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ORIGINAL ARTICLE

The effect of intravesical single-dose Mitomycin C in recurrent superficial bladder cancer

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KEYWORDS
Mitomycin C;
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Summary
Objectives: This study was designed to evaluate the efficacy of the intravesical instillation of single-dose Mitomycin C post-ablation of purely recurrent tumours.
Patients and methods: Two patient groups with small-volume, low-grade (1 or 2), superficial (pTa) recurrent disease were studied. Sixty-seven patients at one institution received a single intravesical dose of Mitomycin C following tumour ablation using a Holmium YAG Laser. The other institution provided a control patient group of 68 patients treated with laser ablation alone. Patients were reviewed with regular flexible cystoscopies throughout the study period.
Results: The groups were matched for age and the number and grade of tumours. Recurrence rates were lower, yet not to statistical significance, in the group receiving Mitomycin C post-intervention (48% vs. 62% ($p = 0.14$) at 12 months and 76% vs. 82% at 24 months ($p = 0.64$)). The observed beneficial effect at 12 months appeared to depreciate by 24 months. There was no significant improvement in the recurrence-free interval for the Mitomycin C group (log rank test $p = 0.28$).

Abbreviations: TCC, transitional cell carcinoma; TUR, transurethral resection; TURBT, transurethral resection of bladder tumour; MMC, Mitomycin C.

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Conclusions: This study has failed to demonstrate a beneficial trend for the use of single-dose of Mitomycin C after ablation of recurrent superficial bladder cancer. Further evaluation in the form of a prospective trial is indicated.

Introduction

The majority of transitional cell carcinomas (TCC) of the bladder are superficial (pTa/pT1) at initial presentation and recurrence rates are generally accepted to be 60—70% after complete transurethral resection (TUR) [1,2]. The proposed explanation for such high rates of recurrence is that disease deemed ''recurrent'' is actually de novo tumour development, induced by a widespread 'field change' to the bladder epithelium secondary to prior urinary carcinogen exposure [3]. Alternatively, malignant cells re-implant after the primary TUR [3—5]. Regardless of the precise mode of recurrence, patients under follow-up represent a significant proportion of a urology department's workload. Any simple prophylactic treatment that could limit the frequency and total number of recurrences experienced could subsequently have clear beneficial implications for patients, as well as easing the pressure on urological services [6].

Numerous trials have now looked at the use of intravesical chemotherapy to limit recurrence [7—9]. Mitomycin C (MMC) has emerged as one of the most popular agents. Tolley et al. demonstrated that a single instillation of intravesical MMC led to longer recurrence-free intervals and lower recurrence rates after endoscopic treatment of primary tumours, when compared with patients treated by TUR alone [10,11]. Multiple-dose MMC maintenance regimes also have a positive role to play with improved outcomes demonstrated in patients who have already suffered recurrence [12—15].

Since 2001, the two institutions from the North West of England in this study have been using flexible cystoscopy laser ablation to manage patients with small-volume, low-grade, superficial recurrent TCC of the bladder. This has been particularly useful in treating those patients who have small volume recurrences but are considered unfit for general anaesthesia because of significant co-morbidities. Using this patient cohort, this study aimed to evaluate the use of a single instillation of MMC in patients with purely recurrent TCC of the bladder.

Patients and methods

Patients treated with laser ablation between October 2001 and May 2005 were identified from the operating theatre logbooks and entered into a computer spreadsheet (Microsoft Office Excel©). A retrospective review of the case notes and pathology records was subsequently performed. Patients were only included in the analysis if they had superficial, non-invasive (pTa) disease of grade 1 or 2 after their original TUR and had subsequently suffered recurrence requiring laser ablation. Patients were excluded if they had received any previous courses of radiotherapy or chemotherapy other than a single-dose of MMC after the original TUR, which was standard practice at both institutions.

Patients at both institutions were treated by laser ablation using a Holmium-YAG laser delivered through a 365-nm fibre. Institution B routinely administered a single-dose of MMC (40 mg/40 ml saline) post-procedure. Individuals were instructed to retain the MMC for at least 1 h post-procedure. Patients were reviewed and examined for recurrence with a 17-French gauge flexible cystoscope on multiple occasions between 4 and 24 months.

The principal endpoints used to assess the chemotherapeutic efficacy of a single-dose of MMC against the control group were the recurrence rates at 12 and 24 months and the recurrence-free interval. Recurrence-free intervals were defined as the time from the laser treatment to the first recurrence being detected. Patients who had died or been lost to follow-up during the study period were excluded from this analysis. Kaplan—Meier curves were then calculated.

Once a patient had recurred they were often re-treated with laser ablation. Data from an initial pilot study suggested that recurrence rates were improved when such patients were included in the series again. It was however not felt statistically valid to treat these additional episodes as independent. Thus only the first set of data for each patient was analysed (i.e. only patients with their first episode of recurrence that was treated by laser ablation). With 68 and 67 respectively in the two groups, the study has 80% power to detect differences in recurrence-free rates of 24% or more