

A controlled study of the use of autologous platelet gel for the treatment of diabetic foot ulcers

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Dear Editor,

Diabetic foot ulcerations are multifactorial in origin and are known for their slow healing rate and resistance to treatment; complications, such as infection and gangrene, are frequent and amputation is often necessary (1). A better understanding of the biologic processes involved in wound repair and tissue regeneration has led to improvement in wound care. The topical application of recombinant human platelet-derived growth factor gel has been used with some success to treat chronic pressure sores and diabetic foot ulcers (2, 3). Platelet releasate, an autologous product easily manufactured and less expensive, has proved safe and effective in accelerating healing of surgical wounds (4). There is evidence from an observational, retrospective, study that platelet releasate may also be effective for the treatment of diabetic foot ulceration (5). Difficulties in controlling for selection biases and systematic differences in other treatments represent major limitations of observational retrospective studies and, to our knowledge, the effectiveness of autologous platelet gel for the treatment of diabetic foot ulceration has never been tested in a controlled study. We report controlled observations on the safety and effectiveness of autologous platelet gel application in addition to standard care for the treatment of chronic diabetic foot ulcers.

Fourteen diabetic patients (6 males and 8 females) consecutively seen at the diabetic foot clinic were studied. Eligible

for the study were patients with grade II/III ulcers according to Wagner (6), lasting for at least 8 weeks and with no signs of infection at recruitment. Participants gave their informed consent and were randomly assigned to one of two groups: standard care (ST) or standard care plus weekly topic application of autologous platelet gel (PG) for five weeks. As a measure of peripheral vascular disease the ankle-brachial pressure index was measured for all participants and a stratified randomisation procedure was used to avoid unbalance in the ankle/brachial pressure index between the two treatment groups. Participants were seen at weekly intervals, appointments were scheduled on different weekdays for those allocated to platelet gel or standard care. Five weeks observation was set as the end point. The wounds area was estimated by considering the wound like an ellipses whose diameters were the largest and shortest dimensions of the wound (7). Wounds area was measured at the beginning of treatment (initial area) and after 5 weeks (final area); the "reduction rate" was calculated as [(final area (mm²) – initial area (mm²) / initial area (mm²)] (8). Observers were blind with respect to treatment assignment. Continuous variables were compared using non parametric tests, due to major deviation from normal distribution; Fisher exact test and Mc Nemar test were used to compare proportions. The two treatment groups were fairly comparable with respect to age, sex distribution, diabetes duration and glycosylated hemoglobin.

Glucose control was assessed by self monitoring and optimized in both groups during the observation period. All but one patient per group had ankle/brachial pressure index below 0.9. Average wound area was not significantly different in the two treatment groups (273 vs 170 mm²). The average reduction rate after five weeks was significantly larger in patients treated with platelet gel (Table 1). All seven patients assigned to PG improved: two ulcers healed

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TABLE 1

Pertinent clinical data of participants and wounds dimension by treatment group.

	Platelet gel (n=7)	Standard care (n=7)	p
Sex (males)	4 (57.1%)	2 (28.6%)	0.592
Age (years)	61.1±9.4	58.1±7.8	0.528
Diabetes duration (years)	16.3±7.9	19.7±9.9	0.487
Ankle/arm index	0.95 ± 0.18	1.02±0.10	0.349
HbA _{1c} (%)	9.5±1.7	8.8±1.7	0.446
Initial wound area (mm ²)	273±156	170±89	0.156
Wound area at 5 weeks (mm ²)	80±75	162±168	0.269
Initial area – area at five weeks (mm ²)	193±117	8±108	0.010
% reduction rate	71.9±22.5	9.2±67.8	0.039
Complete healing or reduction of at least 50%*	5 (71.4%)	2 (28.6%)	0.286

*OR vs standard care 6.2 (95% CI 0.6 – 63)

completely; for the remaining five the wound area was significantly reduced as compared to baseline - from 273 to 80 mm², $p=0.005$ - In the ST group one ulcer healed, one worsened and in five the wound area remained unchanged (170 vs 162 mm², $p=0.858$). The proportion of complete healing or reduction of 50% or more was 71% and 29% respectively in the platelet gel group and standard care group (OR 6.2; 95% CI 0.6-63). To our knowledge this is the first controlled observation on the effectiveness and safety of autologous platelet gel for the treatment of diabetic foot ulceration. No adverse effects were observed in patients treated with platelet gel, furthermore a significant reduction of the wound area was observed in this group but not in the standard care group in a short period of observation. We used five weeks time as an end point as this is usually too short a time to expect significant improvement of diabetic foot ulcerations with standard care alone. Platelets are a major source of growth factors families (GF): epidermal GF, transforming GF and platelet derived GF, which are all involved in the biologic processes of wound repair and tissue regeneration (2). Platelet releasate is an autologous product, that does not expose patients to iatrogenic

infections or immunologic reactions; its manufacture is rapid, easy and considerably less expensive as compared to the costs of recombinant growth factors products (3). Current evidence of the efficacy of platelet releasate for the treatment of diabetic foot ulcers mainly comes from a large observational study which has retrospectively evaluated the impact of platelet releasate on the outcome of neuropathic diabetic foot ulceration in a period of 32 weeks (5). Unlike controlled studies, observational studies are liable to selection biases and furthermore proper control for systematic differences in other concomitant treatments is not always possible. Our results from a controlled study, although obtained in a small group of patients, strongly support safety and effectiveness of platelet gel in addition to standard care as a means for accelerating the healing process in diabetic foot ulcerations, thus reducing cost of treatment and patient's discomfort. Although not significant the difference in initial wound area would, if anything, lead to a conservative estimate of the effect of platelet gel. Observations on larger samples, as well as data on hard end points such as complete healing and prevention of amputation are needed before the effectiveness of autologous platelet gel is unequivocally established.

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