INTESTINAL MICROBIOTA CHANGES TO BE PROTECTIVE DURING INDOMETHACIN INDUCED SMALL INTESTINAL INJURY

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Background: In intestine, commensal microbiota outnumbers host cells at least nine folds and is mutually beneficial with host. NSAIDs is a widely used clinical drug, but by now, there is no effective treatment for NSAIDs induced small intestinal injury other than withdrawal. We hypothesize that after indomethacin treatment, intestinal microbiota would change and attend NSAIDs enteropathy. Aims and Methods: To study the changes of intestinal microbiota during indomethacin enteropathy, male C57/BL mice were divided into donors and acceptors. For donors, 10mg/kg indomethacin was given by gavage for 2 days, and stool were collected on the 1st (before treatment, NC stool) and 3rd day (IND stool), for the following experiments and 16sRNA sequencing. Acceptor mice included 4 groups with 5 days fecal transplantation: IFT (IND stool treated, n=6-8), NFT (control group, n=6), IFT/IND (IND stool plus 10mg/kg indomethacin once, n=8-12), NFT/IND (NFT stool plus 10mg/kg indomethacin once, n=8-12). Small intestine was collected for injury and inflammation examination. Results: Sequencing data showed changes in intestinal microbiota after indomethacin treated. And IFT mice were found to have a higher PGE2 and COX-1 expression than NFT, while body weight and inflammatory factors showed no difference. Comparing to NFT/IND mice, the small intestine of IFT/IND mice was less damaged, as shown in lower fecal hemoglobin concentration, smaller ulcer percentage, milder histological changes and necropsy score. Moreover, lower expressions of NF-κBp65, IL-1β and TNF-α indicated less inflammation in the IFT/IND mice. Conclusion: Intestinal microbiota was changed to be protective after indomethacin treatment in mice.