Ambulatory Photodynamic Therapy for Superficial Basal Cell Carcinoma: An Effective Light Source?

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Photodynamic therapy (PDT) is a non-invasive treatment for several (pre)malignant superficial skin cancers, such as superficial basal cell carcinoma (sBCC), Bowen's disease (BD) and actinic keratosis (AK) (1, 2). PDT is traditionally known as an in-clinic treatment that can be time-consuming for both patients and healthcare personnel. Conventional PDT (cPDT) can be painful (3). In order to optimize comfort during treatment, new photosensitizing agents and light sources have been studied over the past decades.

Moseley et al. (4) reported on the use of a portable low-irradiance illumination source for sBCC. This ambulatory PDT (aPDT) device delivers a standard light dose at low irradiance (7 mW/cm^2) over a prolonged period of time, compared with other devices, such as the Aktilite (80–90 mW/cm^2, Galderma SA, Lausanne, Switzerland) (5). It is considered a patient-friendly, out-of-clinic treatment with lower pain scores compared with regular PDT (4–6).

This aim of this study was to evaluate retrospectively the risk of recurrence in patients treated with aPDT for primary sBCC, and the effect of tumour size on recurrence.

MATERIALS AND METHODS

Medical files of patients treated with aPDT between 1 February 2012 and 31 May 2013 in the Catharina Hospital, the Netherlands, were reviewed retrospectively. Inclusion criteria for this study were: patients with a histologically confirmed primary sBCC with a maximum diameter of 2 cm (due to size limitation of the portable PDT device). Exclusion criteria were: patients with genetic disorders causing skin cancer and those using immunosuppressive medication. The primary outcome measure was 1-year probability of remaining tumour-free. Treatment failure was defined as the presence of residual or recurrent tumour during follow-up visits. Follow-up visits were scheduled according to the local hospital protocol 3 and 12 months post-treatment. Secondary outcome measures were cumulative probability of recurrence-free survival at 6 and 18 months, and incidence of adverse events.

In case of slight hyperkeratosis, lesions were prepared by curettage using a wooden spatula to remove scales and crusts, to increase penetration of the active agent. Consecutively methylaminolaevulinic acid (Metvix 16%, Galderma SA, Penn Pharmaceutical Services, Gwent, UK) was applied to the tumour itself and a 5-mm margin of surrounding normal tissue. A transparent occlusive bandage (Tegaderm®, 3M Healthcare, Minnesota, USA), was applied, after which the portable PDT device (Ambulight®, Ambicare Health, Livingston, Scotland, UK) was attached. The device remained switched off for 3 h. Subsequently, it switched on automatically and remained switched on for another 3 h, thereby delivering a total light dose of 75 J/cm^2, with 7 mW/cm^2 irradiance.

The distribution of baseline characteristics was described by absolute numbers and percentages for categorical variables and mean ± standard deviation for age. Kaplan–Meier survival analyses were used to assess the cumulative probability of recurrence-free survival with 95% confidence intervals (CI) at 6, 12 and 18 months. Differences in recurrence-free survival between groups were tested for significance using the log-rank test. Follow-up ended at the date of a treatment failure or the date of the last follow-up visit. A 2-sided p-value ≤ 0.05 was considered to indicate statistical significance. Analyses were performed using SPSS version 23.0 and Stata version 14.0.

RESULTS

During the study period 125 patients with 143 sBCC were treated with aPDT. The first diagnosed tumour per patient was included for analysis. In case a patient was treated for 2 or more primary sBCC on the same day, the largest tumour was chosen for analysis. A total of 104 patients had a histologically confirmed primary sBCC. Three patients were lost to follow-up directly post-treatment, because they preferred follow-up elsewhere. Thus, 101 patients remained for analysis. Baseline characteristics are shown in Table SI[1].

Median follow-up time was 13 months (range 2–23 months) with 59.4% of patients having completed a follow-up time of at least 12 months and 27% more than 18 months. In 11 patients treatment failure was observed based on clinical observation, from which 9 occurred within 12 months. Eight of the clinically suspect recurrences were confirmed by histopathological examination, and 3 tumours were re-treated without histological confirmation. A total of 11 recurrences were included in the analysis.

At 3 months there were no patients with residual tumour. At 6, 12 and 18 months the cumulative probability of recurrence-free survival was 93.6% (95% CI 86.3–97.1%), 89.9% (95% CI 81.5–94.7%) and 87.6% (95% CI 77.4–93.3%). For 74 patients data on tumour size was available. These patients were categorized according to tumour size: ≤5, 6–10, and >10 mm. The 1-year probability of recurrence-free survival was 100% for the ≤5 mm size group and 92% (95% CI 78.5–97.6%) and 72.9% (95% CI 42.6–89.0%) for the 6–10 mm and >10 mm groups, respectively, $p = 0.014$ (Fig. S1[1]).

Adverse events were reported in 2 patients: one reported blistering and erosions post-treatment, and the other had a bacterial skin infection, which was treated with topical antibacterial ointment.

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DISCUSSION

The current study suggests that aPDT is an effective treatment for primary sBCC, with clearance rates of 89.9% at 12-month follow-up. It is most effective in sBCC smaller than 10 mm.

The probability of recurrence-free survival following aPDT compares favourably with results reported by studies on cPDT. Roozeboom et al. (7) found a 1-year cumulative probability of 84% (95% CI 78–90%) based on pooled estimates of recurrence-free survival in a systematic review on cPDT treatment of sBCC. In a recent prospective randomized controlled trial probability of recurrence-free survival of 72.8% (95% CI 66.8–79.4%) was reported at 12 months following methyl aminolevulinate (MAL)-PDT (8). A possible explanation for better results of aPDT might be the different irradiance in aPDT. The aPDT device emits red light at low irradiance over a longer period of time. It is hypothesized that this low irradiance is more cytotoxic and has a greater photobleaching efficiency and therefore could lead to a higher efficacy, with lower pain scores (9–11). However, the lack of a control group in this study prohibits direct comparison with cPDT.

In 2 cases blistering was observed; 1 due to bacterial infection. It is possible that the blistering in the second patient was also caused by a local skin infection rather than by the PDT itself, but this was not explicitly reported in the patient file.

An interesting finding of the current study is that aPDT is especially effective in tumours < 10 mm. The decrease in treatment success in larger tumours has already been reported by Atilli et al. (6) in a small, open, pilot study with aPDT. They observed that lesions larger than 1.5 cm were more likely to show recurrence. One could argue that smaller sBCC, in general, respond better to treatment compared with larger ones. However, the literature on PDT is not consistent regarding the association between tumour size and effectiveness of PDT (12–16).

An important limitation of this study is its retrospective nature. Reports were often brief and post-treatment photography was usually not conducted. For this reason, recurrences may have been misclassified and adverse events may have been under-reported. Currently, aPDT is not widely implemented in daily practice in Dutch hospitals.

A limitation of the device is its inability to treat tumours located on convex or concave areas (e.g. nose, fingers) or tumours >2 cm. Since there are viable and more cost-effective alternative therapeutic options, such as imiquimod or 5-fluourouracil, the position of aPDT has to be established. aPDT could be a preferred mode of PDT for the working population, for whom in-clinic treatment might not be preferable and for patients who are not able or willing to apply a cream. Another advantage could be the good tolerance during illumination, in contrast to cPDT, in which a burning sensation is more often reported (5, 6).

Thus far, there is insufficient evidence to implement aPDT on a wide scale and comparison with other existing effective treatments in a randomized controlled setting is warranted.

The authors declare no conflicts of interest.

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