



Cross cultural perspectives on ethics and regulation of fecal microbiota for transplantation

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When reading the article titled “Ethical Issues in Fecal Microbiota Transplantation in Practice” (1) written by Dr. Ma and her colleagues, I was impressed by their delicate analysis of these issues as well as the potential prospect of the fecal microbiota for transplantation (FMT) as a new approach to treatment. It is rather amazing that the experiences of treating gastro-intestinal diseases with human feces were recorded both in the East and West though there being a time difference, now FMT has being practiced in both places with different cultures. As early as 4th century a Taoist doctor named Ge Hong described the “Yellow Dragon broth”, a smart name of human feces which was used to treat food poison and diarrhea in his book titles as *A Handbook of Prescription for Emergency*. Interestingly, the same book contains a description of using the juice made of the plant sweet wormwood (*artemisia apiacea*) which Dr. Youyou Tu used the chemical analysis methods to identify and extract the efficacious components from the plant and prepared the medicine called artemisinin, and then proved its safety and efficacy with randomized controlled trials. Her work led to save millions people’s lives in the world and she was then awarded the Nobel Prize. Both the facts suggest us that Chinese medicine is really a great gold mine to explore for modern medicine, and also the exploring of the mine to get gold needs to use scientific methods including chemical analysis, RCT and others (2,3).

Both ethics and regulation aims at protecting patients as well as promote the application of science and technology into medicine to develop safer and more efficacious interventions to diagnose, treat and prevent diseases. However, an ethical issue is not arisen in a vacuum, but in a social and cultural context which may affect the perception

and solution of the same issue. There may be the same in some aspects, but different in the others. As for whether FMT is a drug or a biological product, the answer may have the moral significance to its regulation (4). However, it is not necessarily so. Stem cell is a biological product, but in China the clinical application of stem cells is strictly regulated as any drug, and both National Commission on Health and Family Planning (NCHFP, the former MOH) and China’s FDA are responsible for the regulation of stem cell clinical trials and application. A stem cell therapy can be only approved to apply in clinical practices until its safety and efficacy are proved by preclinical and clinical research. One of reasons is that during 2005–2012 hundreds hospitals including a lot of public hospitals provided unproven and unregulated so-called “stem cell therapy” (just injection of undifferentiated adult stem cells into patients’ body), and boosted that it is a panacea to treat any disease from diabetes, spinal injuries to autism and cancers to exploit desperate patients. The result is the patient’s condition getting worse, and the patient with her/his family was caught in financial catastrophe. This practice also led to notorious stem cell tourism with thousands of foreign patients seeking magic bullet to China. Eventually there is no medically or scientific valuable result except great financial profits get from hundred thousands of patients by doctors, hospitals and biotech companies. As the result this unsavory scandal discredited stem cell therapy, and Chinese patients became very sensitive to it (5). In this context we need to take appropriate measures to prevent any new method such as FMT from the similar malpractice as “stem cell therapy” for patient’s good especially because of insufficient budget provided by the government public

hospitals are tending to make money from patients by the overuse of drugs, or the misuse of innovative therapy, and give the priority to their own interest over patient's. Thus in Chinese context even FMT is not taken a drug, it is appropriate to treat it as a drug which should be subject to GCP promulgated by China's FDA and Regulations on Ethical Review of Biomedical Research promulgated by NCHPL in which it is stipulated that when any method including physical, chemical, biological, traditionally medical or psychological method is planned to use to diagnose, treat and prevent diseases, it shall be subjected to clinical research and its protocol should be reviewed by IRB.

Although we need to balance the protection of patients and the access to care, and this balance is roughly embodied in US FDA's recent "Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation to Treat Clostridium difficile Infection Not Responsive to Standard Therapies" (6) in which FDA intend to exercise enforcement discretion under limited conditions, regarding the investigational new drug (IND) requirements for the use of FMT to treat Clostridium difficile (C. difficile) infection not responding to standard therapies. FDA intends to exercise this discretion, provided some conditions. However, in view of that the efficacy and safety profiles of this intervention have not yet been fully evaluated in controlled clinical trials, the mechanism of the interaction between microbiota and human body is largely unknown, and moreover, the community of clinical experts have not reach the consensus on the safety and efficacy of FMT as well as many patients still don't believe FMT in China, for patient's good and improving FMT technology we still need to put great stress on FMT clinical trials as well as on basic scientific research, which is the scientific backbone to understand better the relationships between human health and the microbiota in and on human body, and the interaction between genome, microbiota, environment and life style (1,7). And the crucial among the others is to conduct RCT. Only RCT will give us the objective and scientific evidences to prove that FMT is safer and more efficacious than other conventional therapies in treating certain diseases. Only then the community of clinical experts will reach consensus on FMT's safety and efficacy, and the majority of patients are willing to, or can be persuaded to accept FMT. Otherwise it is difficult to obtain informed consent from patients and physicians may prefer other therapy rather than FMT.

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