Diabetologia (2006) 49:2813–2814
DOI 10.1007/s00125-006-0453-7

LETTER

Comment on: White PJ, Marette A (2006) Is omega-3 key to unlocking inflammation in obesity? Diabetologia 49:1999–2001

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Received: 8 August 2006 / Accepted: 14 August 2006 / Published online: 19 September 2006

To the Editor:

We read with great interest the commentary by White and Marette in *Diabetologia* [1]. The authors correctly emphasised a key role of adipose tissue, and its inflammatory background, in the development of obesity-related metabolic disorders, particularly insulin resistance and the metabolic syndrome. Of the multitude of potential mechanisms involved, the authors highlighted the role of a negative modulation of macrophage function through activation of peroxisome proliferator-activator receptor γ (PPARγ) [1]. Dietary supplementation with omega-3 might prevent macrophage infiltration into adipose tissue and the related increase in inflammatory gene expression and proinflammatory cytokine production [2]. In agreement with their statement, and on the basis of our previous investigations [3, 4], we would like to add some comments on the regulation of monocyte function, discussing the possible application of these mediators (omega-3) in other fields, such as the prevention of obesity-related cardiac remodelling.

Monocyte recruitment from blood vessels, primarily by monocyte chemoattractant protein 1 (MCP-1), and subsequent macrophage infiltration and accumulation in the myocardium seem to play a pivotal role in cardiac remodelling [5]. It has been shown that serum MCP-1 levels and visceral adipose tissue (VAT) are associated with morphological and functional echocardiographic abnormalities, and these observations provide evidence that visceral fat predisposes to cardiac dysfunction, possibly through low-grade inflammation [4]. Moreover, the strong association between VAT and cardiac dysfunction has been highlighted in the absence of obesity-related complications, such as hypertension and insulin resistance [4].

Although previous studies have implied a role for insulin resistance in the pathogenesis of left ventricular hypertrophy, adjustment for BMI appeared to considerably attenuate this relationship, rendering it statistically non-significant under conditions of normal glucose tolerance [6].

It is against this background that an inflammatory link between VAT and cardiac remodelling has been suggested [4]. Given that human adipose tissue is metabolically active and able to secrete different bioactive proteins, a proportional increase of circulating cytokines with adiposity can be assumed. Thus, chronic exposure to inflammatory stimuli might lead to progressive macrophage infiltration and the gradual impairment of both diastolic function and cardiac morphology [4]. We believe that greater attention should be paid to this hypothesis, particularly when considering that adipose tissue macrophage activities are suggested to occur after the increase in adiposity but prior to the development of insulin resistance [7]. Activation of anti-inflammatory pathways seems to play a key role in prevention, and these effects may be achievable not only in adipose tissue but also in the myocardium. It has previously been observed that PPARγ agonists suppress monocyte elaboration of inflammatory cytokines [8]. In addition, PPARγ activation reduces macrophage infiltration and inhibits left ventricular remodelling, with a concomitant reduction in detrimental hypertrophy and fibrosis [5].

Thus, if the unlocking of inflammatory activation in adipose tissue through the use of omega-3 has been considered, this may also be hypothesised within the

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myocardium via different mechanism, such as reducing monocyte infiltration and macrophage accumulation, or downregulating gene expression and monocyte function. It should be noted, however, that the presented application of omega-3 is currently only theoretical and requires further investigation. The only conclusion that can be drawn from the currently available data is a clear suggestion to adopt a healthy dietary pattern.

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