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## A d d e n d u m

### Children with familial hypercholesterolemia express inflammatory markers. Statin effect on neopterin

T Ueland<sup>1</sup>, A Wiegman<sup>5</sup>, J Rodenburg<sup>5</sup>, B.A. Hutten<sup>5</sup>, L Gullestad<sup>4</sup>,  
L Ose<sup>2</sup>, JJP Kastelein<sup>5</sup>, P Aukrust<sup>3</sup>, AG Semb<sup>2</sup>

Research Institute for Internal Medicine<sup>1</sup>, Section of Lipidology and  
atherosclerosis<sup>2</sup>, and Section of Clinical Immunology and Infectious diseases<sup>3</sup>,  
Rikshospitalet, Oslo, Medical department, Bærum Hospital<sup>4</sup> Norway,  
Department of Vascular Medicine, Academic Medical Center<sup>5</sup>, Amsterdam,  
The Netherlands



## Background

Atherosclerotic disease involves inflammatory and immunologic mechanisms, but the sequence of immunomodulatory steps and which molecule(s) having key roles early in atherogenesis is not clear. Micro C-reactive protein ( $\mu$ -CRP) is established as an inflammatory marker of atherosclerosis. Neopterin, a marker of cellular immune activation, is produced by human macrophages. HMG-Co A reductase inhibitors, statins, have been recognized as immunomodulators and reduce cardiovascular events and mortality.

## Objectives

In this study we examined the levels of neopterin and  $\mu$ -CRP in children with heterozygous familial hypercholesterolemia (FH) because FH has been regarded as a model of atherosclerosis. We evaluated the impact of pravastatin.

## Methods

Children aged 8-18 years, with FH (n=214), were randomised in a double blind fashion and given pravastatin 20 to 40 mg bid (n=106) or placebo (n=108) and followed for 2 years. Their (n=85) unaffected siblings were followed on a yearly base as well.

## Results

There were no differences between the groups concerning demographic data. The children with FH had a significant ( $p<0.009$ ) elevated level of neopterin compared to normal siblings ( $4.89\pm 0.21$  vs  $4.33\pm 0.14$  nmol/L respectively). Furthermore, 2 years of pravastatin therapy reduced the neopterin level with 15% to  $4.23\pm 0.13$  nmol/L compared to placebo which had a 7 % reduction ( $4.6\pm 0.18$  nmol/L)( $p<0.001$ ). There were no difference between the FH-children ( $0.11\pm 0.02$ ), siblings ( $0.10\pm 0.03$ ) and controls ( $0.07\pm 0.03$ ), concerning  $\mu$ -CRP at baseline. Furthermore,  $\mu$ -CRP increase significantly in both FH-children receiving pravastatin ( $0.25\pm 0.09$ ) and placebo ( $0.17\pm 0.095$ )( $p<0.05$ ).

## Conclusion

Our findings suggest that the cellular inflammatory marker neopterin is an early marker in the atherosclerotic process shown in this study in children with FH. This inflammatory response is modified by statins.

