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Effects of icodextrin on the integrin-mediated wound healing of peritoneal mesothelial cells

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Chronic exposure to peritoneal dialysis fluid (PDF) causes structural alterations in the peritoneal membrane such as the loss of the mesothelial cell monolayer. Remesothelialization can be suppressed by high content levels of glucose and glucose degradation products in PDF. In the present study, we investigated the effect of icodextrin on wound healing of peritoneal mesothelial cells and determined the mechanisms involved. We examined the effects of icodextrin on the regeneration process of the peritoneal mesothelial cell monolayer by an in vitro wound healing assay in cultured rat peritoneal mesothelial cells (RPMC) treated with 0% to 70% vol/vol solutions of icodextrin- or glucose-containing PDF. To evaluate the sole effect of icodextrin, remesothelialization was also examined in RPMC exposed to an icodextrin-dissolved culture medium without PDF. The effects of icodextrin on the activation of integrin-mediated intracellular signaling molecules were examined by Western blotting, immunocytochemistry, and a cell spreading assay, respectively. Conventional acidic, lactate buffered glucose-containing PDF (Dianeal) inhibited cell migration over fibronectin in a concentration-dependent manner, however, icodextrin-containing PDF (Extraneal) had no significant inhibitory effect. The inhibitory effect of glucose-containing PDF on cell migration was stronger than that of the identical glucose concentration. The culture medium containing 2.5% glucose inhibited remesothelialization, cell spreading, and formation of focal adhesions as confirmed by vinculin immunostaining, however, the culture medium containing 7.5% icodextrin had no inhibitory effect on any of these mesothelial cell functions. Furthermore, glucose suppressed the tyrosine phosphorylation of focal adhesion kinase (FAK), a key mediator in integrin-mediated intracellular signaling, while icodextrin had no effect on the phosphorylation of FAK. Our results demonstrated that icodextrin had a beneficial effect on the wound healing of peritoneal mesothelial cells by preserving integrin-mediated cell adhesion, thus suggesting that icodextrin-containing PDF may be more biocompatible than conventional glucose-containing PDF.