



Brief Report

Resource® Arginaid® Extra

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Important Note: This brief report summarises information on Resource® Arginaid® Extra. It has not been systematically developed according to a predefined methodology. It is not intended to replace clinical judgement, or be used as a clinical protocol. A reasonable attempt has been made to find and review papers relevant to the focus of this report. It does not claim to be exhaustive.

Introduction

The purpose of this report is to provide information concerning the efficacy of Resource® Arginaid® Extra with respect to wound healing; in particular, for pressure ulcers. ACC has recently received a request to fund Resource® Arginaid® EXTRA for pressure ulcer management. If funded, this product would be supplied through medical consumables.

Resource® Arginaid® EXTRA is an enteral nutritional supplement marketed by Novartis Pharmaceuticals to promote wound healing¹. The product is sold in ready to drink 237ml tetrapaks and also as a powder for mixing with water/juice or using in cooking. It has supplemental levels of l-arginine – a semi-essential amino acid, zinc and vitamins C and E.

Background

Arginine is said to be “indispensable... in the process of wound healing and maintenance of a positive nitrogen balance”². This may be because it provides a substrate for collagen synthesis at the wound site leading to increased wound strength and increased collagen deposition. It may also stimulate T-cell function, the activity of which is essential for wound healing².

Investigation

The following databases were searched: Medline (OVID, 1966-Sept 2006), CINAHL (1982-Sept 06), the Cochrane Database for Systematic Reviews (CDSR), Cochrane Controlled Trials Register (CCTR), Database of Abstracts of Reviews of Effectiveness (DARE), Turning Research into Practise (TRIP) and Embase. In addition, other sites were accessed for additional general information and current clinical guidelines. These included: National Institute for Health and Clinical Excellence, <http://www.nice.org.uk/>; The European Pressure Ulcer Advisory Panel, <http://www.epuap.org/>; The American Food and Drug Administration, <http://www.fda.gov/> and the Scottish Intercollegiate Guidelines Network, <http://www.sign.ac.uk/>.

The search strategy included “arginaid extra”, “arginine supplements”, “wound healing”, “pressure sore/ulcer”, “venous/arterial sore/ulcer”, and combinations of these and other terms. This search excluded animal and non-english studies. Please also note that although Resource® Arginaid® EXTRA is marketed for the management of ulcers and burn wounds, the search was confined to pressure ulcer care as per the EBH request. Despite this, no articles concerning burn wound healing were excluded after database searching. Due to the limited literature for Resource® Arginaid® EXTRA studies concerning arginine-containing supplements were also reviewed.

Results

One study only was identified from the literature search relating to Resource® Arginaid® EXTRA³. This study was a randomised controlled trial investigating the effects of different dietary interventions on nutritional status and pressure ulcer healing in a group of hospital inpatients with existing pressure ulcers

Population: Ten males and six females between the ages of 37-92 were recruited from the aged care or spinal injury wards over a 6 month period from a public hospital and randomised using a computer generated list of random numbers. Pressure ulcer severity varied from stage 2-4.

Inclusion/Exclusion Criteria: Patients with osteomyelitis or diabetes mellitus were excluded as were patients already receiving enteral or parenteral nutritional support. Patients prescribed >10mg steroids or hydroxyurea were also excluded due to the effect on wound healing.

Intervention: Subjects were randomised into one of three dietary groups: (a) standard hospital diet; (b) standard hospital diet + 2 x tetrapaks daily of a high protein, high energy supplement (Total daily supplementation = 500k/cal, 18g protein, 0g fat, 72mg vitamin C, 7.5mg zinc – Resource® Fruit Beverage); or (c) standard hospital diet + 2 x tetrapaks daily Resource® Arginaid® EXTRA (Total daily supplementation = 500k/cal, 21g protein, 0g fat, 500mg vitamin C, 30mg zinc, 9g arginine). All patients underwent two-hourly turning schedules, had a dynamic air mattress for their bed and a gel cushion for sitting. Dressing types depended on wound position, exudate and the presence or absence of infection.

Outcomes: An assessor blinded to group allocation measured ulcer size and severity using the Pressure Ulcer Scale of Healing⁴ (PUSH). This scores the ulcer on wound

size (cm²), exudates and tissue type. Patient weight, total dietary intake and blood biochemistry (protein, zinc and vitamin C levels) were also measured. Measurements were recorded at 0, 1, 2 and 3 weeks.

Results: Overall PUSH scores were significantly reduced in the Resource® Arginaid® EXTRA group from baseline to 3 weeks as well as between groups at 3 weeks. The results represent a “2.5 fold greater improvement in pressure ulcer healing after 3 weeks compared to the other two diet groups”.

Study Summary: Baseline characteristics were dissimilar with respect to body mass index (BMI) and age. Dietary compliance was reported as 94%. The authors did not report how the losses to follow-up (n=3) were managed in terms of statistical analysis. It must be noted this study is of poor quality as there was no reporting of patient or investigator blinding or allocation concealment nor did they specify the use of the intention to treat analysis. The study numbers were very small.

Of Note

Two other studies⁵⁻⁷ (One RCT and one prospective case series) also investigated the specific use of arginine-containing supplements (but not Resource® Arginaid® EXTRA) in patients with pressure ulcers. Both studies that investigated those with existing pressure ulcers reported positive results in terms of pressure ulcer size and severity reduction. Benati et al used a product containing 500k/cal energy; 37g protein, 7.5g arginine, 25mg Zinc and anti-oxidants whilst the latter two studies used Cubitan (Novartis) (Quantities per 100ml: 125kcal, 10g protein, 1.5g l-arginine, 5.0g zinc, 125mg vitamin C, 50mg vitamin E and 1mg Carotenoids). Houwing et al investigated the effect of Cubitan on the development of pressure ulcers following hip fractures. No statistical significance was reported between the intervention and control groups (4 wks intervention or till discharge).

Although not included in this paper's population of interest, two final studies^{8,9} of low quality (RCT's) found lower fistula⁹ and general infection^{8,9} rates in a group of patients following head and neck cancer surgery using arginine-containing supplements.

Conclusions

Dietary supplementation for patients with pressure ulcers using Resource® Arginaid® EXTRA has been reported in one study only to date. This study was positive for the use of the product to assist pressure ulcer healing. Although this study was a randomised controlled trial, the study was of low quality and the sample size was very small. There is other limited evidence for the effectiveness of other arginine-containing supplements. This evidence is not, however, robust. Based on the current literature the clinical effectiveness of Resource® Arginaid® EXTRA is unknown. There is a need for more randomised controlled trials to investigate this further.

Characteristics of Included Studies

Author	Design	Population	Intervention	Outcomes	Level of Evidence/Comments
Desneves, Todorovic, Cassar et al (2005)	Single blind Randomised controlled trial	<ul style="list-style-type: none"> • 16 patients (37-92 yrs), 10 male and 6 female, with stage 2, 3 or 4 pressure ulcers. • Excluded Diabetics 	Patients randomised to 1 of 3 groups; (1) standard hospital diet (n=6); (2) standard diet + high protein supplement (n=5; and (3) standard diet + 2 tetrapaks arginine daily(n=5)	<p>Pressure ulcer size and severity using Pressure Ulcer Scale for Healing (PUSH) at baseline, 1,2 and 3 weeks after dietary changes; Blood biochemistry at above times.</p> <p>PUSH scores improved from baseline (p<0.01) in arginaid extra group; Week 3 results significantly lower than other diets (p<0.05). No significant changes in biochemical markers in any group at 3 weeks.</p>	<p>Unknown allocation concealment or subject blinding. Loss to follow-up, n =3, no report ITT. Small numbers Score = 1-</p>

References

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