Treatment of Acute Radiodermatitis with *Cryptomphalus Aspersa* Secretion

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SUMMARY

Presentation of a clinical study in 100 patients with acute radiodermatitis, treated with *Cryptomphalus Aspersa* secretion (n=50) or the vehicle (n=50) for three months. Patients were evaluated at one week, and one, two, three and six months after start of therapy. The group treated with *Cryptomphalus Aspersa* showed a statistically significant clinical improvement in rash, itching and burning, both at one week and after one month on therapy.

These results open a door into the future treatment of acute radiodermatitis. *Cryptomphalus Aspersa* is an alternative therapy for many patients diagnosed of malignant tumors which require radiotherapy, with specially good results in breast and neck radiodermatitis.

Introduction

Radiation dermatitis usually develops after a latency period of 6 to 12 days. It may occur in different degrees in the form of rash, edema, blisters and/or skin necrosis. Lesions reach peak intensity at 2-3 weeks (1). There is no specific and standardized therapy for radiodermatitis, and although incidence has decreased with the use of mega-voltage instruments it can influence the therapeutic schedule and impair the patients' quality of life (2). Treatment generally involves the use of topical emollients and/or corticoids (3, 4).

Cryptomphalus Aspersa, is a mollusk, exceptionally preserved throughout evolution. When subjected to different kinds of stress or biological alarm (recalling a previous evolutionary situation) it secretes a substance which has been termed *Cryptomphalus Aspersa* secretion (CAS). CAS has a dual mechanism of action: firstly, a collagenase activity against type IV collagen facilitates the remodeling of the skin's basal membrane (since denaturalized collagen is more susceptible to collagenase activity) and, secondly, the stimulation of fibroblast proliferation facilitates biochemical mechanisms that reconstruct the skin (5). The antioxidant properties of this substance have been recently identified, due to its glutathione-S-transferase and superoxide dismutase activity (6).

Based on the above, a topical treatment for acute radiodermatitis using CAS (in a cream-gel form) was proposed (7).

Material and Methods

Open, controlled study: *Cryptomphalus Aspersa* (Endocare® gelcrem biorepar, Industrial Farmacéutica Cantabria) compared with its vehicle.

A total of 100 patients (mean age: 59.09 ± 12.81 years, 63 female and 37 male) were included in the study. The patients had been diagnosed with acute radiodermatitis and were undergoing mega-voltage radiotherapy, 1.3 MeV (Cobalt-60 high energy source), or had completed treatment the previous month. Total mean dose given to patients was 5219.23 ± 57.85 cGy, and mean duration of treatment was 6 weeks.

Phototype distribution of patients included in the study was as follows: III (65%), II (24%) and IV (11%).

A total of 61% were diagnosed with breast cancer. The remaining 39% were diagnosed with other types of cancer (Table 1).

Patients had to apply Endocare® gelcrem (n = 50) or the vehicle (n = 50) once a night, for 3 months. The groups were similar as regards

age, gender, phototype and total dose received.

A clinical and photographic assessment of the patients were performed at the Dermatological Department, Hospital Ramón y Cajal, baseline and at one week, one month, two months and three months from start of treatment. Then, follow-up monitoring was carried out at 3 months from discontinuation of treatment. The clinical parameters included: rash, desquamation, pigmentation, pruritus and burning, graded according to the following scale:

0: none
1: mild
2: moderate
3: severe
4: very severe

In the descriptive statistical study the mean, standard deviation and frequency (percentage) were calculated. A univariate analysis using the Mantel-Haenszel chi-squared test was performed for the comparative study.

The relationships of Endocare®/vehicle therapy with rash, desquamation, pigmentation, pruritus and burning sensation were assessed.

Likewise, to determine a possible effect of treatment on the clinical signs and symptoms with regard to the baseline dose (cGy), 5 groups were studied: 1000-2000, 2000-3000, 3000-4000, 4000-5000, 5000-6000.

Other parameters included in the analysis were: total dose received and combination or no combination with chemotherapy during the treatment.

The presence or absence of combination with chemotherapy was analyzed in two ways:

1. Relationship between chemotherapy and clinical signs and symptoms, taking into account the two treatment groups.
2. Effect of Endocare® gelcrem, on the clinical signs and symptoms, taking into account whether patients were receiving chemotherapy or not.

Results

The clinical study demonstrated a statistically significant clinical improvement in the group of 50 patients treated with Endocare® gelcrem compared to the group of 50 patients who received the vehicle alone, in the following parameters:

- *RASH:*
22.16% (p=0.009) at one week; 54.78% (p=0.016) at one month.
- *PRURITUS:*
42.88% (p=0.004) at one week; 66.4% (p=0.013) at one month.
- *BURNING:*
48.48% (p=0.001) at one week; 87.87% (p=0.001) at one month.

Improvement of these three parameters was significant at one week and one month from start of treatment. The results obtained after 3 months of treatment with Endocare® gelcrem were maintained at three months after completion of the study, with pigmentation gradually improving in all cases.

As regards the effect of Endocare in relation to baseline dose of radiotherapy at the beginning of treatment, the percentage improvement of rash was higher with baseline radiotherapy doses of above 5000 cGy. Pruritus and burning improved at one week and one month, regardless of the baseline dose. However, an statistical evaluation was not feasible due to the small size of the sample in each group.

There were no statistically significant differences in each treatment group as regards the total dose of radiotherapy received.

Chemotherapy had no significant effect on the clinical signs and symptoms of radiodermatitis. Neither were there any differences found in terms of response to treatment with Endocare in patients undergoing chemotherapy.

None of the patients included in the study experienced adverse reactions during Endocare® and/or vehicle treatment.

Discussion

This study demonstrates that the clinical improvement of acute radiodermatitis with *Cryptomphalus Aspersa* secretion therapy, is most remarkable in those signs and symptoms that cause the most discomfort in patients undergoing radiotherapy: rash, pruritus and burning.

The best results of Endocare® gelcrem treatment are statistically significant at one week and one month of radiotherapy, for the three parameters mentioned above. In the case of rash differences were also seen after two months of Endocare® gelcrem application. The vehicle group had a similar response and their radiodermatitis gradually improved (3rd month of treatment).

Creams, ointments, gels and foams are not generally used in radiotherapy regimens because of the potential adverse effects due to

TABLE 1- DIAGNOSES

Breast cancer 61% (n = 61)

Carcinomas in the cervical spine region 24.6% (n = 13)

- Cavum (n=1)
- Larynx (n=1)
- Nasopharynx (n=1)
- Tongue (n=3)
- Maxillary (n=1)
- Floor of the mouth (n=1)
- Cervical metastasis of a tumor of unknown origin (n=3)
- Orapharynx (n=1)
- Parotid gland (n=1)

Other tumors 22.4% (n=17)

greater radiation penetration. However, no changes have been observed in this regard, neither in the Endocare® group nor the vehicle group. These results raise the possibility of the vehicles being responsible for these changes.

Improvement in pruritus and burning in this study appear to be independent from the baseline dose of radiotherapy at the start of therapy, although rash showed higher percent improvement with baseline doses of 5000 rads.

Furthermore, the concomitant use of Endocare® with chemotherapy did not effect the degree of radiodermatitis nor the therapeutic response to Endocare® (8).

These results open a door for future acute radiodermatitis therapy but further, more controlled studies are warranted. *Cryptomphalus Aspersa* secretion is a therapeutic alternative for a large group of patients diagnosed with malignant tumors undergoing radiotherapy, and has shown particularly good results in breast and neck radiodermatitis.

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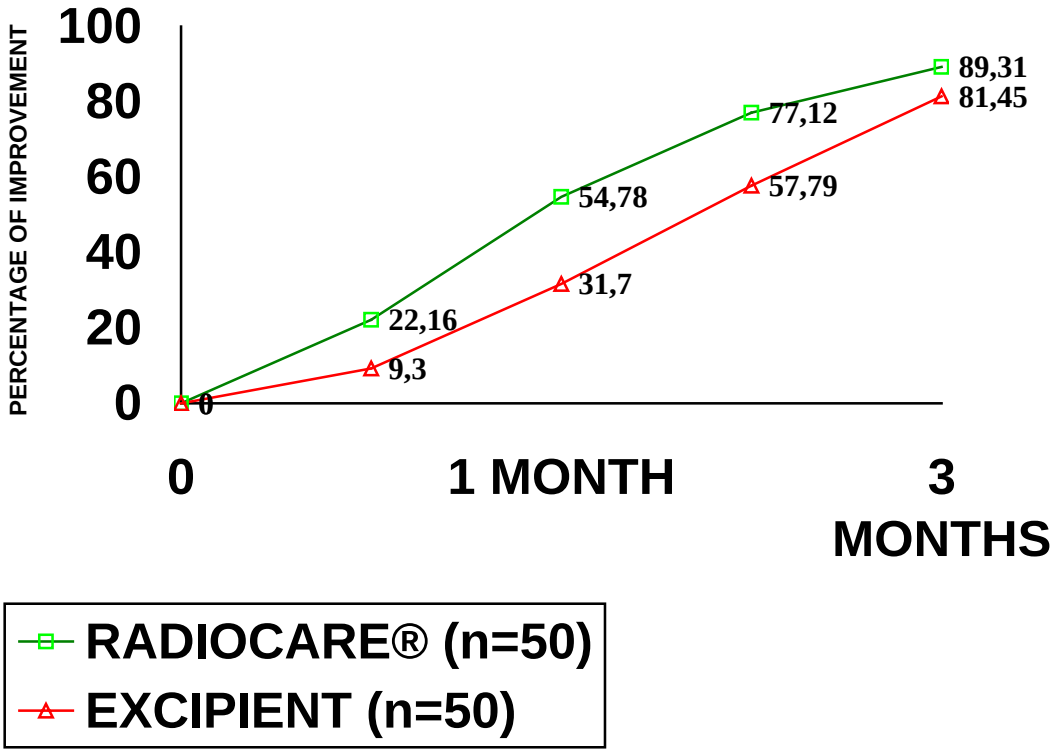
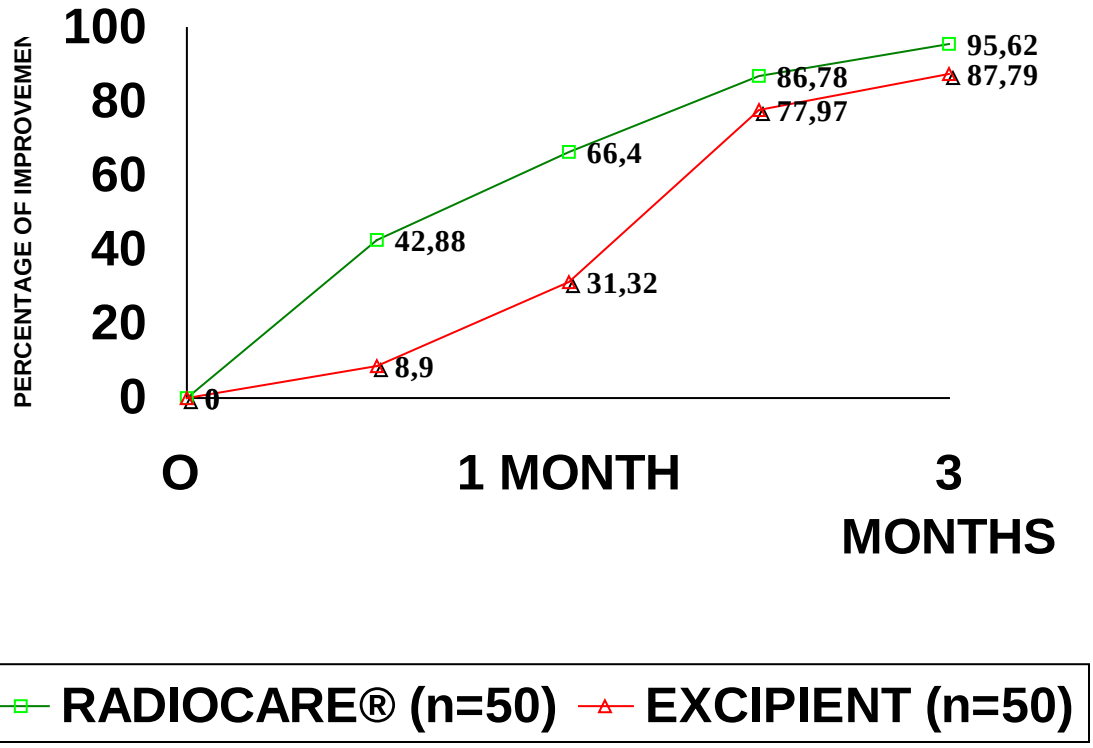
GRAPH 1: RASH


PERCENTAGE OF IMPROVEMENT
100
80
60
40
20
0
0
1 MONTH
3 MONTHS
89,31
81,45
77,12
57,79
54,78
31,7
22,16
9,3
0
RADIOCARE® (n=50)
EXCIPIENT (n=50)

GRAPH 2: PRURITUS



GRAPH 3: BURNING