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# Nutritional regulation of wound healing: the role of different amino acid mixture composition intake in wound repair. A preliminary study

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The ability of the skin to repair wounds requires immediate changes in metabolism and expression and silencing of the genes controlling cell proliferation, migration, adhesion and differentiation.

The energetic costs of wounds repair are enormous (1). Collagen represent around 50% of skin weight (about 20Kg), and synthesis costs are around 4 ATPs for any single amino acid (AA) inserted into the final composition of collagen (2). Moreover, the AA availability is indispensable to ensure the correct repair of the wound. Indeed, the poor state of dermal collagenous matrix is largely responsible for both the propensity to injury and slowness to heal observed in the elderly.

To test whether different formulation of AA mixture could improve wound repair, we fed male rats (14 months old) with three balanced diet containing 1) 100% essential AA mixture (EAA); 2) EAA 10% plus 90% non-essential (NE) AA (deficient diet - D) and 3) EAA 40% plus NEAA 60% (casein like diet – CL) for 30 days. Then, four excisional wound (diameter 5mm) were surgically made on dorsal skin of each animal. After 3, 15 and 30 post wound days (pwd) the wound area were measured, collected and analyzed by Sirius Red and IHC methods for TGFβ1 and Collagen 1. The D diet reduced weight of the animals up to 30% in 60 days although there was an increase of >18% of spontaneous caloric introduction, whereas the EAA and CL diets increased the rat weight of 6% and 12% respectively. Three pwd, the injured area in EAA and CL diets was 92% and 98% respect to day 0 (100%); whereas it was larger (120%) in D diet. Fifteen pwd, the wounds were completely closed with EAA diet, whereas with CL and D diets the open area were 14% and 45% respectively. Thirty pwd, all wounds were closed but large scars were observed in D diet. TGFβ1 was early and strongly expressed in D diet, whereas it was much less expressed in EAA and CL diets. Sirius-red staining showed that the collagen architecture was more organized with EAA diet and less organized with D diet. Collagen was strongly expressed 15 pwd in CL diet and less expressed in D and EAA diets, whereas 30 pwd an intense staining was observed only in EAA diet. Our data show for the first time that malnutrition, diet rich in NEAA, seriously affects metabolism, leading to rapid decay of the animals and slows down the wound closure, due to dermal collagenous matrix impairment and collagen production, and possibly related to excessive TGFβ1 expression. On the contrary, EAA diet controls expression of TGFβ1 and collagen production, accelerating the wound repair and blunting scarring.

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