EFECTIVENESS AND SAFETY OF HIGH DOSE-RATE BRACHYTERAPY IN KELOIDS: SYSTEMATIC REWIEW

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Spanish full text

Introducción: Keloids are benign tumours that originate because of an alteration in the normal healing process commonly after surgical injury or tissue trauma. Although frequently they only have aesthetic consequences, they can lead to symptomatology and important functional limitations. When they are severe, they can cause psychological trauma, with important repercussions on the patient's quality of life. Treatment is usually complex because of the high recurrent rate. The most commonly used therapies include intralesional corticosteroid infiltrations, pressotherapy, cryotherapy, laser, silicone gel, antichemotherapy and surgery combined with radiotherapy or other procedures, as surgery alone is not considered effective. Radiation therapy may be administered by external beam therapy (EBT), high dose-rate brachytherapy (HDR-BT) or low dose-rate brachytherapy (LDR-BT), with adjuvant HDR-BT being one of the most recommended techniques when the keloids do not respond to conventional treatments.

Aims: to evaluate the safety and effectiveness of adjuvant HDR-BT in the treatment of keloids compared to other therapeutic alternatives.

Methods: an exhaustive search of the scientific literature was carried out until March 2018 in the main medical databases, including Medline, Embase, CRD, Prospero and Cochrane. The selection of articles was made according to previously established inclusion/exclusion criteria. Relevant data were collected in evidence tables, and a summary of the evidence was carried out using the GRADE system. Recurrence and cutaneous toxicity grade 3 and 4 were considered critical variables. In order to evaluate the risk of bias of the studies, specific tools were used according to the type of study. Both the selection of the studies, as well as the extraction of data and evaluation of the evidence was carried out by two researchers independently and blindly.

Results: Nineteen studies were selected that evaluated 1474 patients treated with surgery and adjuvant HDR-BT. The recurrence rate in these studies ranged from 0% to 46% (weighted mean: 14.84% ±9.5%). The recurrence rate was significantly higher in the sternum (86%) than in other locations ($p<0.05$). Keloid size, burns as aetiology and pretreatment were significantly associated with the risk of recurrence in some studies but not in others. The patient scored the scar condition between 12.5 and 24.3, with 6 corresponding to normal skin and 60 to the worst possible condition (POSAS Scale). The score given by clinicians ranged from 4.7 to 17. In the only clinical trial performed, the scar condition improved significantly after the intervention. (67.2 to 22.3 ($p<0.001$). Between 51% and 71% of the intervened patients were satisfied with the cosmetic results. In a few

studies it was observed that pruritus improved/disappeared in 78.6%-95.3% of cases, pain in 80% to 88.9% and burning in 69%-83%. A small percentage of patients suffered these conditions for the first time after treatment.

In terms of safety, three studies were found to report skin toxicity ≥ grade 3 (weighted mean ± SD=6.66 ±3.4). The frequency of infections ranged from 0% to 20% (weighted mean ± SD=6.66 ±3.4) and dehiscences from 0% to 23.3% (weighted mean ± SD=12.99 ±8.39). In general, the most commonly described chronic complications were telangiectasias (weighted mean ± DE=15.4 ± 3.3) and pigment alterations (weighted mean ± DE=24.37 ± 28.16). Isolated cases of fibrosis, chronic wounds, dermatitis, ulcers and erythema were also reported. Only one of the studies refers to cases of neoplasia.

Discussion: The studies included in the current systematic review are of very low methodological quality. They are mostly retrospective series with a high risk of bias, as they are based on information that has mostly been derived from clinical databases or medical histories. Two of the compared cohort studies are also retrospective, and the other two have significant biases. There is only one randomized clinical trial, and this only includes 7 patients treated with adjuvant HDR-BT, having been aborted prematurely due to the poor results obtained with intralesional cryotherapy, which was the technique being evaluated.

Conclusions: The results suggest that the application of HDR-BT in combination with surgery may be more effective than other conventional therapies in preventing recurrences in individuals with recalcitrant or recurrent keloids, although there are no expected differences from other types of radiotherapy. It is considered to be a relatively safe and well tolerated technique, although the possibility of severe toxicity is not ruled out. At present, it has not been demonstrated that the risk of complications or carcinogenesis is reduced in comparison with other radiotherapy techniques. The main benefit of HDR-BT over LDR-BT lies in the fact that it can be performed on an outpatient basis, without requiring the patient to be immobilized or isolated. There are important questions remaining regarding optimal dosage and treatment guidelines. Existing studies are not adequate to evaluate how adjuvant HDR compares to other therapies that could be applied after surgical excision, such as triamcinolone/5-fluouracil. In the absence of these studies, it is not possible to draw firm conclusions regarding the role that HDR-BT could play in the therapeutic management of keloids.

Recommendations: HDR-BT is not recommended as a first-choice test. In view of the uncertainty regarding toxicity and risk of carcinogenesis, as well as dosage patterns, if applied, t would be advisable to establish a procedure for case follow-up in order to assess cosmetic outcomes, recurrences and serious adverse events. The implementation

of well-designed randomised clinical trials comparing effectiveness and safety against other therapeutic modalities is essential to establish a treatment algorithm