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The translational research of adrenomedullin as a potential therapeutic agent for ulcerative colitis

Adrenomedullin (AM) is a potent vasodilatory peptide ubiquitously produced in organs throughout the human body. AM shows multi-functional properties including diuresis, angiogenesis, inhibition of aldosterone secretion and anti-inflammatory activity. AM production and secretion can be induced by pro-inflammatory cytokines such as tumor necrosis factor- α and interleukin-1 and by lipopolysaccharide. Conversely, AM causes the down regulation of inflammatory cytokines in cultured cells. Furthermore, AM down regulates inflammatory processes in a variety of different colitis models, including acetic acid-induced colitis and dextran sulfate sodium induced colitis. AM works by exerting anti-inflammatory and antibacterial effects and by stimulating mucosal regeneration and supporting maintenance of the colonic epithelial barrier. We assessed the safety and preliminary efficacy of exogenous AM administered to patients with refractory ulcerative colitis in an open-labeled exploratory trial. AM (1.5 pmol/kg/min) was administered intravenously for 8 hours daily for 12-14 days. Disease activity index (DAI) score and endoscopic findings were evaluated before and after administration of AM. We enrolled seven patients with active ulcerative colitis, refractory to usual combination medical therapy. In all patients, DAI score after AM therapy was improved compared with that at baseline. The average DAI score of all patients improved from 9.3 ± 1.5 points at baseline to 4.7 ± 2.2 points at two weeks and to 1.2 ± 1.1 points at 12 weeks. Endoscopic findings also showed remarkable amelioration with mucosal healing and scarring. During infusion of AM, hemodynamics kept almost stable, and no adverse effect has shown clinically. In conclusion, AM is a promising agent for patients with refractory ulcerative colitis.

Biography

Kazuo Kitamura graduated from Miyazaki Medical College with MD and received his PhD in Biochemistry from Miyazaki Medical College. He worked as a Post-doctorate at the University of Texas Southwestern Medical Center from 1985 until 1988. From 1988 to 1995, he was Assistant Professor of Miyazaki Medical College, which is where he discovered adrenomedullin in human pheochromocytoma tissue. Since 2006, he has been a Professor in the Department of Internal Medicine in the University of Miyazaki. His areas of research interest are translational researches in cardiovascular disorders as well as inflammatory bowel diseases.

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