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Photodynamic therapy for multiple basal cell carcinomas

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Abstract

In this work we describe the use of two chlorin e-6 based photosensitizers (Radachlorin® and Photolon®) to treat multiple basal cell carcinomas. Photodynamic therapy method was applied for two patients with 31 superficial basal cell carcinomas. The presented data show a positive response with an overall rate of 100% complete regression in all treated lesions, and acceptable aesthetic results without serious side-effects or complications during or after treatments. Therefore the photodynamic therapy method with chlorin derivatives appears to be good promising option for the treatment of multiple basal cell carcinomas.

Keywords: photodynamic therapy, photosensitizer, Radachlorin®, Photolon®, carcinomas.

Terapia fotodinámica de carcinomas basocelulares múltiples

Resumen

En este trabajo se describe el uso de dos fotosensilizadores derivados de las clorinas e-6 (Radachlorin® and Photolon®) para tratar carcinomas basocelulares múltiples. El método de terapia fotodinámica se aplicó a dos pacientes con 31 carcinomas basocelulares superficiales. Los datos presentados muestran una respuesta positiva con 100% de regresión completa en todas las lesiones tratadas, y resultados estéticos aceptables sin efectos colaterales serios o complicaciones durante o posterior al tratamiento. Por lo tanto el método de terapia fotodinámica con derivados de las clorinas vislumbra como una opción prometedora para el tratamiento de carcinomas basocelulares múltiples.

Palabras clave: terapia fotodinámica, fotosensibilizador, Radaclorin®, Photolon®, carcinomas.

Introduction

Skin cancer is the most wide-spread type of malignant neoplasm among the population. The global incidence has been increasing in epidemic proportions being exposure to sun light the main cause connected with this appearance, although these

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tumors may develop in areas of the body protected from solar radiation. Basal cell carcinomas (BCCs) are the most common form of skin cancers with high and increasing incidence rates which reaches 60% frequency in cases treated at the Plastic Surgery Department of the Hospital Oncology Service, IVSS (1). For the last ten years photodynamic therapy (PDT) has become one of the best alternative methods of skin cancer treatment that provides a high degree recovery and excellent aesthetic results with low cost (2,3). PDT is likely to be used primarily for patients with special problems, that is, those with multiple and frequently occurring lesions, and others with numerous lesions not amenable to standard treatment (4). Patients with multiple BCCs require numerous surgical procedures that over time leave them with multiple disfiguring scars.

The chlorin group photosensitizers are characterized by high photodynamic activity and therapeutic efficiency (5, 6). They are being rapidly eliminated from the organism, and due to this they do not cause a long-term photosensitization of skin (7, 8). It completely solves a problem of the long lasting skin phototoxicity that is a main disadvantage of the first-generation photosensitizers (9).

The objective of this study was to present two patients with multiple superficial BCCs treated successfully with Radachlorin®-PDT and Photolon®-PDT method.

Materials and methods

Patients

The present research was carried out at the Plastic Surgery Unit, Hospital Oncology Service, (IVSS, Caracas, Venezuela) with patients that attended the hospital facility and were found suitable for this study. Each patient was evaluated clinically and by histopathology before and after treatment. Informed consent was obtained from both patients, according to the approved protocol by the institutional Ethics Committee, and each patient was given specific instructions about photosensitivity and the precautions to be taken with light after treatment.

The first case treated was a 55 years old Caucasian man with twenty histopathologically documented superficial BCCs (figure 1). The patient had several recurrent lesions previously treated with cryosurgery as well as other multiple primaries, and then was consented to PDT at the Oncologic Surgery Department. The second patient was a 54 years old woman with eleven lesions and skin type III (figure 2). Of all 31 BCCs lesions treated, 20 (64.5%) were localized in the head and neck area, while 11 (35.5%) were at the trunk.

Photodynamic therapy

The study protocol was in agreement to the guidelines of the 1975 Declaration of Helsinki.

PDT was carry out with the commercial chlorin derivatives photosensitizers, Radachlorin® (produced by Rada-pharma, Co. Ltd., Russia) (10) and Photolon® (produced by Scientific Pharmaceutical Center of RUE "Belmedpreparaty", Minsk, Belarus) (11). The drug doses were 1 mg/kg (for Radachlorin®) and 1.6 mg/kg (for Photolon®) body weight diluted in 200 cc of saline solution by intravenous injections slowly in a 20 minutes period. Then the patients were irradiated by the diode laser (ML-662-SP, Russia) with 662 nm wavelength with light dose 250 J/cm^2 (for Radachlorin®) and 200 J/cm^2 (for Photolon®) 2 and 3 hours after the drug injection, respectively. The treatment parameters were chosen on the basis of previous phase dose-ranging studies (10, 12).

Tumors were irradiated one by one with a spot size which covered only the detected lesion. Each treatment was conducted under proper shielding of the sur-

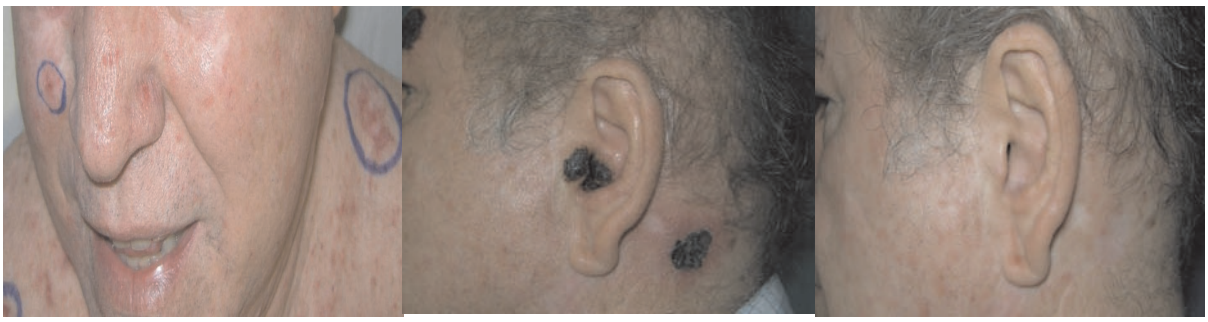

Figure 1. 55-years old Caucasian patient with multiple BCCs before Radachlorin®-PDT treatment (a). Ten days after treatment. Tumors crusted ulcer formation was observed (b). Complete wound healing, cicatrization and epithelization eight weeks following treatment (c).

rounding skin area and eye protection for both patients and medical personnel. PDT was performed under outpatient conditions without anesthesia, and all patients were kept in sunlight-protected rooms from the time of drug administration until they leave the Hospital in the night.

Results

Patient 1

In August 2009, a treatment with PDT using Radachlorin® was performed in an attempt to eradicate 15 BCCs, but five new were observed during the 6-month follow-up period in areas no treated with PDT before; then the patient was submitted to second session with Photolon®. No serious side-effects or complications during or after treatments were observed, other than transient mild local pain, moderate edema, followed by a crusted ulcer formation after one week. In 2-4 weeks the necrosis turn away and then there began gradual cicatrization and epithelization which completed to 5th-8th weeks.

As a representative case we present a photographic sequence documentation of this patient.

Figure 1a shows some of the twenty multiple BCC before Radachlorin®-PDT treatment. Crusted ulcer formation occurred ten days after treatment (Figure 1b), and then this crusted zone disappeared with gradual cicatrization and epithelization which was completed in 8 weeks (figure 1c).

We observed a complete response rate of 100% with acceptable aesthetic results among the twenty lesions treated, clinically and histopathologically corroborated. The patient has been followed-up for thirty two months without recurrence.

Patient 2

In the second case the Photolon®-PDT treatment was performed on eleven lesions (figure 2a). Crusted ulcer formation occurred ten days after treatment (figure 2b), and disappeared with gradual cicatrization and epithelization which was completed in 8 weeks (figure 2c). The patient has been free of recurrence for 28 months. There was confirmation of the absence of oncologic disease by clinical evaluation and histopathology.

Side effects

There were no signs of serious complications and allergic reactions during or after treatment, only we registered transient mild or moderate local pains at the treatment site, moderate edema and hyperemia during 2-3 days. The patients kept a restricted light regimen 3 days after PDT, and the use of analgesics was no required. No skin photo toxicity was observed.

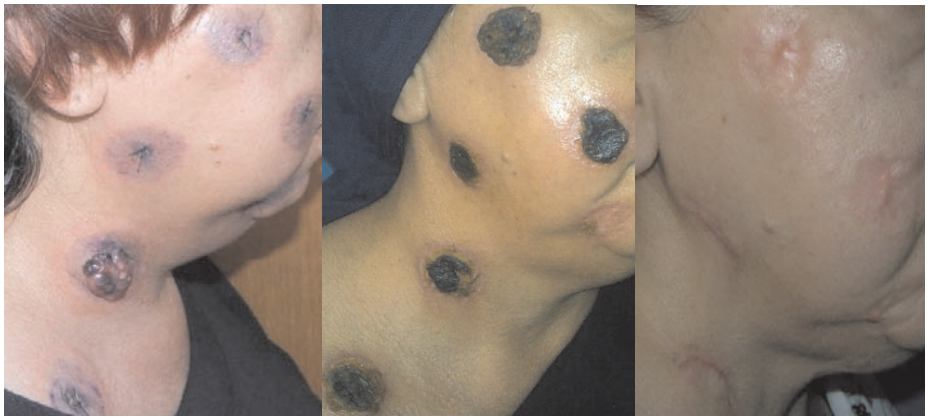

Figure 2. 54-year-old woman with multiple BCC before Photolon®-PDT treatment (a). Crusted ulcer formation 10 days after treatment (b). Healing with cicatrization and epithelization 8 weeks after treatment (c).

Discussion

In the first case presented, a complete regression of tumors was achieved in 15 (100%) from all treated lesions with Radachlorin®, and in the case of Photolon® the complete regression was also 100% in the 5 treated BCCs. The evolution of the patients was satisfactory without differences regarding to the use one or another drug, with similar results. Therefore both drugs were within the expected results as also was demonstrate in other similar studies (1, 10, 12).

The evolution of the second patient treated with Photolon® was also satisfactory and the results comparable with the results obtained by other clinical studies (12), 100% complete regression was obtained demonstrating the efficacy of this photosensitizer for multiple BCCs treatment.

Conclusion

The results of this study suggest that the combination of Radachlorin® and Photolon® -PDT appears to be a good promising option for multiple or frequently occurring BCC, and offers a tissue sparing modality with low morbidity and acceptable aesthetics results, leading us to recommend that clinicians consider Radachlorin® and Photolon®-PDT as a first-line option for multiple superficial BCCs of the head and neck area in our populations.

Bibliographical references

1. CRASTRO J., RINCÓN J.N., GORDON P.M., MARCANO A., ARANGUREN L. ***Rev Venez Oncol*** 19: 3-19. 2007.
2. HENDERSON B.W., DOUGHERT T.J. ***Photochem Photobiol*** 55: 145-57. 1992.
3. COPPER M.C., BING T.I., OPPELAAR H., *RUEVEKAM M.C., STEWART F.A.* ***Arch Otolaryngol Head Neck Surg*** 129: 709-711. 2003.
4. MORTON C.A., BURDEN A.D. ***Clin Exp Dermatol*** 26: 33-36. 2001.
5. EDITORIAL, ***Photodiagnosis Photodyn Ther*** 6: 94-96. 2009.
6. ISTOMIN Y.P., LAPZEVICH T.P., CHALAU V.N., SHLIAKHTSIN S.V., TRUKHACHOVA T.V. ***Photodiagnosis Photodyn Ther***; 7: 144-151. 2010.
7. CHIN W.W.L., PAUL P.W.S., BHUVANESWARI R. LAU W.K., OLIVO M. ***Photochem Photobiol Sci 5***: 1031-1037. 2006.

8. ALLISON R.R., SIBATA C.H. ***Photodiagnosis Photodyn Ther***, 7: 61-75. 2010.
9. MOAN J., STEEN H.B., FEREN K. CHRISTENSEN T. ***Canc Lett***. 14: 291-296. 1981.
10. KOCHNEVA E.V., FILONENKOV E.V., VAKULOVSKAYAC E.G., SCHERBAKOVAD E.G., SELIVERSTOV O.V., MARKICHEVE N.A., RESHETNICKOV A.V. ***Photodiagnosis Photodyn Ther***. 7: 258-267. 2010.
11. ISAKAU H.A., PARKHATS M.V., KNYUKSHTO V.N., DZHAGAROV B.M., PETROV E.P., PETROV P.T. ***J Photochem Photobiol. B*** 92: 165-174. 2008.
12. ISTOMIN Y.P., KAPLANB M.A., SHLIAKHTSIN S. V., LAPZEVICHA T.P., CERCOVSKYA D. A., MARCHANKAD L. N., FEDULOVD A. S., TRUKHACHOVAC T. V. ***Proc. of SPIE*** 7380, 73806V1-8. 2009.