Photodiagnosis and Photodynamic Therapy 13 (2016) 261–266

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

Photodynamic therapy: Progress toward a scientific and clinical network in Latin America

Hilde H. Buzzá[a,*,1], Ana Paula da Silva[a,1], José Dirceu Vollet Filho[a], Dora Patricia Ramirez[a], José Roberto Trujillo[b], Natalia M. Inada[a], Lilian T. Moriyama[a], Cristina Kurachi[a], Vanderlei S. Bagnato[a]

[a] São Carlos Institute of Physics, University of São Paulo (USP), P.O. Box 369, 13560-970 São Carlos, São Paulo, Brazil
[b] Trubios, Johns Hopkins University, Rockville, MD, United States

ARTICLE INFO

Article history:
Received 23 March 2015
Received in revised form 12 August 2015
Accepted 13 August 2015
Available online 18 August 2015

Keywords:
Photodynamic therapy
Latin America
Scientific network
Public health program
Non-melanoma skin cancer

ABSTRACT

Cancer is one of the major challenges for Latin America health services, since the skin cancer is the most frequent lesion. This manuscript addresses an initiative for the treatment of basal cell carcinomas (BCC) by photodynamic therapy (PDT) based on a government-funded national program in Brazil. The program provides clinical training and facilitates access to drugs/equipment and significantly reduces PDT costs. It also lays foundations for the establishment of a Latin American research network to improve prevention, early detection and treatment of diseases. Centers have been established by direct contact (conferences, visits to healthcare facilities and official departments). A local training was divided into complementary theoretical and practical parts. This is an ongoing project that has involved 10 countries: Brazil, Bolivia Chile, Ecuador, El Salvador, Colombia, Cuba, Mexico, Peru and Venezuela, The initial results are encouraging and have provided assessment of Latin America patients relating, for example, the most common skin phototypes with incidence of BCC in such countries. The network is expected to produce relevant scientific information for PDT introduction in many countries. The experience acquired by local teams shall enable them to innovate PDT protocols and increase the number of skilled contributors/researchers to broaden knowledge on the ever-crescent PDT field in Latin America. The establishment of a collaboration network and introduction of other projects and experience exchange shall become an easier process with time. This PDT clinical research network is a start for the strengthening of Science in South Hemisphere countries.

1. Introduction

Non-melanoma skin cancer (NMSC) is the most common type of cancer in Brazil and accounts for 25% of all malignant tumors registered. In 2014, 182,000 new cases per year had been estimated in Brazil, which makes NMSC the type of largest incidence in the country. An early detection provides high rates of cure for those lesions. Among skin tumors, the non-melanoma type is the most prevalent, although it is associated with the lowest mortality rate [1]. Skin is the largest organ in the human body and exhibits significant heterogeneity and, therefore, NMSC shows up tumors of different lineages. The most common lesions are basal cell carcinomas, which account for 70% of the diagnosed lesions, and epidermoid carcinomas, which represent 25% of the reported cases [1]. Although basal cell carcinoma (BCC) is the most common, it is also the least aggressive, but has an important destructive power if it is not treated. A higher incidence of BCC is observed in fair-skinned individuals living in tropical climates [2–4]. NMSC can evolve and cause physical deformities and severe ulceration that lead to anatomical and functional impairments and whose management overburdens health services [5,6]. Skin cancer is usually more common in individuals over 40 years old and relatively rare in children and African descendants, except for those already diagnosed with previous skin diseases. Risk factors include fair skin, clear eyes and light hair, propensity to sunburn and sun sensitivity. People with such characteristics are usually under increased risk of developing ulcers or previous skin diseases and, therefore, are the most afflicted ones [2,7,8]. Other factors, as age, length of exposure to sun, rural activity and family history are considered potential risks [7,8,10].

Developed countries are usually provided with well-established NMSC prevention and early diagnosis programs. Latin America

* Corresponding author. Fax: +1 55 1633739811.
E-mail address: hilde.buzza@usp.br (H.H. Buzzá).
[1] Both authors contributed equally to this work.

http://dx.doi.org/10.1016/j.pdpdt.2015.08.004
1572-1000/

countries lack such effective programs, therefore, most cases are diagnosed at later stages [2,8]. In 1988, Fitzpatrick developed a questionnaire for the classification of skin types based on phenotype and reaction to sun exposure, which enabled their correlation with lesions incidence [9].

However, new approaches must be established for the management of skin cancer, especially in Latin America, and include new or improved technologies for the treatment of the lesions, according to the reality of local infrastructure and investment available. Countries should also devote efforts to support access and affordability of drugs and equipment. The Brazilian experience with photodynamic therapy (PDT) indicates this technique is a possible tool for the start of an initiative to solve the skin cancer problem. The PDT procedures have fitted most conditions and can enable the handling of a large variety of skin lesions and specialized healthcare services to concentrate on more complex situations.

In Latin America, cancer is usually detected only in advanced stages, because most of the population has low access to specialized healthcare services [10–12]. This manuscript addresses an association between PDT and fluorescence diagnosis techniques as a low-cost approach for the treatment of NMSC, reducing waiting lists for minor surgeries and providing improvement in healthcare services [13,17].

PDT has been investigated for various applications and widely used for the treatment of skin cancer, particularly as a relevant treatment option for BCC [12,13,17]. The technique consists of three main elements: presence of a photosensitizer (PS), i.e., a molecule that absorbs light to initiate a series of photochemical reactions, a light source of a specific wavelength that is absorbed by the PS, and availability of molecular oxygen in the tissue under treatment [5,24]. This combination results in the production of oxidative cytotoxic agents and leads the treated cells to death by necrosis, autophagy, or apoptosis when irreversible damage has occurred [5].

The optical diagnosis with fluorescence is a valuable tool to enable healthcare professionals to identify lesion borders and monitor PS production/delivery and bleaching during PDT treatments in real time, ensuring the treatment is efficiently delivered [2].

The initial clinical implementation of PDT in Brazil was hindered due to the low accessibility to drugs and other treatment devices produced abroad, importation bureaucracy and prohibitive costs. Therefore, a national program has been created to provide clinical training and more feasible access to national drugs and equipment, which significantly reduce the cost of a PDT application and bring PDT closer to Brazilian and Latin American population realities. This Brazilian government-funded program provides more favorable conditions for the increase in the use of PDT as a treatment option.

This study not only proposes a solution for skin cancer in developing countries, but also lays foundations for the establishment of a Latin American network of research to improve prevention, early detection and treatment of diseases, with the engagement of scientific community and clinical application of the technique.

Our research group has extensive experience in PDT, with clinical applications to several diseases and, since 1997, has conducted studies on the application of PDT to dermatology [14–16]. Relevant papers in this area and on synthesis of photosensitizers [13,18,21], fluorescence spectroscopy [20], optical imaging [21,22] and evaluation of vascular effects of PDT [23] have been produced. The group has accumulated sufficient know-how and the whole physical structure to lead both national and international large-sized clinical projects, with a constantly increasing contact network. summarizes the differences among the protocols adopted in the three countries with reported results and number of patients treated and Table 2

2. Materials and methods

2.1. Contacting centers

Several methods have been used for the establishment of an initial contact with the centers, from direct contacts made after communication during conferences to the promotion of propagation activities, such as visits to healthcare facilities and communication via official departments of healthcare management and well-established healthcare institutions. The visits were based on a Brazilian version of the project [13] and promoted opportunities for the organization of local workshops and contact with interested researchers for training them and their staff through the transmission of information on PDT. During such training meetings, held locally at the upcoming centers, the equipment was delivered along with the photosensitizing drugs and the first patients were treated for the introduction of PDT and the clinical protocols.

During the visits, the training team can assess the structure each new center provides and help to properly adapt the facilities for the treatment sessions. Moreover, if a lack of experience or infrastructure is identified by the leading team, the progress of treatments is constantly followed to complement training with video conferences and contact on a daily basis, if necessary.

2.2. Personnel training

The training was divided into two complementary parts, namely theory and practice, according to the Brazilian program of PDT for the treatment of NMSC.

A physician in charge of the newly created team must attend the full training and be responsible for all reports and diagnostic procedures. Therefore, the participation of a dermatologist or oncologist is essential, so that adequate lesion screening and indication to PDT can be provided. The leading team stimulates nurses, technicians and other healthcare personnel to take part in the full training, including the treatment procedure, since patient management can be performed by these professionals under medical supervision.

The theoretical training consisted of a classroom lecture on the physical concepts of PDT and fluorescence diagnosis and the pharmacological concepts involving the explanation of how methyl aminolevulinate (m-ALA) is transformed into protoporphyrin IX (PpIX, the PS molecule itself) and accumulated in cells. The lecture also addressed the clinical protocol and the equipment operation step by step, with examples of the expected results and potential complications of the treatment, such as severe pain during irradiation, inflammation, post-irradiation allergies or infection, and management procedures in each case. Biosafety care procedures, such as use of protective eyewear for the specific wavelengths for both patient and caregiver, and pain management were also emphasized. The lecture also informed and detailed the collection and periodic submission of the treatment information to the leading team in the form of monitoring reports made by each local team.

The training lecture is essential, as it enables the transmission of the fundamental PDT concepts, so that the personnel under training can conduct research and produce knowledge by properly observing and interpreting clinical results. They can also perform their first treatment under the supervision of the leading team to ensure the understanding of each step. The training also involved the preparation of adequate material to be submitted to the Ethic Committee for research in humans, when required.