MONITORING OF HEMATOPORPHYRIN INJECTED IN HUMANS AND CLINICAL PROSPECTS OF ITS USE IN GYNECOLOGIC ONCOLOGY

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INTRODUCTION
The use of hematoporphyrin (HP) and its water soluble derivatives (HPD) as tumor localizers and sensitizers for phototherapy of neoplasias is well documented and receiving rapidly increasing interest.

Gynecologic oncology is an important area of application of porphyrins in association with visible light for both early diagnosis and phototreatment, owing to the large occurrence and the wide variety of tumors easily accessible to coherent or non-coherent light sources, eventually coupled to fiber optic endoscopes. Ready to start a plan of clinical experiments of diagnosis and phototreatment of gynecologic tumors with hematoporphyrin-visible light, we have studied, in some selected patients undergoing surgical ablation of the tumor masses, the location of administered HP in the neoplastic and surrounding tissues and the whole processes of clearance of the dye from the patients bodies. Actually the present extension of the method to different oncologic fields and to different stages of neoplastic growth and invasion requires a precise knowledge of the rates and extents of distribution of the sensitizers in different normal and malignant tissues, to optimize phototreatment and diagnostic procedures. Moreover the clearance rates and features of the dye from the body are essential parameters to control and prevent side effects.
Finally these clinical studies may provide essential contributions to the elucidation of the mechanisms of photodinamic effects of porphyrins in vivo.

PROCEDURES AND RESULTS

Administration and monitoring of HP

HP for clinical use was prepared from a lot of hematoporphyrin IX hydrochloride (Porphyrin Products, Logan, Utah, U.S.A.), estimated 95-97% pure by high pressure liquid chromatography. The product, dissolved with sterile isotonic saline and filtered through millipore under nitrogen pressure, was administered by intravenous injection at the dose of either 2.5 or 5 mg/Kg of body weight.

For the first set of clinical experiments, two patients with primary vulvar tumors, undergoing total vulvectomy, were selected. Previous clinical examination and laboratory tests excluded alterations of liver and kidneys functions. Since the time of HP injection the patients were kept 10 days in a room with darkened lights, the eyes being protected by sunglasses. The patients were then warned not to expose to direct sunlight for the additional two weeks. At regular intervals from HP injection the monitoring of HP concentrations in serum, faeces and urine was performed throughout 24 days. The HP concentrations in tumor and normal surrounding tissues were also determined, following dissection under a magnifier and separated extractions of fresh samples obtained from bioptic or surgical specimens.

The concentrations of HP in solid tissues and body fluids were measured spectrophotofluorometrically, following extraction or dilution with buffered 1% sodium dodecylsulfate.

Preferential distribution of injected HP in malignant tissue, and in vivo detection of HP fluorescence

The comparative distribution of injected HP in tumor and in the normal surrounding tissues confirmed that the preferential affinity of malignant cells for porphyrins observed in isolated cells and in animal tissues in vivo, can be demonstrated also in humans. Fig.1 shows a typical spectrophotofluorometric assay of HP content in a surgical specimen of a vulvar squamous cell carcinoma, in comparison with the control normal skin tissue. The differential HP concentrations in vulvar tumor masses with respect to the surrounding tissues allowed us to observe and photograph the characteristic