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Fluorescence and peritoneal cancer: are we close to clinical use?

Introduction

Fluorescence can be spontaneous (auto fluorescence) or enhanced by an exogenous precursor such as 5-aminolevulinic acid (ALA). Administration of exogenous ALA induces a temporary accumulation of PpIX in malignant cells of epithelial origin. PpIX selectively concentrates in tumor cells and generates red fluorescence when excited by blue light revealing a distinct contrast to the surrounding normal tissues. Photodiagnostic has received significant interest in surgical oncology for improving the early detection of urological (1), pulmonary (2), dermatologic (3) and gastrointestinal (4) cancers. Fluorescence imaging is still undeveloped in gynecology and requires others experimental and clinical studies. Sixty-five percent of ovarian cancers are diagnosed at stages III or IV. After optimal treatment with no residual tumor, 55% of patients will present a recurrence. These results raised the question of the efficiency of initial laparoscopic staging. Despite attempts at improving staging (computed tomography, magnetic resonance imaging), the detection of residual micrometastatic disease remains a challenge to the gynecologic oncologist. Therefore any approach that might improve the sensitivity of staging procedure and radical surgery would be very attractive as a mean of improving the management of these patients.

Photodynamic diagnosis and ovarian cancer

The use of fluorescence in order to diagnose precancerous or cancerous disease is also called photodynamic diagnosis. A review of the literature concerning the use of photodynamic diagnosis in ovarian cancer in clinical and experimental studies was made in order to assess the current status of this technique in gynecologic oncology (5).

In a randomized experimental study, Canis et al showed how improved was the detection of peritoneal metastases of ovarian cancer using ALA-induced fluorescence. Intra peritoneal ALA injection was made three hours before the laparoscopic procedure. The mean number of metastases detected during laparoscopy was statistically higher with blue light (fluorescence mode) compared to white light (conventional light mode) (6). In 2002, Chan et al found that fluorescent laparoscopic detection of micrometastatic ovarian cancer using ALA was significantly more sensitive than white-light laparoscopy in detecting smaller cancerous lesions in an ovarian cancer rat model (7). Cancerous lesions showed significantly higher fluorescent intensity compared to non cancerous lesions which was confirmed in several publications in which hexaminolevulinatate (He-ALA), a promising and new photosensitizer was used (8-10). He-ALA gave the highest PpIX fluorescence contrast between normal and tumoral peritoneal tissues. Imaging with He-ALA improved the detection of peritoneal metastases compared to ALA.

In gynecology, very few clinical studies have been performed evaluating the usefulness of fluorescence based detection of ovarian cancer (11-13). Nevertheless, Loning et al found that ALA-induced PpIX fluorescence was confined to ovarian cancer tumor tissue sparing stromal tissues with a sensitivity of 100% and a positive predictive value of 91% (13). In another clinical study evaluating in vivo fluorescence detection of ovarian carcinoma metastases in a second-look laparoscopic procedure after intraperitoneally applied 5-aminolevulinic acid (ALA), Loning et al showed that laparoscopic fluorescence detection of endogenous PpIX after intraperitoneal application of ALA may provide a higher sensitivity of finding peritoneal metastases of epithelial ovarian carcinoma compared with conventional laparoscopy. Direct visualization of in vivo fluorescence after ALA application may improve the early detection of intraperitoneal ovarian carcinoma micrometastases. The high tissue selectivity of PpIX accumulation in tumor tissue specimens also offers the opportunity for therapeutic approaches using photodynamic therapy in the future (12,14,15).

Conclusion

Fluorescence imaging improves sensibility and accuracy of the diagnosis of advanced ovarian cancer as it was demonstrated in several experimental and clinical studies. These results justify the development of PDD in gynecology. A randomized phase III trial of hexaminolevulinat photodynamic diagnosis in patients with advanced ovarian cancer has just begun in Lille University Hospital. This study aims to assess laparoscopic fluorescence detection of carcinosis compared to white light laparoscopy in order to optimize the management of these patients.

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