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“Drug holiday” in DRONJ (Denosumab Related Osteonecrosis of the Jaws) patients : real benefit in surgical or non surgical therapeutic approach ?

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Abstract

One of the most frequent monoclonal antibodies linked to MRONJ is Denosumab. In our study, attention was focused on different therapeutic approaches considering patients treated only with Denosumab or in combination with other drugs associated with the genesis of ONJ. We considered two different clinical approaches: sites treated without surgery; sites treated with traditional surgery or Er:YAG laser (2940nm, 250mJ, 20Hz). In our study, the discontinuation of the drug was evaluated in relation to treatment outcomes.

Background

A rare adverse event of pharmacological therapy with anti-resorptive and / or anti-angiogenic drugs is known as medication-related osteonecrosis of the jaw (MRONJ). One of the most frequent monoclonal antibodies linked to MRONJ is Denosumab. In our study, attention was focused on different therapeutic approaches considering patients treated only with Denosumab or in combination with other drugs associated with the genesis of ONJ. We also considered the drug holiday in relation to treatment outcomes ^[1].

Materials and methods

Thirty-one patients affected by DRONJ are included in the present evaluation. Among these, 22 (71%) female and 9 (29%) male, 23 (74.2%) cancer and 8 (25.8%) non-cancer. Considering the patients included in this study, we analyzed thirty-six DRONJ sites. Among these, 28 (77.8%) associated to cancer and 8 (22.2%) non cancer. Based on the AAOMS classification (update 2014), the present study included 1 (2.8%) site in stage 0, 9 (25%) sites in stage I, 18 (50%) in stage II and 8 (22.2%) in stage III ^[2]. We considered two different clinical approaches: T1: 15 (41.7%) sites treated without surgery; T2: 21 (58.3%) treated with traditional surgery or Er:YAG laser (2940nm, 250mJ, 20Hz). T1 and T2 were all treated with Amoxicillin 1g twice a day in association with Metronidazole 500mg twice a day for three weeks. We have performed five weekly sessions of low level laser therapy (LLLTT, 1064nm, 1.25w, 15 Hz) using Nd:YAG laser. In T1, 11 (73.3%) sites are localized in patients that have stopped Denosumab two months before our treatment and 4 (26.7%) in patients that have continued Denosumab. In T2, 14 (66.7%) sites are localized in patients which have stopped Denosumab two months before treatment and 7 (33.3%) in patients that have continued Denosumab.

Results

In T1, up to 73.3% of sites improved clinically and up to 33.3% got complete healing. In T2 100% of sites improved clinically and got complete healing. Considering the suspension or not of Denosumab in T1: up to 63.6% of sites that have interrupted Denosumab before treatment improved clinically and up to 36.4% got complete healing; 100% of sites that have continued Denosumab improved clinically and up 25% got complete healing. In T2: 100% of sites that have interrupted Denosumab improved clinically and got complete healing; similar results were obtained in sites of T2 that have continued Denosumab.

Conclusions

In the literature there is no unambiguous opinion on how to discontinue the drug before treatment. Considering our study, the surgical treatment is more effective than the conservative approach ^[3]. Discontinuation of Denosumab before treatment does not appear strongly significant for complete healing and especially in clinical improvement (that is a transition from an upper to a lower stage) in the case of a conservative approach. The “drug holiday” does not show significant differences in terms of treatment outcome considering patients treated surgically.

References

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