

Gut Microbiota in Patients with Opioid Use Disorder: A 12-week Follow up Study

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Abstract : Aim: Opioid use disorder is often characterized by repetitive drug-seeking and drug-taking behaviors with severe public health consequences. Animal model showed that opioid-induced perturbations in the gut microbiota causally relate to neuroinflammation, deficits in reward responding, and opioid tolerance, possibly due to changes in gut microbiota. Therefore, we propose that the dysbiosis of gut microbiota can be associated with pathogenesis of opioid dependence. In this current study, we explored the differences in gut microbiota between patients and normal controls and in patients before and after initiation of methadone treatment program for 12 weeks. Methods: Patients with opioid use disorder between 20 and 65 years were recruited from the methadone maintenance outpatient clinic in 2 medical centers in the Southern Taiwan. Healthy controls without any family history of major psychiatric disorders (schizophrenia, bipolar disorder and major depressive disorder) were recruited from the community. After initial screening, 15 patients with opioid use disorder joined the study for initial evaluation (Week 0), 12 of them completed the 12-week follow-up while receiving methadone treatment and ceased heroin use (Week 12). Fecal samples were collected from the patients at baseline and the end of 12th week. A one-time fecal sample was collected from the healthy controls. The microbiota of fecal samples were investigated using 16S rRNA V3V4 amplicon sequencing, followed by bioinformatics and statistical analyses. Results: We found no significant differences in species diversity in opioid dependent patients between Week 0 and Week 12, nor compared between patients at both points and controls. For beta diversity, using principal component analysis, we found no significant differences between patients at Week 0 and Week 12, however, both patient groups showed significant differences compared to control ($P=0.011$). Furthermore, the linear discriminant analysis effect size (LEfSe) analysis was used to identify differentially enriched bacteria between opioid use patients and healthy controls. Compared to controls, the relative abundance of Lactobacillaceae Lactobacillus (L. Lactobacillus), Megasphaera Megasphaerahexanoica (M. Megasphaerahexanoica) and Caecibacter Caecibactermassiliensis (C Caecibactermassiliensis) were increased in patients at Week 0, while Coriobacteriales Atopobiaceae (C. Atopobiaceae), Acidaminococcus Acidaminococcusintestini (A. Acidaminococcusintestini) and Tractidigestivibacter Tractidigestivibacterscatoligenes (T. Tractidigestivibacterscatoligenes) were increased in patients at Week 12. Conclusion: In conclusion, we suggest that the gut microbiome community maybe linked to opioid use disorder, such differences may not be altered even after 12-week of cessation of opioid use.

Keywords : opioid use disorder, gut microbiota, methadone treatment, follow up study

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