

Hexyl Aminolevulinate in the Detection of Bladder Cancer

A Viewpoint by Dirk Zaak and Christian G. Stief

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Although many aspects of the management of non-muscle-invasive bladder cancer are now well established, there are still significant challenges, which influence patient outcome, to overcome. Early detection and treatment of recurrent disease is required to optimise bladder preservation, reduce patient morbidity and increase both health-related quality of life and survival. Conventional (white-light) cystoscopy and cytology are considered to be the standard methods for the detection of bladder cancer. However, their sensitivities and specificities are far from satisfactory, leading to incomplete detection of primary or recurrent papillary or flat urothelial lesions.

Since the beginning of the 1990s, fluorescence (endo)cystoscopy, often referred to as 'photodynamic diagnosis' (PDD), has been investigated in order to maximally enhance the detection rate of overlooked tumours. Based on biopsy-correlated evaluations, several studies evaluating PDD with 5-aminolevulinic acid as an adjunct to conventional cys-

toscopy have demonstrated a significant increase in sensitivity for the diagnosis of both flat carcinomas and papillary tumours. However, because of the lipid bilayer of the urothelial cell membranes, the cellular uptake of charged molecules such as 5-aminolevulinic acid is limited. Hexyl aminolevulinate, a more lipophilic 5-aminolevulinic acid ester derivative with high potency and selectivity, has been studied extensively. Prospective clinical trials have indicated a sensitivity of >90% with PDD using hexyl aminolevulinate for the detection of flat urothelial lesions, such as carcinoma in situ (CIS), compared with 46–77% for conventional cystoscopy. Therefore, PDD (e.g. using hexyl aminolevulinate) is recommended by the guidelines of the European Association of Urology for the detection of CIS; hexyl aminolevulinate has been approved for the detection of bladder cancer in many European countries.

PDD can also be used to evaluate transurethral resection sites for completeness of resection and to detect early treatment failures after intravesical therapy. However, a decrease in the recurrence rate with PDD using hexyl aminolevulinate versus conventional cystoscopy (as has already been demonstrated for PDD using 5-aminolevulinic acid) awaits verification in ongoing, prospective, randomised trials. ▲