Healing action of nerve growth factor on lameness in adult goats

Nicola COSTA (a), Marco FIORE (b) and Luigi ALOE (b)

(a) Facoltà di Farmacia, Università degli Studi “Magna Graecia”, Catanzaro, Italy
(b) Istituto di Neurobiologia, Consiglio Nazionale delle Ricerche, Rome, Italy

Summary. - We investigated the effect of nerve growth factor in goats affected by lameness, a condition that is associated with cutaneous ulcers, abscesses and granulomas. Lesions were treated daily with 1 µg of nerve growth factor (NGF), dissolved in 100 µl of sesame oil or with sesame oil only. Healthy controls were treated with sesame oil only for periods ranging from two to four weeks and behavioral, biochemical and histopathological conditions were evaluated. Topical application of NGF, but not sesame oil, promoted ulcer healing in all goats within two-three weeks of treatment. The effect of NGF was to re-establish in about 60 days normal locomotion and indirectly to improve feeding behavior and milk production. These findings suggest that NGF might be clinically useful for healing damaged skin in goats and confirm previous studies on human corneal ulcers.

Key words: ulcer, NGF, lameness, skin, behavior, goat.

Riassunto (La molecola NGF promuove la guarigione della pododermatite nella capra adulta). - La pododermatite (PDD) è una malattia molto diffusa tra caprini, ovini e bovini, caratterizzata da una progressiva distruzione necrotica del derma mentre il nerve growth factor (NGF) promuove la guarigione di ulcere oculari e cutanee nell’uomo. Partendo da questi dati sperimentali sedici capre adulte affette da PDD sono state trattate con 1 µg al giorno di NGF per tre settimane. Otto capre affette da PDD sono state trattate con il solvente e utilizzate come controllo. Otto capre sane sono state trattate con il solvente come ulteriore gruppo di controllo. I risultati dimostrano che l’NGF induce la guarigione delle ulcere podali mentre tale effetto non si nota nei controlli. I nostri studi suggeriscono un potenziale ruolo terapeutico dell’NGF nella PDD dei caprini.

Parole chiave: ulcera, NGF, pododermatite, cute, comportamento, capra.

Introduction

In numerous farm animals and particularly in goats and sheep, lameness is associated with the presence of cutaneous ulcers, abscesses, and granulomas in the interdigital and sole area of the anterior and posterior feet [1-4]. Footpain caused by lameness impairs locomotor activity, alters feeding behavior and decreases body weight [1, 5]. Several factors, including housing and flooring, nutritional, environmental, genetic and contagious factors are believed to be involved in the pathogenesis of lameness [3]. Indeed, lameness in goats may be induced by anaerobic gram-negative bacteria such as Dichelobacter nodosus. At present, the mechanism(s) implicated in this condition remain largely unknown, and the available therapies do not promote complete healing of lesions. In adult female goat lameness can cause decreased milk production, poor fertility, and affect the care of offspring. Therefore, the economic costs are very high and there is a pressing need to understand the mechanism(s) involved in ulcer formation and to identify pharmacological compounds that can be used to promote healing. Thus, the identification of any molecule that is able to block the lesions and/or to promote healing would be of therapeutic interest. It has been reported that topical application of nerve growth factor (NGF), a polypeptide exerting a variety of biological activities on neuronal and non-neuronal cells [6-8] is able to stimulate healing in human corneal and pressure ulcers [9, 10]. Other studies carried out in animal models have also shown that NGF accelerates the rate of wound healing, exerts therapeutic action on damaged peripheral nerve and promotes tissue repair in ocular inflammation [11-14]. These and other studies indicate that the effects of NGF are mediated by NGF receptors present on cutaneous cells, such as fibroblasts, keratinocytes, mast cells and immunocompetent cells [12-16]. Taken together, these observations raised the question whether NGF can exert a similar reparative action on cutaneous lesions of domestic and/or farm animals. To test the validity of this hypothesis, we investigated the effect of topical

Indirizzo per la corrispondenza (Address for correspondence): Luigi Aloe, Istituto di Neurobiologia, CNR, Viale Marx, 15/43, 00137 Rome, Italy. E-mail: aloe@in.rm.cnr.it