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Photodynamic Therapy

Nowadays great progress has been achieved in basic researches that has given us a better understanding of tumor biology. Despite it, there are many serious diseases, for example cancer, effective treatment of which is associated with certain difficulties. Besides, the number of new clinically approved drugs is extremely low. This information suggests that it is necessary to pay attention to existing therapies, that can be used to fight cancer. One of them is photodynamic therapy.

Photodynamic therapy (PDT) was the first drug-device combination approved by the US Food and Drug Administration (FDA) almost 2 decades ago, but even so remains underutilized clinically [1].

Photodynamic therapy (PDT) – a method of treatment tumors, in particular cancer, the essence of which is the electoral impact on biological tissues as a result of photochemical reactions. Light energy is the catalyst of these reactions [2]. PDT consists of 3 essential components: photosensitizer, light, and oxygen. It is obviously that no one of these is individually toxic, but together they initiate a photochemical reaction that culminates in the generation of a highly reactive product termed singlet oxygen and number of free radicals. This singlet oxygen activates the cytotoxic effects, which is a specific mechanism of damage vital cells functions by formation of deep structural and functional changes of the cell membranes and processes occurring within them and as result these cells die [1].

The earliest recorded treatments that exploited a photosensitizer and a light source, in this case sunlight, for medical effect can be found in ancient Egyptian and Indian sources. Over 3000 years ago vegetables and plants were used as substances to produce photoreactions in skin and caused therapeutic effect.

The first serious scientific evidence that agents, photosensitive synthetic dyes, in combination with a light source and oxygen could have potential therapeutic effect was made at the beginning of the 20th century by von Tappeiner and Rabb in Germany. Historically this was a time when Germany was leading the world in the industrial synthesis of dyes. Subsequent work in the laboratory of von Tappeiner showed that oxygen was essential for the 'photodynamic action' – it is the term, which was coined by von Tappeiner. However, in the early twentieth century technological progress was not developed enough to create medical devices for photodynamic therapy [3].

Much later, in the 1990s the Russian scientists developed a laser copper vapor system, radiation of which was able to provide clinical impact. Besides, one early Russian development was a new photosensitizer called Photogem which was derived from haematoporphyrin in 1990 by Professor Andrey F. Mironov and coworkers in Moscow. Photogem was approved by the Ministry of Health of Russia and tested clinically from February 1992 to 1996. A pronounced therapeutic effect was observed in 91 percent of the 1500 patients that underwent PDT using Photogem, with 62 percent having a total tumor resolution. Of the remaining patients, a further 29 percent had a partial tumor resolution, where the tumour at least halved in size. In those patients that had been diagnosed early, 92 percent of the patients showed complete resolution of the tumour [3].

PDT is a 2-stage procedure. The first stage is an administration of a light-sensitive photosensitizer into biological tissues. A photosensitizer is used to make the cells sensitive to light. The second stage represents the tumor irradiation by light. It should be noted that light sources for the photodynamic therapy may be either laser or non-laser. It may be xenon and mercury lamps and the latest developments represent a matrix of LEDs. The laser systems in turn are divided by type of the active substance. There are gas laser systems developed in Russia, which are used to treat skin diseases. For example, a laser medical device Yakhroma-Med copper bromide has a direct clinical impact [4].

There are also real laser systems (eg, Yahroma-2) in which the copper vapor lasers are used for optical pumping dye lasers. There is dye Rhodamine B, which is characterized by high efficiency, which is about 20 %. The wavelength at which the activated rhodamine B is 510.8 nm, which corresponds exactly to the emission of copper vapor lasers [4].

There is another very important point: each photosensitizer is activated at a particular wavelength. For example, Photofrin is a very widely applied photosensitizing agent, which is activated by the light with the wavelength 628 nm. The radiation by laser beam can be delivered with the help of optical devices. In this way, flexible light sources are more preferred embodiment of the use due to the fact that it can deliver light energy to virtually any organ in the body with good homogeneity of light delivery [2].

Optical fibers were originally developed to transmit light energy with minimum losses to their distal ends which emit like semi-point light sources. If electromagnetic radiation is confined inside the core of the fiber and propagates along the fiber, this type of optical fibers is called Distal End Emitting Optical Fibers.

There is another type of this device, which has side-emission effect. This effect represents a leaking light from the fiber's core to its cladding and further via the outer jacket to the surrounding medium. It mean that conducting light can leak from the side of fiber. These optical fibers are called Side-Emitting Optical Fibers (SEOF). The main effect of forming a leak path is changing of the refractive index.

There are different types of creation this effect. For example formation of leakage channels by changing the shape of the fiber or macro-bending in certain part of fiber because the decay of light along the fiber depends on the bending angle. Also, the channel leakage can be created by the optical tunneling method or by outside impact interference that may be cause a change refractive index [2].

Paradoxically, the highly localized nature of PDT is one of its current

limitations, because the treatment is ineffective against metastatic lesions, which are the most frequent cause of death in cancer patients.

As it was mentioned earlier, each photosensitizer has a high absorption peak at a particular wavelength of light. Most of the photosensitizers, which are actively used for FDT, have a high absorption peak between 600 and 800 nanometers. This is because absorption of photons with wavelengths longer than 800 nm does not provide enough energy to excite oxygen to its singlet state and in this case cytotoxic effects does not occur.

Almost all photosensitizers used in cancer therapy are based on a tetrapyrrole structure, similar to that of the protoporphyrin contained in hemoglobin.

References

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