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Nutrients for Enhancing Wound Healing in Veterinary Patients

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Abstract

Wound healing entails many biological and molecular processes such as clotting, inflammation, migration-proliferation and remodeling. Vitamins like A, B, C and D; minerals including zinc, magnesium and iron, protein and amino acids are necessary to reduce the inflammatory process and enhance collagen synthesis and ultimately add in enhancement of wound healing without scar formation. Veterinarians should include these nutrients in prescription for effective management of traumatic or surgical wounds.

Keywords: Amino acid, Protein, Trace element, Vitamin, Wound healing

Introduction

Nutrition is one of the most important aspects for management of either natural or surgical wounds and is often overlooked as an issue in Veterinary patients handling. Malnutrition is well identified risk factor for recovery must be identified and should be corrected pre-operatively. Attention to basic nutrition and provision of adequate supplements will help to cure chronic wounds. In 1932, Cuthbertson defined the concept of peripheral to visceral redistribution of metabolic substrates as part of adaptive mechanism to heal wounds in critically ill trauma patients. Nutrients required in the body in minute quantities such as vitamins and trace elements are known as micro-nutrients. These minerals are often referred to as trace elements. Certain minerals, such as calcium, magnesium and phosphorus, which are present in large quantities in the bone and other tissues, are included in the category macro minerals. One of the most common functions of trace elements and certain macro minerals, is to serve as cofactors for enzymatic reactions (Teitelbaum *et al.,* 2005). On the other hand, those nutrients that cannot be synthesized in the body, such as Vitamin C and minerals are called as essential/ indispensable nutrients and those nutrients that are necessary in the diet under defined metabolic circumstances where the needs of body cannot be met by endogenous synthesis mechanisms are known as conditionally

essential conditionally indispensable nutrients providing optimal nutrition must be understood as a dynamic process as need of the animal changes on the basis of amount of exercise they do, stage of production, pregnancy and certain disease conditions. For example, an adequately nourished patient may become acutely malnourished over a short period of time due to increased metabolic needs of an injury or sepsis. Under these circumstances, a wound that is healing perfectly may be diminished until nutritional deficits can be met. A complete history and physical examination alone has been found to be 80-90 percent accurate in evaluating patient nutritional status. Mal-nutrited patients are predisposed to increased septic complications, pneumonia or impaired wound healing (Raslan *et al.,* 2010). Brief periods of nutritional intervention in malnourished patients can fully restore collagen synthesis ability. There have been multiple prospective studies to demonstrate that enteral feeding is superior to parenteral feeding in reducing from septic complications (e.g. pneumonia, abdominal abscesses, sepsis) in those patients requiring nutritional supplementation (Sena *et al.,* 2008). Wound healing process includes a complex series of interactions between different blood cells, cytokine mediators and extracellular matrix. As we know that best wound healing requires adequate blood supply and nutrients at the damaged site, the overall health and nutritional status of animal influences ultimate outcome of injured tissue. Increased metabolic demands caused by inflammation and cellular activity in healing wound requires increased protein or amino acids, vitamins and minerals (Stadelmann *et al.*, 1998).

Vitamins and Minerals

Researchers working on the complex process of wound healing have identified several nutritional co-factors involved in tissue healing and regeneration, including Vitamins A, C and E, zinc, arginine, glutamine and glucosamine.

Vitamins for Wound Healing

Vitamin A

Vitamin A functions as a hormone and alters the activity of epithelial cells, melanocytes, fibroblasts and endothelial cells (Reichrath *et al.*, 2007). Vitamin A is used topically in dermatology for many years for treating sun burns, psoriasis and dermabrasion. It maintains the epithelial cells on skin surface and the mucous membranes. It stimulates the immune system and increases collagen and extracellular matrix formation, fibroplasia, glycoprotein and proteoglycan formation. It increases cross-linking of newly formed collagen. It also heals fractures, burns, bowel and radiation induced injury (Gropper *et al.,* 2009). It reverses the anti-inflammatory effects of corticosteroids on wound healing. Chickens diet supplemented with Vitamin A (150,000 IU/kg chicken chow) has twice wound- breaking

strength (Greenwald *et al.,* 1990). Sepsis, tendon damage and fractures benefit from peri- operative vitamin A supplementation. Vitamin A enhances non-steroid induced, post-operative immune system.

Vitamin E

Vitamin E promotes cellular membrane growth, protecting against damage by oxidation. It reduces injury to wound by excessive free radicals (Shukla *et al.,* 1997). Vitamin E as a free radical removes inflammatory cascades in necrotic tissue, tissue colonized with microbial flora, ischemic tissue, and chronic wounds. It increases breaking strength and collagen content of the wound by inhibiting lipid peroxidation (Galeano *et al.,* 2001). Vitamin E makes more stable cell membrane by preventing lipid peroxidation. It also includes stabilization of lysomal membrane and reverses several deleterious effects of glucocorticoids (Ehrlich *et al.,* 1973).Vitamin E normalizes healing of wounds exposed to pre-operative irradiation and decrease the development of intraperitoneal adhesions in animals (Kagoma *et al.,* 1985).

Vitamin C

Vitamin C is an important co-factor for synthesis of skeleton, cutaneous tissues, collagen, capillary walls, proteoglycans and other connective tissues. Its deficiency leads to abnormal collagen fibers and alterations of intracellular matrix (DaRocha *et al.,* 2002). Vitamin C is the prime necessity for the hydroxylation of proline and lysine residues in procollagen, which is necessary for its release and conversion to collagen. Apart from this, Vitamin C increases the function of neutrophil and enhances neovascularization in healing tissues (Nicosia *et al.,* 1991). It functions as a very good antioxidant (Frei *et al.,* 1988) and is necessary for a normal response to injury. Ascorbic acid increases during times of injury or stress (Pugliese, 1998) and increase in reactive oxygen species (ROS) has been observed within wounds; therefore, substances that enhance the level of antioxidants in tissue are thought to benefit wound healing (Gupta *et al.,* 2002). Various etiologies leading to wounds, including trauma and surgery, are worked as physiological stressors that have also been correlated with a decrease in the level of plasma ascorbic acid (Hemila and Douglas, 1999). Thus, the acute stress experienced by trauma or surgery patients may unmask marginal Vitamin C deficiencies which are responsible for deficiency symptoms. It was observed that skin healing wounds have lower ascorbic acid content than normal intact tissue.

Vitamin D

Vitamins D also has beneficial effects on wound healing. Modulation of structural integrity and transport across epithelial barriers is the key role of Vitamin D. It has been used potentially for the treatment of venous and pressure ulcers (Kalava *et al.,* 2011; Ribas and Santosh, 2012).

Minerals for Wound Healing

Zinc

Zinc is an essential trace mineral for synthesis of DNA and protein and act as co-factor for RNA and DNA polymerase (Prasad, 1995). It is also necessary for cell division and for tissue regeneration and repair. Zinc deficiency leads to decreased protein and collagen synthesis during healing. This results in poor wound healing and poor breaking strength of wounds (Agren and Franzen, 1990). Zinc levels were 50 percent higher in muscle and skin as compared to abdominal wounds of rats during wound healing (Senapati and Thompson, 1985). Requirement of zinc is highest from time of wounding throughout the early inflammatory phase. Just after wounding, zinc levels increased and highest level was noticed on fifth day at a time of high inflammation, granulation tissue formation and epidermal cell proliferation (Lansdown *et al.*, 1999). By seventh day, zinc concentrations returned to normal, when inflammation had subsided. Surgery and wounding increases local demand for zinc and topical use of zinc to surgical wounds consistently augment wound healing (Lansdown *et al.*, 2007). Zinc heals wound in both animals and humans. Repletion of zinc to normal levels promotes fibroblast proliferation and collagen synthesis. Zinc levels can be depleted in settings of severe stress and in patients receiving long-term steroids. Both Vitamin A and Zinc supplements improve wound healing. The recommended daily allowance for Zinc is 15 mg.

Magnesium

Protein and collagen formation and tissue growth requires magnesium as an important trace element that functions as a co-factor (Arnold and Barbul, 2006). Collagen synthesis is done by Magnesium, when it interacts with adenosine triphosphate. About 53 percent of Magnesium is present in skeleton and 45 percent in soft tissues. Overall, 99 percent of Magnesium is associated with the connective tissue (Elin, 1987).

Copper

Of the numerous trace elements present in body. Copper, zinc and iron have the closest relationship to wound healing. Copper is a required cofactor for cytochrome oxidase and cytosolic antioxidant superoxide dismutase. Lysyl oxidase is a key copper enzyme used in development of connective tissue, where it catalyzes the crosslinking of collagen and strengthens the collagen framework (Stipanuk and Caudill, 2013).

Silver

Silver and its oxide are used in wound healing effectively. Silver nanoparticle has antimicrobial activity (Lara *et al.,* 2011) and improves tensile properties of wound by alignment of collagen (Kwan *et al.,* 2011) Silver nanoparticles with chondroitin sulfate and acharan sulfate stimulate wound healing and accelerate collagen deposition and new tissue formation in the wound area (im *et al.,* 2013).

Other Dietary Supplements for Wound Healing

Bromelain

Bromelain is a family of proteolytic enzymes derived from pineapple plant. It reduces edema, bruising, pain and healing time following trauma and surgical procedures (Tassman *et al.,* 1965). This is probably related to its anti-inflammatory action rather than a direct analgesic effect (Austin *et al.,* 1999). It increases resorption rate of hematomas.

Glucosamine

Hyaluronic acid, a glycolsaminoglycans is an integrated component of extracellular matrix (ECM) and secreted during tissue repair. During the proliferative stage of wound healing, hyaluronic acid in production by fibroblasts stimulates the migration and mitosis of fibroblasts and epithelial cells at the healing site. Glucosamine is the rate limiting substrate for synthesis of hyaluronic acid (McCarty, 1996). Glucosamine stimulates the synthesis of glycosaminoglycans and collagen (Zupanets *et al.,* 2002). Lehto and Jarvinen (1985) observed that the level of glycosaminoglycans within the site of partially wounded muscles peaks on fifth day of trauma and thereafter decreased to normalcy. Glucosamine supplementation is recommended during this period for maximum therapeutic impact on wounds. Administration of glucosamine through oral route both pre-operative and post-operative or just after trauma will enhance hyaluronic acid production at the wound site and wound will heal faster with fewer complications related to scarring.

Proteins

Adequate protein intake is essential for optimum growth of the animal and wound healing Protein deficiency may increase morbidity and mortality in the surgical/trauma patients. It affects almost all the stages of wound healing and deficiency leading to delay in wound healing by prolongation of inflammatory phase. In proliferative phase, its deficiency inhibits fibroplasia, collagen and proteoglycan synthesis, and neovascularization. Remodeling phase is also affected and leads to decrease in tensile strength of wounds (Haydock *et al.,* 1988). Individuals with either low serum protein or serum albumin had significantly weaker wounds than those with normal protein values. Thus, it is emphasized to

increase protein quantity in diet to optimize healing and immune function, and to prevent post-surgical complications in these Individuals having wound (Correia and Waitzberg, 2003). Minor surgery may not significantly increase the protein requirement of the healthy patients; however, if the animal is protein malnourished, wound healing will be delayed unless dietary protein intake is increased. The protein requirements after major surgery should be increased by 10 percent. The animal with multiple traumas may need percent more protein. The animals with burn wound require high protein supplements.

Amino Acids

Arginine

Arginine is a non-essential amino acid that plays a very important role in protein and amino acid synthesis. Sufficient arginine in the tissue is essential for efficient wound healing and immune response (Toriosian, 1994). It increases the level of hydroxyproline and subsequent collagen deposition at the wound site. It helps in activating lymphocyte response as well as insulin-like growth factor-1, which controls wound healing process (Kirk *et al.*, 1993).

Glutamine

Glutamine plays a very important role in wound healing process. It is utilized by inflammatory cells and fibroblasts within the wound for proliferation as well as a source of energy (Newsholme, 2001). Fibroblasts use glutamine for these same purposes, as well as for protein and nucleic acid synthesis. Glutamine is released from skeletal muscle following Injury or surgery. Intravenous glutamine in surgery patients as an alanine-glutamine dipeptide showed consistently better post-operative results (Souba, 1992).

Conclusion

For better wound healing with minimum scar formation, it is essential to fulfill the nutritional requirement of the wounded patient. We should recommend minerals, vitamins and other food supplements for early and better wound healing without scar formation.

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