Monocyte suppressing action of fenofibrate

Bogusław Okopień, Jan Kowalski, Robert Krysiak, Krzysztof Łabuzek, Aldona Stachura-Kutach, Andrzej Kutach, Marek Zieliński, Zbigniew S. Herman

Correspondence: Bogusław Okopień, e-mail: mtbbokop@p.pl

Abstract:
Since atherosclerosis has been proven to be an inflammatory disease, it is obvious that the proper treatment for dyslipidemia should not only correct lipid parameters but also inhibit inflammation. Monocytes and monocyte-derived proinflammatory cytokines are widely known to be involved in the formation and rupture of the atherosclerotic plaque. The aim of our study was to assess the effect of fenofibrate, a commonly used hypolipidemic drug, on the release of interleukin 1β (IL-1β), interleukin 6 (IL-6) and monocyte chemoattractant protein 1 (MCP-1) by monocytes from patients with combined hyperlipidemia. Fourteen patients with biochemically confirmed type IIb dyslipidemia who did not respond to a low-fat diet were treated with micronized fenofibrate for 1 month. The control group included 12 healthy, normolipidemic, age-matched subjects. To accurately evaluate the levels of the inflammatory cytokines, we excluded patients with any inflammatory disease. Monocytes were isolated from peripheral blood before and after the treatment. IL-1β, IL-6 and MCP-1 release was measured by enzyme-linked immunosorbent assay (ELISA) after lipopolysaccharide stimulation.

IL-1β, IL-6 and MCP-1 levels were significantly higher in hyperlipidemic patients compared to the control (143.9 ± 6.5 vs. 74.4 ± 4.4 pg/ml; 8212 ± 285 vs. 6110 ± 170 pg/ml; 19.6 ± 0.9 vs. 12.3 ± 0.6 ng/ml, respectively). Thirty-day fenofibrate treatment decreased the release of IL-1β by 43% (143.9 ± 6.5 vs. 86.2 ± 5.9 pg/ml), of IL-6 by 22% (8212 ± 285 vs. 6330 ± 234 pg/ml), and of MCP-1 by 29% (19.6 ± 0.9 vs. 14.0 ± 0.8 ng/ml).

The evaluated cytokines were markedly elevated in patients with type IIb dyslipidemia. Effective fenofibrate therapy had a significant inhibitory effect on the release of monocyte-derived inflammatory cytokines.

Key words: dyslipidemia, atherosclerosis, fibrate, proinflammatory cytokines, monocyte

Abbreviations: IL-6 – interleukin 6; IL-1β – interleukin 1β; MCP-1 – monocyte chemoattractant protein 1

Introduction

Atherosclerotic cardiovascular disease is the principal cause of death and disability nowadays. Recent years have witnessed many studies indicating that some inflammatory factors play a significant role in the initiation and growth of the atherosclerotic plaque. Such immune cells as monocytes, macrophages and T lymphocytes belong to the most important constituents of the atherosclerotic plaque [24]. Activated immune cells produce and secrete such cytokines as monocyte chemoattractant protein 1 (MCP-1), interleukin 1β (IL-1β) and interleukin 6 (IL-6). It has been proved that the migration of monocytes into the subendothelial space and the release of proinflammatory cytokines initiate atherosclerotic injury to the arterial wall [19].