En las biopsias iniciales se describen elementos característicos del proceso de cicatrización de la piel dañada. En las muestras de la última cura se describe una arquitectura epidérmica y dérmica normal. No se evidenció presencia de metaplasia. Un resultado similar fue reportado en un modelo animal en biopsias de lesiones tratadas con EGF (1).

REFERENCIAS

1. BROWN, G. L.; L. CURTSINGER III *et al.* (1986) *J. Exp. Med., 163:1319-1324*
2. GONZÁLEZ, T.; L. C PÉREZ *et al.* (1993) *Biotecnología Aplicada, 10:8*
3. VÁZQUEZ, J.; M. FREYRE *et al.* (1990) *Biotecnología Aplicada, 7:42-51*

ORAL HUMAN RECOMBINANT EPIDERMAL GROWTH FACTOR IN PATIENTS WITH DUODENAL ULCER

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INTRODUCTION

Peptic gastroduondenal ulcer is a recurrent disease with economic repercussion as it mainly affects adults during their productive years. The role of Epidermal Growth Factor (EGF) in the physiology of regeneration and protection of the digestive tract has been thoroughly studied. Oral EGF accelerates healing of gastroduodenal ulcers in animals (1, 2). However, there are no reports showing the effect of oral EGF in humans.

METHODOLOGY

An open, randomized, positively controlled trial was conducted. Inclusion criteria were: endoscopic diagnosis of duodenal ulcer, major diameter between 0.5 and 1.5 cm, age between 18 and 75 years, and written consent to participate. Patients with H_2 blockers during the previous 2 weeks were excluded. Seventy five patients were randomly distributed in three groups to receive oral human recombinant EGF in 1% carboxymethyl cellulose at two different doses (450 mg or 600 mg/day), or cimetidine. Treatment was administered up to 6 weeks. The most important assessment criteria was the proportion of patients healed after 2, 4 and 6 weeks of treatment determined by endoscopy. Biopsies were taken from 30 patients at each evaluation. One patient, erroneously included because of actually having a pre-pyloric ulcer, was withdrawn.

RESULTS

Distribution of the patients characteristics in trial groups was homogeneous. More than 50% of the patients were between 35 and 54 years old, and a predo-

Group	Patients with healed ulcer						Failures		Total
	Week 2		Week 4		Week 6				
	No.	%	No.	%	No.	%	No.	%	
A	5	20.8	13	54.1	19	79.1	5	20.8	24
B	3	13.0*	10	43.4*	17	73.9	6	26.0	23
C	11	40.7	21	77.7	25	92.5	2	7.4	27
Total	19	25.6	44	59.4	62	82.4	13	17.5	74

*Statistically significant difference with group C ($p = 0.03$). No. = Number

minance of white males was observed. Similar clinical improvement ratios were obtained in the three groups after 6 weeks of treatment.

Healing ratios compared by χ^2 or Fishers exact tests showed a significant difference between group B and group C during the first 4 weeks of treatment, but differences after 6 weeks were not significant (table). Adverse reactions were not detected in any of the patients. Abnormal histological modifications were not found in any of the biopsies performed.

DISCUSSION

The healing percent obtained with EGF was within the range reported for effective medications in the treatment of peptic ulcersm, 70 to 90% after 6 to 8 weeks of treatment (3). The rate of healed patients in the groups treated with EGF increased with time, lowering the difference as compared to cimetidine group. This may indicate that EGF has a long-term healing effect. A similar finding has been reported by Olsen *et al* (1). Higher doses of EGF or a higher concentration of carboxymethyl cellulose could be more effective. Itoh *et al* (4) proved effectiveness of EGF combined with 2% hydroxypropyl cellulose, as compared to EGF alone. To our knowledge, this is the first report on the oral use of EGF in humans.

REFERENCES

1. OLSEN, P. S.; S. S POULSEN *et al.*, (1986) *Gastroenterology* **90**:911-917.
2. KONTUREK, S. J.; A DEMBINSKI,. *et al.*,(1988) *Gastroenterolgy* **94**:1300-1307.
3. HIXSON, L. J.; C. L KELLEY; W. N JONES *et al.*, (1992) *Arch Interm. Med.***152**:726-732.
4. ITOH, M.; S. IMAI, (1992) *et al., J. Clin. Gastroenterol.* **14 (Suppl 1)**: S127-130.

APLICACION TOPICA DE FACTOR DE CRECIMIENTO EPIDERMICO HUMANO RECOMBINANTE EN ULCERAS POST-FLEBITICAS

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INTRODUCCION

El Factor de Crecimiento Epidérmico (EGF) está involucrado en la proliferación celular. Se ha reportado un tiempo de cicatrización más corto en pacientes portadores de úlceras cutáneas de diferentes etiologías, al ser tratados con EGF tópico (1, 2). En el presente estudio se evalúa el efecto del EGF, sólo o combinado con sulfadiacina de plata, en la cicatrización de úlceras postflebíticas.

METODOLOGIA

Se realizó un ensayo clínico controlado, aleatorizado, a doble ciegas. Se incluyeron 60 pacientes con diagnóstico de úlcera post-flebítica de más de 3 cm de diámetro y que dieron su consentimiento. Los pacientes con antecedentes de alergia a la sulfadiacina, diabetes mellitus o embarazadas fueron excluidos. Se diseñaron tres grupos de tratamiento tópico: crema de EGF con sulfadiacina de plata (EGF + SDP), crema de EGF (EGF) y crema de sulfadiacina de planta (SDP). Se utilizó EGF humano recombinante a 10 μg/g y SDP al 1%. Las curas se realizaron tres veces por semana de manera ambulatoria, hasta 6 semanas. La evaluación se consideró BUENA si la lesión cicatrizó en más del 50%, REGULAR si cicatrizó en menos del 50% y MALA si no cicatrizó, empeoró o el paciente abandonó el estudio. Se calculó el área de la úlcera antes y a las 2, 4 y 6 semanas de tratamiento, pesando recortes de papel con el calcado de las lesiones, y transformando los valores a área (1 cm^2 = 8,6 mg).

RESULTADOS

La distribución de pacientes por grupo, en cuanto a edad, sexo y área inicial de las úlceras, fue homogénea. Un paciente abandonó.

La tabla muestra el número de pacientes (y porciento) en cada evaluación por grupos. El análisis estadístico no reveló diferencias, χ^2 = 1.667, p = 0,4346.