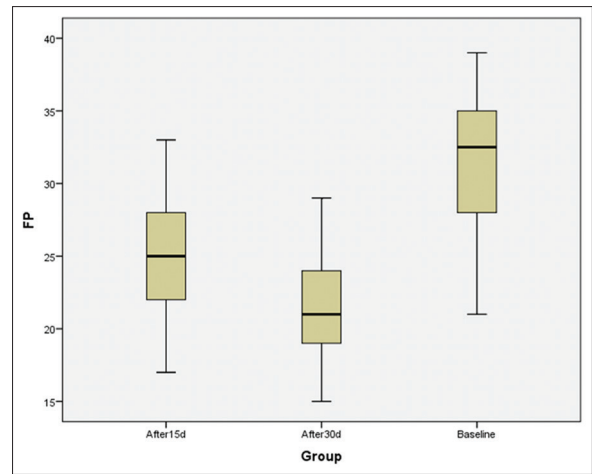


Figure 3: Posttest wound healing within combined intervention group (foot care education and platelet derived growth factor)

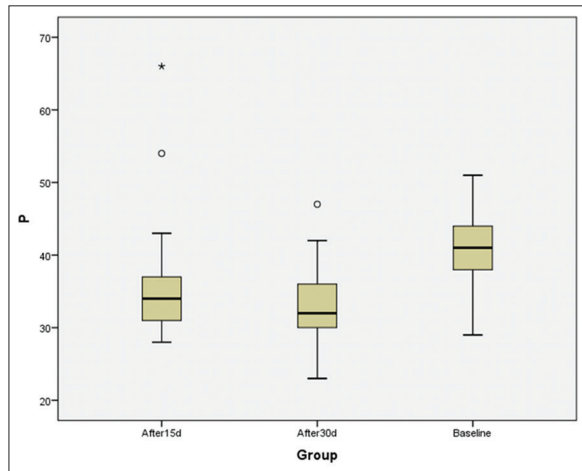


Figure 4: Posttest wound healing status within the medication intervention group (recombinant human platelet-derived growth factor)

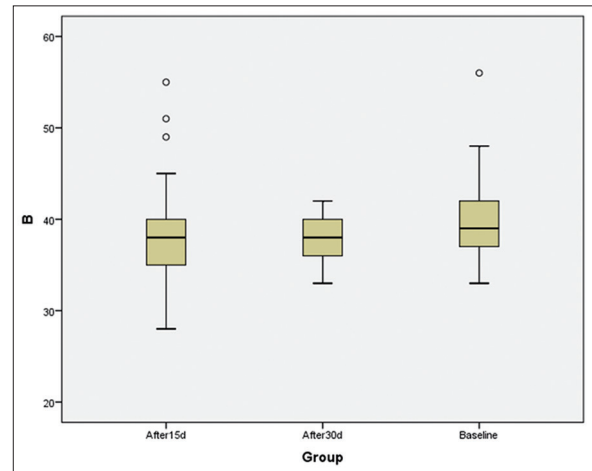


Figure 5: Posttest wound healing status within the control group (Betadine)

there is a significant difference in wound healing. Factor 1* group among the adults with T2D in the CIG, MIG, and CG show significant difference in the effectiveness of foot care education and rhPDGF among adults with T2D in the CIG, compared to those adults in the MIG and CG.

Tests of within-subject effects

Measure 1 shows the transferred variable average [Table 3]. Factor 1 shows the significant difference in foot care education and wound healing in foot ulcers among the CIG, MIG, and CG.

DISCUSSION

In this study, total wound healing status was significantly higher with better clinical outcomes such as short treatment periods and total wound closure among adults in the CIG (foot care education

and PDGF) compared to MIG and CG. Other studies reported the same with fewer complications during rhPDGF treatment.^[18-25] Higher mean scores were found with foot care education.^[26]

In this study, adults with T2D in the CIG had a good reduction of wound characteristics compared to MIG and CG. CIG showed major changes in wound characteristics on day 15 and 30 when compared to CIG and CG. Other studies showed that off-loading with nonremovable devices were effective for ulcer healing.^[27,28]

Total wound healing was higher among adults with T2D in the CIG (foot care education and PDGF) compared to MIG and CG. PDGF was more effective in changing exudates type over foot ulcer compared to Betadine.^[29] Significant differences existed between CIG, MIG, and CG, with PDGF showing reduced exudate amount compared to Betadine. Other studies

Table 2: Multivariate test^a among the combined intervention, medication intervention and control groups

Effect	Value	F	Hypothesis df	Error df	Significance
Factor 1					
Pillai's trace	0.647	133.608 ^b	2.000	146.000	0.000*
Wilks' lambda	0.353	133.608 ^b	2.000	146.000	0.000*
Hotelling's trace	1.830	133.608 ^b	2.000	146.000	0.000*
Roy's largest root	1.830	133.608 ^b	2.000	146.000	0.000*
Factor 1* group					
Pillai's trace	0.316	13.813	4.000	294.000	0.000*
Wilks' lambda	0.684	15.259 ^b	4.000	292.000	0.000*
Hotelling's trace	0.461	16.710	4.000	290.000	0.000*
Roy's largest root	0.459	33.758 ^c	2.000	147.000	0.000*

^aDesign: Intercept + Group. Within Subjects Design: factor1. ^bExact statistic. ^cStatistic is an upper bound on F that yields a lower bound on the significance level.
*P<0.001

Table 3: Tests of Within-Subjects Effects among combined intervention, medication intervention and control groups

Measure: Measure_1					
Source	Type III sum of squares	df	Mean square	F	Significance
Factor 1					
Sphericity assumed	3494.253	2	1747.127	110.958	0.000*
Greenhouse-Geisser	3494.253	1.887	1852.152	110.958	0.000*
Huynh-Feldt	3494.253	1.936	1804.568	110.958	0.000*
Lower-bound	3494.253	1.000	3494.253	110.958	0.000*
Factor 1* group					
Sphericity Assumed	863.133	4	215.783	13.704	0.000*
Greenhouse-Geisser	863.133	3.773	228.755	13.704	0.000*
Huynh-Feldt	863.133	3.873	222.878	13.704	0.000*
Lower-bound	863.133	2.000	431.567	13.704	0.000*
Error (Factor 1)					
Sphericity assumed	4629.280	294	15.746		0.000*
Greenhouse-Geisser	4629.280	277.329	16.692		0.000*
Huynh-Feldt	4629.280	284.642	16.264		0.000*
Lower-bound	4629.280	147.000	31.492		0.000*

*P<0.001

reported the similar findings with use of PDGF.^[11,30,31] There was an improvement in ulcer healing with best foot care practice guidelines^[32,33] and foot care education improved foot care practice.^[34-36] Local effects and systemic absorption was not reported among the adults with T2D in the three groups.

The mechanism of action of rhPDGF in wound-healing and tissue-forming ability in foot ulcers [Figure 6] is by chemotaxis, binding to tyrosine kinase receptors, paracrine action, fibroblast, and smooth muscle cell proliferation and differentiation.^[12,37-39] Angiogenesis, intracellular matrix deposition and extracellular matrix production, immune modulation, and remodeling take place.^[39] This enhances granulation tissue and epithelialization among adults with T2D. This has been seen in other studies.^[12,37-39] Significant wound healing was seen among adults with T2D in the CIG as compared to

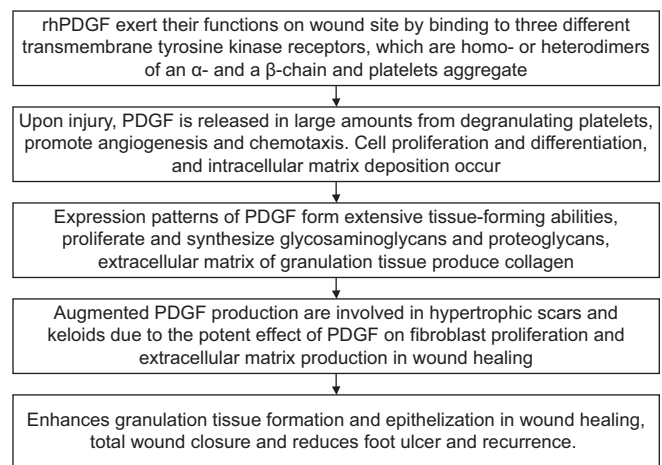


Figure 6: Mechanism of action of recombinant human platelet-derived growth factor on wound healing in foot ulcer among adults with type 2 diabetes

MIG and Betadine, especially for the mean peripheral tissue edema and induration.^[40]

CONCLUSION

In this study, combined foot care education and PDGF in the CIG resulted in complete wound healing of foot ulcers with mean time of 15.4 days compared to MIG and CG among adults with T2D. This study showed that higher wound healing with off-loading or reducing pressure sensitivity and nonweight bearing in foot ulcers was effective. Early screening, initiation of wound care, and monitoring blood glucose ensures improvements in the total wound healing and wound healing characteristics. These best foot care practices are beneficial for reducing complications of foot ulcers. Hence, this study shows that combined foot care education and PDGF was found to be safe and highly effective in healing Grade 1 and 2 foot ulcers and had significantly better healing compared to use of PDGF alone and Betadine.

Limitations of the study are small sample size for comparing best wound care clinical practices and cost-effectiveness among adults with foot ulcers.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Margolis DJ, Malay DS, Hoffstad OJ, Leonard CE, MaCurdy T, de Nava KL, *et al.* Incidence of diabetic foot ulcer and lower extremity amputation among Medicare beneficiaries, 2006 to 2008. In: Data Points Publication Series [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2011.
- Christman AL, Selvin E, Margolis DJ, Lazarus GS, Garza LA. Hemoglobin A1c predicts healing rate in diabetic wounds. *J Invest Dermatol* 2011;131:2121-7.
- Margolis DJ, Malay DS, Hoffstad OJ, Leonard CE, MaCurdy T, Tan Y, *et al.* Economic burden of diabetic foot ulcers and amputations. In: Data Points Publication Series [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2011.
- Baba M, Davis WA, Davis TM. A longitudinal study of foot ulceration and its risk factors in community-based patients with type 2 diabetes: The Fremantle Diabetes Study. *Diabetes Res Clin Pract* 2014;106:42-9.
- Baba M, Duff J, Foley L, Davis WA, Davis TM. A comparison of two methods of foot health education: The Fremantle Diabetes Study Phase II. *Prim Care Diabetes* 2015;9:155-62.
- Bruun C, Guassora AD, Nielsen AB, Siersma V, Holstein PE, de Fine Olivarius N. Motivation, effort and life circumstances as predictors of foot ulcers and amputations in people with Type 2 diabetes mellitus. *Diabet Med* 2014;31:1468-76.
- D'Souza MS, Venkatesaperumal R, Karkada SN, Amirtharaj A. Determinants of glycosylated haemoglobin among adults with type 2 diabetes mellitus. *J Diabetes Metab* 2013;4:2.
- Powers CJ, McLeskey SW, Wellstein A. Fibroblast growth factors, their receptors and signaling. *Endocr Relat Cancer* 2000;7:165-97.
- Trengove NJ, Bielefeldt-Ohmann H, Stacey MC. Mitogenic activity and cytokine levels in non-healing and healing chronic leg ulcers. *Wound Repair Regen* 2000;8:13-25.
- Margolis DJ, Hoffstad O, Nafash J, Leonard CE, Freeman CP, Hennessy S, *et al.* Location, location, location: Geographic clustering of lower-extremity amputation among Medicare beneficiaries with diabetes. *Diabetes Care* 2011;34:2363-7.
- Larijani L, Ranjbar H. Overview of diabetic foot; novel treatments in diabetic foot ulcer. *Daru* 2008;16 Suppl 1:1-6.
- Papanas N, Maltezos E. Becaplermin gel in the treatment of diabetic neuropathic foot ulcers. *Clin Interv Aging* 2008;3:233-40.
- Chan YH. Randomised controlled trials (RCTs) – Sample size: The magic number? *Singapore Med J* 2003;44:172-4.
- Bates-Jensen BM, McNeess P. Toward an intelligent wound assessment system. *Ostomy Wound Manage* 1995;41 7A Suppl: 80S-6S.
- Bates-Jensen BM, Vredevoe DL, Brecht ML. Validity and reliability of the Pressure Sore Status Tool. *Decubitus* 1992;5:20-8.
- Harris C, Bates-Jensen B, Parslow N, Raizman R, Singh M, Ketchen R. Bates-Jensen wound assessment tool: Pictorial guide validation project. *J Wound Ostomy Continence Nurs* 2010;37:253-9.
- Tabachnick BG, Fidell LS. *Using Multivariate Statistics*. Boston, MA: Pearson Education Inc.; 2007.
- Jaiswal SS, Gambhir RP, Agrawal A, Harish S. Efficacy of topical recombinant human platelet derived growth factor on wound healing in patients with chronic diabetic lower limb ulcers. *Indian J Surg* 2010;72:27-31.
- Embil JM, Rose G, Trepman E, Math MC, Duerksen F, Simonsen JN, *et al.* Oral antimicrobial therapy for diabetic foot osteomyelitis. *Foot Ankle Int* 2006;27:771-9.
- Margolis DJ, Bartus C, Hoffstad O, Malay S, Berlin JA. Effectiveness of recombinant human platelet-derived growth factor for the treatment of diabetic neuropathic foot ulcers. *Wound Repair Regen* 2005;13:531-6.
- Mi Q, Rivière B, Clermont G, Steed DL, Vodovotz Y. Agent-based model of inflammation and wound healing: Insights into diabetic foot ulcer pathology and the role of transforming growth factor-beta1. *Wound Repair Regen* 2007;15:671-82.
- Fang RC, Galiano RD. A review of becaplermin gel in the treatment of diabetic neuropathic foot ulcers. *Biologics* 2008;2:1-12.
- Langer A, Rogowski W. Systematic review of economic evaluations of human cell-derived wound care products for the treatment of venous leg and diabetic foot ulcers. *BMC Health Serv Res* 2009;9:115.
- Dumville JC, O'Meara S, Deshpande S, Speak K. Hydrogel dressings for healing diabetic foot ulcers. *Cochrane Database Syst Rev* 2011;1469-493X:CD009101.
- Brownrigg JR, Apelqvist J, Bakker K, Schaper NC, Hinchliffe RJ. Evidence-based management of PAD & the diabetic foot. *Eur J Vasc Endovasc Surg* 2013;45:673-81.
- Nemcová J, Hlinková E. The efficacy of diabetic foot care education. *J Clin Nurs* 2014;23:877-82.
- Lewis J, Lipp A. Pressure-relieving interventions for treating diabetic foot ulcers. *Cochrane Database Syst Rev* 2013;1:CD002302.
- Morona JK, Buckley ES, Jones S, Reddin EA, Merlin TL. Comparison of the clinical effectiveness of different off-loading devices for the treatment of neuropathic foot ulcers in patients with diabetes: A systematic review and meta-analysis. *Diabetes Metab Res Rev* 2013;29:183-93.
- Kiwanuka E, Junker J, Eriksson E. Harnessing growth factors to influence wound healing. *Clin Plast Surg* 2012;39:239-48.
- Landsman A, Agnew P, Parish L, Joseph R, Galiano RD. Diabetic foot ulcers treated with becaplermin and TheraGauze, a moisture-controlling smart dressing: A randomized, multicenter, prospective analysis. *J Am Podiatr Med Assoc* 2010;100:155-60.
- Martí-Carvajal AJ, Gluud C, Nicola S, Simancas-Racines D, Reveiz L, Oliva P, *et al.* Growth factors for treating diabetic foot ulcers. *Cochrane Database Syst Rev* 2015;10:CD008548.
- Prentice D, Ritchie L, Crandall J, Harwood L, McAuslan D, Lawrence-Murphy JA, *et al.* Implementation of a diabetic foot management best practice guideline (BPG) in hemodialysis units.

- CANNT J 2009;19:20-4.
33. Fujiwara Y, Kishida K, Terao M, Takahara M, Matsuhisa M, Funahashi T, *et al.* Beneficial effects of foot care nursing for people with diabetes mellitus: An uncontrolled before and after intervention study. *J Adv Nurs* 2011;67:1952-62.
 34. Vatankhah N, Khamseh ME, Noudeh YJ, Aghili R, Baradaran HR, Haeri NS. The effectiveness of foot care education on people with type 2 diabetes in Tehran, Iran. *Prim Care Diabetes* 2009;3:73-7.
 35. Bus SA. Innovations in plantar pressure and foot temperature measurements in diabetes. *Diabetes Metab Res Rev* 2016;32 Suppl 1:221-6.
 36. Saurabh S, Sarkar S, Selvaraj K, Kar SS, Kumar SG, Roy G. Effectiveness of foot care education among people with type 2 diabetes in rural Puducherry, India. *Indian J Endocrinol Metab* 2014;18:106-10.
 37. Papanas N, Maltezos E. Benefit-risk assessment of bescaplermin in the treatment of diabetic foot ulcers. *Drug Saf* 2010;33:455-61.
 38. Kurd SK, Hoffstad OJ, Bilker WB, Margolis DJ. Evaluation of the use of prognostic information for the care of individuals with venous leg ulcers or diabetic neuropathic foot ulcers. *Wound Repair Regen* 2009;17:318-25.
 39. Barrientos S, Brem H, Stojadinovic O, Tomic-Canic M. Clinical application of growth factors and cytokines in wound healing. *Wound Repair Regen* 2014;22:569-78.
 40. Ndip A, Ebah L, Mbako A. Neuropathic diabetic foot ulcers-evidence-to-practice. *Int J Gen Med* 2012;5:129-34.

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