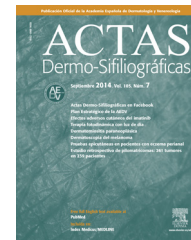




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ORIGINAL ARTICLE

Electrochemotherapy in the Treatment of Melanoma Skin Metastases: A Report on 31 Cases[☆]



J.M. Mir-Bonafé,^{a,*} A. Vilalta,^a I. Alarcón,^a C. Carrera,^a S. Puig,^a J. Malveyh,^a
R. Rull,^b A. Bennàsar^a

^a Servicio de Dermatología, Unidad de Melanoma, Hospital Clínic, Universidad de Barcelona, Barcelona, Spain

^b Servicio de Cirugía General, Hospital Clínic, Universidad de Barcelona, Barcelona, Spain

Received 21 June 2014; accepted 18 October 2014

Available online 1 April 2015

KEYWORDS

Electrochemotherapy;
Metastasis;
Melanoma;
Bleomycin

Abstract

Introduction and objectives: Electrochemotherapy is indicated for the treatment of unresectable cutaneous and subcutaneous tumors. The technique involves the synergistic use of electroporation of cell membranes to increase the cytotoxicity of anticancer drugs delivered to the tumor cells. The aim of this study was to analyze the clinical effectiveness and safety of electrochemotherapy in the treatment of unresectable locoregional recurrent or metastatic melanomas.

Material and methods: We studied 31 patients treated between January 2007 and December 2012. The European Standard Operating Procedures of Electrochemotherapy (ESOPE) were applied in all cases. Treatment response was analyzed as overall patient response (mean response based on results for all lesions treated in a given patient).

Results: Response was classified as partial in 49% of patients and complete in 23%. At 1 year, the level of response achieved had been maintained in 17 patients. Disease progression was observed in 28% of the series. Immediate local complications (pain, swelling, erythema) were mild and resolved within 48 hours in most cases. Eight patients developed subsequent local complications, such as ulcers and secondary infections associated with necrosis of the lesions. These complications were brought under control with topical treatments.

Conclusions: Electrochemotherapy is a very effective, safe, and efficient treatment for advanced locoregional disease in patients with unresectable melanoma lesions.

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[☆] Please cite this article as: Mir-Bonafé J, Vilalta A, Alarcón I, Carrera C, Puig S, Malveyh J, et al. Electroquimioterapia en metástasis cutáneas de melanoma: Experiencia en 31 casos. Actas Dermosifiliogr. 2015;106:285–291.

* Corresponding author.

E-mail address: jmirbonafe@gmail.com (J.M. Mir-Bonafé).

PALABRAS CLAVE

Electroquimioterapia;
Metástasis;
Melanoma;
Bleomicina

Electroquimioterapia en metástasis cutáneas de melanoma: Experiencia en 31 casos**Resumen**

Introducción y objetivos: La electroquimioterapia (EQT) es una técnica terapéutica indicada en tumores cutáneos y subcutáneos no resecables quirúrgicamente. La EQT se fundamenta en la acción sinérgica de un fármaco antineoplásico junto con la electroporación de las membranas celulares para aumentar su citotoxicidad. El objetivo del presente estudio es objetivar la eficacia clínica, así como el perfil de seguridad de la EQT como tratamiento en pacientes con recidivas o metástasis cutáneas locorreionales de melanoma no abordables quirúrgicamente.

Material y métodos: Entre enero de 2007 y diciembre de 2012 se incluyeron 31 pacientes. Todos los tratamientos se realizaron siguiendo las guías de consenso *European Standard Operating Procedures of Electrochemotherapy* (ESOPE). La respuesta se calculó por paciente, obteniendo la media del conjunto de las lesiones.

Resultados: En el 49% de los casos se demostró una respuesta parcial y en el 23% se obtuvo una respuesta completa. Diecisiete pacientes mantuvieron la respuesta al año de seguimiento. En el 28% existió progresión de la enfermedad. Las complicaciones locales inmediatas (dolor, edema, eritema) fueron leves, y se resolvieron en las primeras 48 h en la mayoría de los casos. Ocho pacientes presentaron complicaciones locales posteriores, como ulceración y sobreinfección, secundarias a la necrosis de las lesiones y fueron controladas con tratamientos tópicos.

Conclusiones: La EQT presenta un excelente perfil de eficacia, eficiencia y seguridad, siendo de gran utilidad en el control de la enfermedad locorreional avanzada en el melanoma en lesiones no resecables quirúrgicamente.

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Introduction

Electrochemotherapy (ECT) is a novel therapeutic option indicated for the treatment of unresectable cutaneous and subcutaneous tumors when, due to the site or extent of the disease, the initial treatment fails or no other treatment options are available.¹ This technique combines the electroporation of cell membranes with the administration of anticancer drugs for the treatment and locoregional control of solid tumors. Since its introduction in the early 1980s, electroporation has been used both in vitro and in vivo to deliver water-soluble substances such as nucleotides, peptides, and drugs to the cell interior.² Electroporation is a physical-chemical technique in which the cell membrane is subjected to a pulsed, high-intensity electrical field, which creates transmembrane channels, or pores, through which water-soluble molecules that under normal conditions are non-permeant can be delivered into the cell cytosol.³ This temporary, reversible permeabilization of the cell membrane makes it possible to achieve a higher intracellular drug concentration. In the case of cisplatin and bleomycin, electroporation increases cytotoxicity by a factor of 100 and 1000, respectively.⁴

In 2006, the European Standard Operating Procedures of Electrochemotherapy (ESOPE)⁵ project studied the efficacy, toxicity, dose, and mechanism of action of ECT and established standard procedures for the technique. The ESOPE study was conducted at 4 European cancer centers with patients who had cutaneous metastases of various etiologies. The local tumor control rate for ECT was 88% with intravenous bleomycin, 73% with intratumoral bleomycin, and 75% with intratumoral cisplatin.

The aims of this study were to analyze the response at 1 month and 1 year as well as the possible complications related to ECT as locoregional therapy in patients with unresectable recurrences or cutaneous metastases of melanoma.

Material and Methods

This was an observational study of a case series in which data were collected both prospectively and retrospectively between January 2007 and December 2012 at the Department of Dermatology of Hospital Clínic (Universitat de Barcelona). Patients were included in the study if they had unresectable recurrences or cutaneous metastases of melanoma or if no alternative treatment was available after the failure of previous therapies. Given the critical situation of these patients, no strict exclusion criteria were applied, with the exception of allergy to bleomycin or its derivatives. Patients who had previously received local or systemic therapies were not excluded. All treatments were carried out in accordance with the ESOPE consensus guidelines.⁵

The Cliniporator electroporation device (IGEA, Italy) was used. The electrodes used to treat cutaneous and subcutaneous lesions consisted of 6 needles of variable length (between 1 and 3 cm). Five of the electrode needles were arranged in the shape of a pentagon, with the sixth needle occupying its geometric center. The intensity and amplitude of the electric pulses were kept higher than 400 V/cm² and 1 A, respectively. Pulse length was 100 ms. Amplitude, frequency, and length of pulses were managed automatically using the console of the device, which controlled the power unit in accordance with the ESOPE guidelines. In each application, 8 electric pulses with the aforementioned characteristics and a frequency of 5000 Hz were produced.

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