

# The use of recombinant epidermal growth factor in primary health assistance

## Abstract

**Introduction:** The high morbidity for diabetic foot and its long hospitalization could be solved with the same quality thanks to the level achieved by the Cuban National Health System as well as the proved efficacy of Recombinant Epidermal Growth Factor (EFG) (Heberprot-P) and the training of the personnel who work in the welfare health areas.

**Objective:** To Evaluate the diabetic foot treatment using Heberprot-P in the primary health assistance in Cuba.

**Patients & method:** Our universe was composed by 1551 patients assisted consecutively in four welfare health areas. All of them received 15 to 24 intralesional injections of 75 micrograms each, three times a week. They were under went to surgical operations when required under nerve trunk anesthesia on the leg. An informed consent was signed previously. The variables analyzed were: Age, sex, Wagner classification, doses administered, surgical procedures and final result.

**Results:** In our series 407 debridement were carried out (26%), 77 toe amputations (4, 96 %) and 3 metatarsal amputations (0, 19%). No major amputations were carried out. A satisfactory granulation was achieved in all patients. The adverse reactions were 17 (1, 1%) all of them were mild. Nobody quit the treatment and there were no mortality.

**Conclusions:** Among our patients the treatment were 100% effective the rate of amputations were low. The adverse events were few and mild.

**Keywords:** wagner classification, intralesional injection, primary health assistance, heberprot-P

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## Introduction

Diabetic foot ulcers (DFU) represent a health problem a world wide.<sup>1-3</sup> In some countries its treatment is very expensive and not all the citizens can access to medical centers.<sup>4,5</sup> Since the advent of the epidermal growth factor Heberprot-P a new paradigm has become in DFU treatment. This illness produces a high mortality, morbidity and disability.<sup>6,7</sup>

The patients were referred from primary health physicians. Those who require surgical operations sign an informed consent. The surgical procedures were carried out under nerve trunk anesthesia, according with the site of ulcer. The intraregional injection was performed by personnel trained in the University Hospital three times a week. The patients were evaluated by our doctors weekly through computerized photo program. The adverse reactions were very few. We didn't have quit of the treatment. No major amputations were necessary.

## Patients and method

A longitudinal, retrospective study was carried out including all the patients underwent Heberprot-P Therapy from four primary health areas, assisted consecutively within July 2014 and September 2016. The universe was composed by 1551 diabetic patients suffering gangrene or sole ulcer. All of them were included among stage III or IV of Wagner scale.

They were injected intralesional three times a week with 75 micrograms of Heberprot-p, and evaluated weekly by one specialist

of our group who performs the surgical procedures. The operations were carried out in ambulatory system in one operation room at the university hospital.

**Inclusion criterion:** Patients who didn't have contraindication to use the medicine. Gangrene of toes or sole ulcers. Sign the informed consent. **Exclusion criterion:** Absolute contraindication to use the product. When major amputation was mandatory. Refusal the treatment. The index of granulation and epithelization was evaluated by computerized photo program created to this purpose.

## Results

In Table 1 we found predominance of females with relationship 55% to 45% respect the males. According of age groups among males the main group was 51 to 60 years old while in females was 61 to 70 as other authors said.<sup>8</sup> According with Wagner scale predominated the neuropathic/infected foot among younger patients, while the olders had mainly ischemic injuries, produced by macroangiopathy as well as microangiopathy.

Above 61 years old were seen 388 ulcers Wagner scale IV which represent 86%. Below 70 predominated the Wagner III with 1021 patients, they were 93% like appears in Table 2 we achieved good results in ischemic ulcers as Montequin and cols reported.<sup>9,10</sup> Majority receive about 15 dosages of the drug like appears in Table 3.

The surgical procedures can be observed in Table 4 among them predominate the debridements 83, 57% we have to point that we

consider surgical operations such required anesthesia and we didn't include minor procedures. We gave priority to the minimal procedures as sun as possible to resect all the infected areas before the treatment, as appear in the revised literature.<sup>11-13</sup>

All the surgical procedures were performed after the sign the model about informed consent established in our hospital.<sup>14</sup> Almost the third of patients required a minor operation they were enough radical according with the injury and so conservative to archive a functional foot. See Table 4. The end stage of the patients can be seen in Table 5 the results of epithelization and granulation were highly satisfactory.

**Table 1** Patients according age and sex

Age groups	Male		Female		Totals	
	N°	%	N°	%	N°	%
To 50years	158	22,64	172	20,22	330	22,64
51 a 60	189	27,07	233	27,26	422	27,21
61 a70	183	26,22	241	28,22	424	23,33
71 a 80	123	17,62	147	17,26	270	17,41
81 & more	45	6,45	60	7,04	105	6,77
Totals	698	100	853	100	1551	100

Source: Data base

**Table 2** Distribution about Wagner scale

Age groups	Wagner III		Wagner IV		Totals	
	N°	%	N°	%	N°	%
To 50years	301	91,21	29	8,79	330	21,26
51 a 60	387	91,71	35	8,29	422	27,17
61 a70	333	78,54	91	21,46	424	27,31
71 a 80	72	78,54	198	73,33	270	17,37
81 & more	6	5,71	99	94,29	105	6,89
Totals	1099	71	452	29	1551	100

Source: Data base

**Table 3** Used doses for patient

Used doses for patient		
Doses injected	Number	Percent
To 15 doses	739	47,65
16 a 19	305	19,66
20 a 24	507	32,69
Totals	1551	100

Source: Data base

**Table 4** Surgical procedures carried out

Surgical procedures carried out		
Type	Number	Percent
Debridement	407	83,57
Amputation one toe	50	10,27
Amputation two toes	27	5,54
Metatarsal amputation	3	0,62
Totals	487	100

Source: Data base

**Table 5** Results at the end of study

Final evaluation	Number	Percent
Partial epithelization	558	35,98
Complete epithelization	993	64,02
Complete granulation	1551	100

Source: Data base

## Discussion

In patients with gangrene we use to demarcate the affected area by infiltration of the drug around it, to take advantage of angiogenic effect of the product after the delimitation, had achieved, the surgical procedure was carried out to remove all the necrotic area.

All patients remain with useful foot for marching, those individuals that required an orthesic device were ordered to make a personalized shoe. Some of them required tenotomies or single arthrodesis to achieve an optimal feet to avoid recidivism similar to Lewis recommend.<sup>8</sup>

Photometric evaluation was performed weekly by one of our specialist and recorded in a data base, to evaluate exactly the progress. About one third of our patients required a minor amputation but major wasn't needed. An evaluation of amputation risk was performed in each patient as recommended Khan and others.<sup>15-16</sup>

All comorbidities were evaluated by a multidisciplinary team like appears in some bibliographies.<sup>17-19</sup> In our opinion the extension of diabetic foot treatment to primary health care is highly satisfactory if the personnel is previously educated and checked closely.

## Wagner scale

- Grade 0 Risk foot. Thick callus. Prominent metatarsal bones heads, claw toes, bone deformities.
- Grade I. Superficial ulcer, whole destruction of the skin, superficial cellulitis.
- Grade II. Uncomplicated deep ulcer which affects skin, tendons, fat, ligaments, without osteomyelitis.
- Grade III. Complicated deep ulcer, extensive area, discharge puss, osteomyelitis and abscess.
- Grade IV. Limited gangrene, partial necrosis of the foot.
- Grade V. Extensive gangrene all the foot affected and systemical effects.<sup>20-22</sup>

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None.

## Conflict of interest

The author declares no conflict of interest.

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