[12]. The adjunctive therapies target different stages of the healing process have been proposed because of the suboptimal healing rates often observed in practice, epidermal growth factor (EGF) stimulates the proliferation of fibroblasts, keratinocytes and vascular endothelial cells, which contribute to its scar tissue formation property [13]. Its action is launched by the interaction with specific receptors located on the cellular membrane, expressed on most human cell types including those which play critical roles for wound repair such as fibroblasts, endothelial cells and keratinocytes. The EGF-induced mitogenic, motogenic, and cyto-protective actions are instrumental for healing events that may be summarized as: (a) stimulation of productive cells migration toward the injured area, (b) stimulation of granulation tissue outgrowth–including extracellular matrix accumulation, maturation and de novo angiogenesis, (c) stimulation of wound contraction by myofibroblast

Statistical analyses

The Statistical analyses of the results were performed using SPSS version 19.0 for windows (IBM-SPSS, Inc, Armonk, NY), Exploratory analysis for each variable (main, secondary and control) were performed to evaluate their global behavior and evaluate the hypothesis applying proper statistical tests in the assessment stage. With the quantitative variables the measurements of the central tendency and dispersion were estimated.

For all variables (quantitative and qualitative), the logistic regression model was adjusted to study the influence of each variables and their interactions on the response to the treatment and occurrence of serious adverse events. The hypothesis that there is a difference between independent qualitative variable and dependent quantitative was established by calculation of the Odds ratio(OR), with a probability beta a priori for $p<0.05$.

Ethics

The protocol was approved by the institutional review board (IRBJLT 021/2008) of the Clinic Surgical Hospital "José R. Lopez Tabrane" in Matanzas, Cuba and the IRB of the Matanzas University of Medical Sciences, Matanzas City, Cuba. Patients were fully informed about the aim of the study and they were told that their participation was optional. Written informed consent was obtained from each participant.

Results

Basic characteristics

Sixty-two neuropathic fore foot ulceration in Sixty-four diabetic subjects who met the eligibility criteria (inclusion and exclusion) were included in this study (Table 1). The mean age of the participants was 54.6 ± 6.5 years in the treated and 54.7 ± 6.8 years in controls. In both groups predominate the female, and in the ethnicity the mestizo group, and for the clinical point of view the type 2 of diabetes with a time of evolution of 15.8 ± 3.5 years in group A and 14.9 ± 4.1 years in group B, according to the gradation by Wagner the grade 2 is the most prevalent. According to this finding is possible to establish that the Groups were comparable according to demographic and baseline characteristics.

Variables			**Group A Treatment (n=35)**	**Group B Control (n=27)**
Age (median and standard deviation)			54.6 ± 6.5 years	54.7 ± 6.8 years
Gender	Female		N=19 (54.3%)	n=15 (55,5%)
	Male		n=16 (45.7%)	n=12 (44,5%)
	Yellow		n=2 (5.7%)	n=1 (3.7%)
Ethnicity	White		n=10 (28.6%)	n=8 (29.6%)
	Mestizo		n=17 (48.6%)	n=13 (48.1%)
	African descent	n=6 (17.1%)	n=5 (18.6%)	
Type of DM	Type 1		n=2 (5.7%)	n=1 (3.7%)
	Type 2		n= 33 (94.3%)	n=26 (96.3%)
Time of evolution of the diabetes mellitus (years)			Group A T Time of ev ype 1	

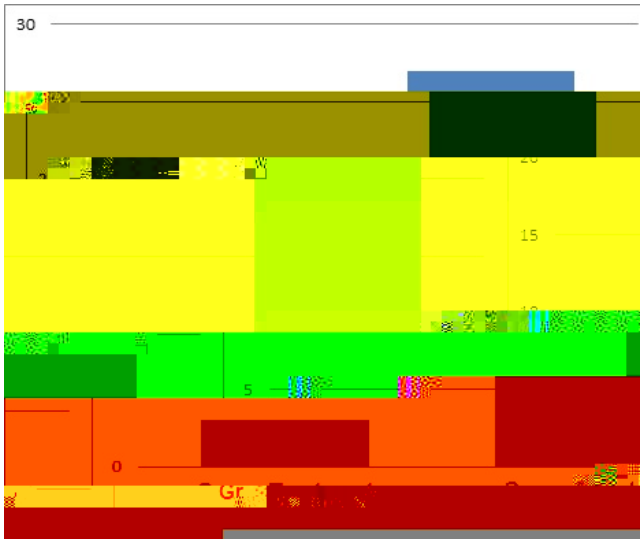

Figure 2: Recidivism of Neuropathic forefoot ulceration after z-platy of Achilles combined or not with intralesional human recombinant Epidermal Growth Factor. Matanzas, 2009-2016.

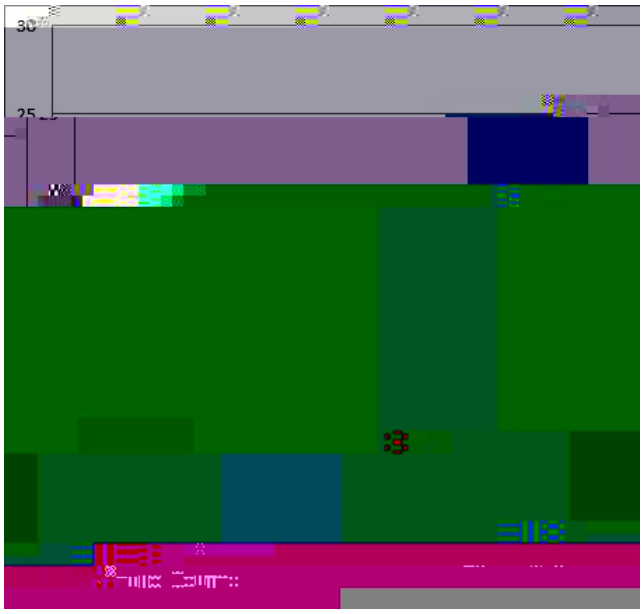

Figure 3: New lessons after z-platy of Achilles combined or not with intralesional human recombinant Epidermal Growth Factor. Matanzas. 2009-2016.

Assessment of the safety results

Safety was monitored daily during treatment and during 6 months after the closure of the study. The most frequent complications (Table 2) in the treatment group was Local pain 5.7% (n=3), local infection of the surgical incision 2.8% (n=1) and shivering 2.8% (n=1). The control group had 14.8% (n=4) of local pain, 7.4% (n=2) of Local infections of the surgical incision and 3.7% (n=1) of border necrosis. The multivariate analysis show risk factors unresolved osteomyelitis (OR, 2.6) and protective factors, gender female (-0,972), insulin therapy (-0,876) and older patient (-0,542). There were not minor or major amputations reported as an outcome of treatment.

Complications	Group A Treatment		Group B Control	
	No	%	No	%
Local infections of the surgical incision	1	2.80%	2	7.40%
Local pain	3	5.70%	4	14.80%
Shivering	1	2.80%	-	-
Border necrosis	-	-	1	3.70%

wounds exhibit other distinctive elements among the variety of chronic wounds [27,28]. HXe Ẑrst to mention is the, which has been shown to correlate with the level of glycated haemoglobin, suggesting a direct relationship between glycaemia and the wound proteolytic proẐle. Locally injected hrEGF could stimulate the survival and repair of cutaneous and adjacent soн tissues in a context of circulatory neurogenic deterioration [14]. Such knowledge prompted the hypothesis that injecting hrEGF deep into the wound base and walls would allow for greater pharmacodynamic response in terms of granulation tissue growth and wound closure. In further studies, single or repeated hrEGF systemic or local injections produced clear-cut cytoprotective and proliferative responses, suggesting an intrinsic ability of hrEGF at supraphysiological concentrations to trigger biological events necessary for tissue repair [29]. HXe Ẑrst clinical evidences on hrEGF inẐltrative treatment involved diabetic foot ulcers and amputation residual bases. All the lesions were chronic, complex

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