An Overview of Photodynamic Therapy (PDT) in Oncology

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Abstract

The development of photodynamic therapy (PDT) for cancer can be broadly divided into two areas. One area concerns the study's ability to localize in cancers. The second area is due to the photodynamic reaction upon the activation of the drug by visible light to achieve selective photochemical destruction of the target tissue. The current status of clinical PDT in oncology is discussed.

Keywords: PDT, photosensitisers, division, oncology

Introduction

The PDT phenomenon and its dependence on a chemical photosensitiser (drug), light of an appropriate wavelength and oxygen was observed and documented at the turn of the 20th Century in the Munich laboratories of Oscar Raab and Hermann von Tappeiner. However, clinical application did not begin until seven decades later. Skin, breast, and lung cancers were some of the first to be included in the early clinical trials by virtue of their accessibility.

In the past 20 years, PDT has received acceptance as a treatment modality for some cancers but not as universally as one would have expected. Resistance by some medical establishments, financial constraints, growing health economic awareness and lack of resources for scientists and clinicians to carry out robust evidence-based trials have all played a part in the slow diffusion process of PDT.

What is the current situation? Starting with the available drugs and devices:

Photosensitisers

There are a number of drugs synthesised and available for PDT in cancer cases, but only a few have passed the necessary clinical trials. The first drug to be clinically available for use in the modern era of PDT was a haematoporphyrin derivative (HPD). Photofrin® (Photosan, poly-haematoporphyrin formulation) is a purified derivative of HPD which is the drug most commonly used for systemic PDT. It is licenced by FDA and the EU.

5-Aminolevulinic acid (5-ALA) is the drug that is licenced for topical PDT. A number of ALA based drugs are now available and used in different parts of the world. Chlorine family; the clinically relevant representative members of this family are Temporfin (Foscan), and Npe 6 (mono-L-aspartyl chlorin e6). Foscan is licenced for head and neck cancer. Many dyes (e.g. Phtalocyanine) have been used in laboratory and clinical trials. However, they do not have the same appeal in Europe as they have in other continents.

Light sources

The photodynamic reaction depends upon the activation of the drug by an intense and appropriate non-thermal light to achieve selective photochemical destruction of the target tissue. In PDT, the wavelength of the light needs to be matched with the absorption band of the drug to produce the PDT effect. Original clinical work in oncology used an Argon-pumped laser. Currently, both lasers and light emitting diodes (LED) are used as PDT light sources. Diode
lasers provide a small frame and the possibility of greater power emission. LED’s are relatively inexpensive and the cost is much lower than for lasers. However, they are generally only suitable for skin and exposed mucous membrane treatments, usually in conjunction with topically administered drugs.

**PDT in oncology**

After many laboratory and experimental studies in the early 1980’s, clinical trials followed that showed PDT to be an effective treatment in a variety of cancers with complete, or at least partial, clearance of lesions. It has many advantages. PDT is a local treatment that can be used in advanced disease stage for palliation of symptoms with survival benefit in some. It is potentially curative for early stage cancer and, therefore, can be used as an alternative to surgical resection when the patient refuses surgical intervention or is ineligible for surgery, PDT can be repeated and used for salvage in some cases where the patient is not suitable for surgery following induction chemo/radiation. Moreover PDT can be used in oncology in conjunction with other treatment modalities. In some cases PDT can be used to downstage potentially inoperable cases (downgrading of T factor). However there are also disadvantages of PDT. Photosensitivity skin reaction is the most important complication of PDT, but this is only in systemic PDT photosensitisation and is largely preventable. Erosion/ulceration and infection can occur following PDT. Haemorrhage can occur after PDT in some instances. Perforation of tubular structures (eg oesophagus) can occur.

**Current status of clinical PDT in oncology**

The current status of PDT in oncology may be described under 3 headings based on the following criteria: 1) efficacy of clinical and pathological response, 2) tried feasibility and availability of methodology (in respect of drugs and their dosage and illumination; light sources, dosimetry and delivery systems and access and ease of application), 3) strength of evidence-based outcomes.

These 3 categories can be thought as the 3 divisions: 1) the premier division comprises indications in which there are many publications showing the effectiveness of PDT (examples: non-melanoma skin cancer, advanced and early stage bronchial cancer (central type lung cancer), advanced and early stage oesophageal cancer, barrett’s dysplastic mucosa and adeno carcinoma, head and neck cancer); 2) division with conditions in which PDT has been tried and tested as an effective treatment. However, neither the methodology is standard nor is there strong material available and publications are rather scanty (they include: cholangiocarcinoma, peripheral lung cancer, local recurrence of breast cancer, some gynaecological cancer, bladder cancer); 3) the last division comprises of cases in which there are logical, laboratory-based evidence of the efficacy of PDT but with only feasibility and initial studies showing safety and response of cancer to PDT. In many of these cases PDT has been used as a last resort and documentation suggests the need for an initial appraisal of the methods. There is uncertainty of the methodology (example of these include: prostate, urothelial cancer, pancreas, colorectal cancer). It must be emphasised that these divisions are not static and that ongoing studies will change the grading according to publication and the strength of the future studies. It is also important to state that Photodagnosis (autofluorescence/or enhanced) is becoming an integral part of PDT.

**Conclusions**

We need better much better drugs, which localise in tumours with greater selectivity.
We need better light sources and delivery system.
We need better applicators.
We need more resources to carry out research.
We need to educate future oncologists to accept integration of PDT in oncological modalities.
We need Clinical Research, Clinical research, and Clinical research.