CLINICAL PERSPECTIVE

Anti-inflammation – just another word for anti-ageing?

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Sarcopenia, the Greek term for 'poverty of flesh', refers to age-associated loss of muscle mass and strength. The cost of ageing is a potential unmanageable burden for society and ageing-related diseases remain a major challenge to the national healthcare systems. However, in order to develop efficient strategies for treating age-related disorders, including sarcopenia, it is mandatory to unravel the mechanisms underlying the biology of ageing (Johnston *et al.* 2008).

Sarcopenia is a multifactorial condition with contributing factors that may include loss of alpha-motoneuron input, changes in anabolic hormones, and decline in physical activity level. The typical sarcopenic phenotype includes a shift in fibre-type distribution, loss in force-generating capacity, loss of muscle mass and strength, and impaired performance of daily-life activities. However, sarcopenia may also be viewed as a condition driven by pro-inflammatory cytokines. Accordingly, a key question is whether sarcopenia is truly a distinct syndrome or a less aggressive form of a cachexia continuum. Muscle loss results from an imbalance between protein synthesis and degradation. This imbalance is not easily detectable when basal rates of protein turnover are measured, but is detected in the postprandial state in old rats and elderly humans, when fed a normal protein meal (Johnston *et al.* 2008).

Although the signalling pathways and mechanisms whereby inflammation inhibits muscle protein synthesis are not fully understood, a recent mechanistic study published in *The Journal of Physiology* (Rieu *et al.* 2009) lends strong support to the hypothesis that chronic inflammation is an important player in sarcopenia and muscle weakness. They demonstrate that prevention of low-grade systemic inflammation by chronic administration of ibuprofen maintains the anabolic effect of food intake on the regulation of muscle protein metabolism in old rats. Both muscle proteolysis and protein synthesis were insensitive to food intake, whereas decrease of low-grade inflammation by ibuprofen restored protein synthesis.

The anti-inflammatory rationale may be of importance not only with regard to maintenance of muscle mass, but with regard to several ageing-associated chronic diseases. Ageing is associated with chronic low-grade systemic inflammation, or '*inflamm-ageing*' and accompanies several chronic non-communicable diseases (CNCDs). Evidence exists that inflammation is involved in mediating insulin resistance, atherosclerosis, neuro-degeneration and tumour growth. In continuation, systemic low-grade inflammation appears to be a key player in the development of type 2 diabetes, cardiovascular diseases, Alzheimer's disease and cancer. Targeting inflammation may therefore provide a potential treatment not only for sarcopenia, but also for the prevention of a number of chronic age-associated diseases (Pedersen, 2009).

While the study by Rieu *et al.* (2009) convincingly provides a link between inflammation and muscle protein metabolism in rats, there is still a gap to fill with regard to the clinical relevance of this finding. It remains to be shown if non-steroidal anti-inflammatory drugs can be safely administered to humans to obtain systemic concentrations that will in fact counteract inflammation-induced inhibition of protein synthesis. The therapeutic potential of high-dose anti-inflammatory drugs has been limited by bleeding risk. However, recent evidence has pointed at the potential of, for example, salsalate, a dimer of salicylic acid, which has an established safety profile and is an equipotent inhibitor of NF-κB while at the same time having a lower bleeding risk than, for example, aspirin. Salsalate has promising effects on inflammation-induced insulin resistance (Fleischman *et al.* 2008). Hopefully, other clinical studies will evaluate whether non-steroidal anti-inflammatory drugs may counteract inflammation-induced loss of muscle mass in humans.

Meanwhile, it is suggested that elderly people should be encouraged to avoid a physically inactive life style. Substantial evidence exists that regular exercise decreases systemic low-grade inflammation. Given that regular exercise offers protection against loss of muscle mass, type 2 diabetes, cardiovascular diseases, Alzheimer's disease and some cancers, it is suggested that regular exercise may exert some of its beneficial health effects by inducing anti-inflammatory actions. Regular exercise, including strength training, represents a low-risk low-cost, but highly efficient mode to combat chronic inflammation in the elderly. In future, targeting inflammation, either with drugs or exercise, may prove to constitute an efficient anti-ageing cure.

References

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