Effects of a high fat diet on intestinal microbiota and gastrointestinal diseases

Mei Zhang, Xiao-Jiao Yang

Mei Zhang, Department of Gastroenterology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China
Xiao-Jiao Yang, McGill University, Montreal, Quebec H3A 0G4, Canada

Author contributions: The authors equally contributed to this work.

Conflict-of-interest statement: There are no potential conflicts of interest and no financial support was given.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Correspondence to: Mei Zhang, MD, Chief Physician, Professor, Department of Gastroenterology, Xuanwu Hospital, Capital Medical University No. 45 Changchun Street, Xuanwu District, Beijing 100053, China. zhang2955@sina.com Telephone: +86-10-83198438

Received: July 1, 2016
Peer-review started: July 4, 2016
First decision: August 2, 2016
Revised: August 15, 2016
Accepted: September 14, 2016
Article in press: September 14, 2016
Published online: October 28, 2016

Abstract
Along with the rapid development of society, lifestyles and diets have gradually changed. Due to overwhelming material abundance, high fat, high sugar and high protein diets are common. Numerous studies have determined that diet and its impact on gut microbiota are closely related to obesity and metabolic diseases. Different dietary components affect gut microbiota, thus impacting gastrointestinal disease occurrence and development. A large number of related studies are progressing rapidly. Gut microbiota may be an important intermediate link, causing gastrointestinal diseases under the influence of changes in diet and genetic predisposition. To promote healthy gut microbiota and to prevent and cure gastrointestinal diseases, diets should be improved and supplemented with probiotics.

Key words: Intestinal microbiota; Gastrointestinal diseases; High fat diet

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Along with the rapid development of society, lifestyles and diets have gradually changed. Due to overwhelming material abundance, high fat, high sugar and high protein diets are common. Numerous studies have determined that diet and its impact on gut microbiota are closely related to obesity and metabolic diseases. Different dietary components affect gut microbiota, thus impacting gastrointestinal disease occurrence and development. A large number of related studies are progressing rapidly. In this review, we summarize the relationship between a high fat diet, gut microbiota and gastrointestinal diseases.

Zhang M, Yang XJ. Effects of a high fat diet on intestinal microbiota and gastrointestinal diseases. World J Gastroenterol 2016; 22(40): 8905-8909. Available from: URL: http://www.wjgnet.com/1007-9327/full/v22/i40/8905.htm DOI: http://dx.doi.org/10.3748/wjg.v22.i40.8905
INTRODUCTION

Along with the rapid development of society, lifestyles and diets have gradually changed. Due to overwhelming material abundance, high fat, high sugar and high protein diets are common. Numerous studies have determined that diet and its impact on gut microbiota are closely related to obesity and metabolic diseases\(^1\). Different dietary components affect gut microbiota, thus impacting gastrointestinal disease occurrence and development. A large number of related studies are progressing rapidly. In this review, we summarize the relationship between a high fat diet, gut microbiota and gastrointestinal diseases.

BASIC COMPOSITION OF INTESTINAL MICROBIOTA

The intestinal tract is the primary site of bacterial colonization in the human body. These complex and diverse bacteria form the gut flora. There are more than 1000 bacterial species in the human gut and this number can reach as high as \(1 \times 10^8\) species. The intestinal flora is primarily composed of anaerobes, facultative anaerobes and aerobes. Anaerobes comprise more than 99% of gut microbes. The intestinal flora of the human body primarily includes Firmicutes, Bacteroidetes, Actinomycetes, Proteobacteria, Verrucomicrobia and Archaeabacteria. More than 90% are Firmicutes or Bacteroidetes. The Firmicutes, Bacteroidetes, Proteobacteria and Actinomycetes comprise 64%, 23%, 8% and 3% of the gut microbiota, respectively\(^2\). The intestinal flora of the human body is established in infancy and gradually stabilizes with age. By approximately 2 years of age, it is similar to the adult intestinal flora\(^3\). The intestinal flora composition differs by age group. The proportion of Firmicutes and Bacteroidetes in infants, adults and the elderly is 0.4, 0.9 and 0.6, respectively\(^4\).

EFFECT OF A HIGH FAT DIET ON INTESTINAL MICROBIOTA

Diet is an important factor determining intestinal flora composition. It plays a critical role in the colonization, maturation and stability of the intestinal flora. Both animal and human experiments have demonstrated that dietary changes can rapidly affect intestinal flora structure. Within 4 d of eating a specific dietary component, the human intestinal flora composition will change significantly\(^1,5\).

Animal experiments have indicated that dietary structure affects intestinal flora. The proportion of Bacteroidetes decreased and the proportion of Firmicutes increased, which increased the proportion of Mollicutes in the intestinal tracts of mice fed a high fat and high sugar diet compared with mice fed a low fat and high sugar diet\(^6\). Intestinal flora diversity is reduced in mice fed a high fat and high sugar diet. However, control diet consumption gradually reversed these changes. Furthermore, one study investigated varying proportions of dietary fatty acids in mice for 8 wk. A diet high in saturated fatty acids led to an increased proportion of intestinal Firmicutes and decreased intestinal flora diversity\(^7\). This study suggests that dietary fats and saturated fatty acid intake may affect intestinal flora composition. One study found that converting a low sugar, low fat diet to a high sugar, high fat diet caused a rapid decline in the number of Bacteroidetes in the intestines\(^8\). Another study also suggested that the number of Bacillus bifidus was reduced in mice fed a high fat diet\(^9\). Animal studies have demonstrated a significant reduction in the number of lactic acid bacteria, Bacillus bifidus and Enterococcus in the intestinal tract of the group fed a high fat diet. Furthermore, the phylum Bacteroidetes displayed a decreasing trend, while the Bacillus fusiformis displayed an increasing trend\(^10,11\).

Human experiments have also demonstrated that dietary composition affects intestinal flora. Compared with Italian children who consume a large amount of plant protein, fat, sugar and starch, the proportion of Bacteroidetes in the intestinal flora of African children was high, while the proportion of Firmicutes was low\(^12\) (Table 1).

RELATIONSHIP BETWEEN INTESTINAL MICROBIOTA AND GASTROINTESTINAL DISEASES

The composition and proportion of gut microbiota are closely related to human health. Upsetting the gut microbiota equilibrium can cause enteric dysbacteriosis and a variety of gastrointestinal and systemic diseases\(^13\).

Intestinal microbiota and inflammatory bowel disease

Inflammatory bowel disease (IBD) comprises a group of inflammatory conditions of the colon and small intestine, including Crohn’s disease (CD) and ulcerative colitis (UC), the cause and pathogenesis of which are not completely understood. Gut microbiota are closely related to IBD occurrence and development. Although the specific bacteria involved in IBD have not been identified, the gut microbiota in patients with IBD differs from those of healthy individuals. One study\(^14\) determined that the total number of mucosa-associated bacteria in the IBD group was higher than that in the control group. In the CD group, Streptococcus was dominant in the inflammatory mucosal region, while in the UC group, lactic acid Bacillus was dominant. Studies have demonstrated that the number of Faecalibacterium prausnitzii decreased in patients with CD\(^15\). Their secretory products have immune regulatory activity in vitro\(^16\). IBD pathogenesis includes intestinal flora imbalance,
increased pathogenic bacteria, toxin damage to the intestinal epithelium, immune function abnormalities and immune tolerance imbalance. Intestinal bacteria can induce epithelial endoplasmic reticulum stress, leading to intestinal mucosal barrier damage and increased intestinal permeability. Probiotic supplements in patients with IBD can effectively alleviate symptoms and delay disease progress\textsuperscript{17,18}. Intestinal microbiota and irritable bowel syndrome

Irritable bowel syndrome (IBS), affecting approximately 5%-25% of the population, comprises a group of symptoms, including abdominal pain and changes in bowel movement patterns, without any evidence of underlying damage. The mechanisms of IBS are unclear. One study found that 3%-36% of intestinal infections can cause persistent symptoms of IBS, which suggests that gut microbiota play an important role in IBS onset\textsuperscript{19}. Intestinal flora may affect gastrointestinal motility, visceral sensitivity, the inflammatory response and the brain-gut axis, which leads to IBS. A number of studies have confirmed that the intestinal flora of patients with IBS differs from that of healthy individuals\textsuperscript{20,21}. At present, however, intestinal flora composition results in patients with IBS have been inconsistent and some have been contradictory. These inconsistencies may be owing to differences in specimen collection, molecular detection methods or definitions of IBS\textsuperscript{22}. The majority of studies have found that the Bacteroidetes are reduced, while the Firmicutes are increased in the intestinal flora of patients with IBS. However, it is not yet determined whether the changes in intestinal flora directly cause or are secondary to IBS. In the future, treatment of the intestinal flora imbalance may become an option for patients with IBS\textsuperscript{23}. Intestinal microbiota and liver disease

Nonalcoholic fatty liver disease (NFALD) is one of the most rapidly growing chronic liver diseases. Studies have indicated that changes in intestinal flora play an important role in liver disease incidence and progression\textsuperscript{31}. Intestinal probiotics can improve liver disease and are now widely used in its clinical treatment\textsuperscript{22}. Nonalcoholic fatty liver disease (NFALD) is one of the most rapidly growing chronic liver diseases. A number of studies have indicated that intestinal flora play an important role in NFALD development\textsuperscript{33}. Bacterial overgrowth and intestinal permeability are the primary mechanisms underlying endotoxemia and inflammatory reaction-initiated liver disease. One study confirmed the relationship between intestinal bacterial overgrowth and NFALD\textsuperscript{34}. In another study, the relationship between intestinal permeability and NFALD was demonstrated in animal experiments\textsuperscript{35}. Alcoholic fatty liver was also associated with gut-derived endotoxemia. Specifically, ethanol intake in the intestinal tract may cause intestinal mucosal injury and intestinal flora disorder, resulting in increased endotoxin-induced intestinal epithelial permeability, bacterial translocation and endotoxemia\textsuperscript{36}. The intestinal flora in patients with liver cirrhosis is dramatically disordered. One study demonstrated

| Table 1 Effect of a high fat diet on intestinal microbiota |
|----------------|----------------|----------------|
| Diet           | Intestinal flora | Animal experiments | Human experiments |
| High fat diet  | Bacteroidetes  | Decreased       | Decreased       |
|                | Firmicutes     | Increased       | Increased       |
| Low fat diet   | Bacteroidetes  | Increased       | Increased       |
|                | Firmicutes     | Decreased       | Decreased       |

Zhang M et al. Effects of a high fat diet
Zhang M et al. Effects of a high fat diet

a significant decrease in *Bacillus bifidus* and lactic acid *Bacillus* in the intestinal tract of patients with liver cirrhosis, suggesting the possibility of intestinal bacterial translocation and increased infection[37]. The occurrence of primary hepatocellular carcinoma is also associated with intestinal flora imbalance[38].

**CONCLUSION**

In summary, gut microbiota may be an important intermediate link, causing gastrointestinal diseases under the influence of changes in diet and genetic predisposition. A diet that is high in fat, especially high in saturated and trans fat, is closely related to obesity, metabolic syndrome and gastrointestinal diseases; polysaturated fats such as omega-3, omega-6 and omega-9 in right proportions are suggested as substitutes. To promote healthy gut microbiota and to prevent and cure gastrointestinal diseases, diets should be improved with low fat, low sugar, high fruit and vegetable intake and complex fibers and supplemented with probiotics or increased fermented dairy product consumption, such as yogurt and buttermilk. It is essential for patients with GI diseases to not only change their dietary composition, but also to establish a healthy eating habit and pattern to promote healthy microbiota as well as to alleviate disease-associated syndromes. Maintenance of normal gut microbiota may be a potentially key means of preventing GI diseases in the future.

**REFERENCES**

1. Tremaroli V, Bäckhed F. Functional interactions between the gut microbiota and host metabolism. *Nature* 2012; **489**: 242-249 [PMID: 22972297 DOI: 10.1038/nature11552]
2. Eckburg PB, Bik EM, Bernstein CN, Purdom E, Dethlefsen L, Sargent M, Gill SR, Nelson KE, Relman DA. Diversity of the human intestinal microbial flora. *Science* 2005; **308**: 1635-1638 [PMID: 15831718 DOI: 10.1126/science.1105911]
3. Palmer C, Bik EM, DiGiulio DB, Relman DA, Brown PO. Development of the human infant intestinal microbiota. *PLoS Biol* 2007; **5**: e177 [PMID: 17594176 DOI: 10.1371/journal.pbio.0050177]
4. Mariat D, Firmesse O, Levenez F, Guimarães V, Sokol H, Doré J, Corthier G, Furet JP. The Firmicutes/Bacteroidetes ratio of the human intestinal microbial flora. *Nature* 2007; **448**: 102-108 [PMID: 17594176 DOI: 10.1038/nrgastro.2007.3]
5. Hildebrandt MA, Hildebrandt SA, Hamady M, Chen YY, Knight R, Ahima RS, Bushman F, DuPont AW, DuPont HL. The intestinal microbiota and chronic disorders of the gut. *Nat Rev Gastroenterol Hepatol* 2011; **8**: 523-531 [PMID: 21844910 DOI: 10.1038/nrgastro.2011.133]
6. Fydercek K, Strus M, Kowalska-Duplaga K, Gosiętski T, Wędyrowicz A, Jedynak-Wasowicz U, Sladek M, Pieczarkowski S, Adamski P, Kochan P, Heczko PB. Mucosal bacterial microflora and mucosal layer thickness in adolescents with inflammatory bowel disease. *World J Gastroenterol* 2009; **15**: 5287-5294 [PMID: 19908336 DOI: 10.3748/wjg.v15.i7]
7. Walker AW, Sanderson JD, Churcher C, Parkes GC, Hudspith BN, Rayment N, Brostoff J, Parkhill J, Dougan G, Petrovska L. High-throughput clone library analysis of the mncosa associated microbiota reveals dysbiosis and differences between inflamed and non-inflamed regions of the intestine in inflammatory bowel disease. *Microbiol* 2011; **17**: 47 [DOI: 10.1096/1471-2180.11-77]
8. Noor SO, Ridgway K, Scovell L, Kemsley EK, Lund EK, Jamieson C, Johnson IT, Narbad A. Ulcerative colitis and irritable bowel patients exhibit distinct abnormalities of the gut microbiota. *BMC Gastroenterol* 2010; **10**: 134 [PMID: 21073731 DOI: 10.1186/1471-230X-10-134]
9. Cary VA, Boullata J. What is the evidence for the use of probiotics in the treatment of inflammatory bowel disease? *J Clin Nurs* 2010; **19**: 904-916 [PMID: 20492035 DOI: 10.1111/j.1365-2702.2009.03123.x]
10. Whelan K. Quigley EM. Probiotics in the management of irritable bowel syndrome and inflammatory bowel disease. *Curr Opin Gastroenterol* 2013; **29**: 184-189 [PMID: 23286925 DOI: 10.1097/MOG.0b013e32835d7bba]
11. Spiller R, Garsed K. Postinfectious irritable bowel syndrome. *Gastroenterology* 2009; **136**: 1979-1988 [PMID: 19457422]
12. Chassard C, Dapoigny M, Scott KP, Crouzet L, Del’homme C, Marquet P, Martin JC, Pickering G, Ardil D, Eschalier A, Dubray C, Flint HJ, Bernalier-Donadille A. Functional dysbiosis within the gut microbiota of patients with constipated-irritable bowel syndrome. *Aliment Pharmacol Ther* 2012; **35**: 828-838 [PMID: 22315951 DOI: 10.1111/j.1365-2036.2012.05007.x]
13. Carroll IM, Ringel-Kulka T, Siddip J, Ringel Y. Alterations in composition and diversity of the intestinal microbiota in patients with diarrhea-predominant irritable bowel syndrome. *Neurogastroenterol Motil* 2012; **24**: 521-530, e248 [PMID: 22339879 DOI: 10.1111/j.1365-2982.2012.01891.x]
14. Parke GC, Brostoff J, Whelan K, Sanderson JD. Gastrointestinal microbiota in irritable bowel syndrome: their role in its pathogenesis and treatment. *Am J Gastroenterol* 2008; **103**: 1557-1567 [PMID: 18513268 DOI: 10.1111/j.1572-0241.2008.01869.x]
15. Ohman L, Simrén M. Intestinal microbiota and its role in irritable bowel syndrome (IBS). *Curr Gastroenterol Rep* 2013; **15**: 323 [PMID: 23590243 DOI: 10.1007/s11894-013-0323-7]
16. Candela M, Guidotti M, Fabbri A, Brigidi P, Franceschi C, Finerti C. Human intestinal microbiota: cross-talk with the host and its potential role in colorectal cancer. *Crit Rev Microbiol* 2011;
Sobhani I, Tap J, Roudot-Thoraval F, Roperch JP, Letulle S, Langella P, Corthier G, Tran Van Nhieu J, Furet JP. Microbial dysbiosis in colorectal cancer (CRC) patients. PLoS One 2011; 6: e16393 [PMID: 21297998 DOI: 10.1371/journal.pone.0016393]

Kostic AD, Gevers D, Pedamallu CS, Michaud M, Duke F, Earl AM, Ojesina AI, Jung J, Bass AJ, Tabernero J, Basela J, Liu C, Shvidasani RA, Ogino S, Birren BW, Huttenhower C, Garrett WS, Meyerson M. Genomic analysis identifies association of Fusobacterium with colorectal carcinoma. Genome Res 2012; 22: 292-298 [PMID: 22009990 DOI: 10.1101/gr.126573.111]

Zackular JP, Baxter NT, Iverson KD, Sadler WD, Petrovitch JF, Chenb GY, Schlossa PD. The gut microbiome modulates colon tumorigenesis. MBio 2013; 4: e00692-13 [PMID: 24194538 DOI: 10.1128/mBio.00692-13]

Sears CL, Pardoll DM. Perspective: alpha-bugs. their microbial partners, and the link to colon cancer. J Infect Dis 2011; 203: 306-311 [PMID: 21208921 DOI: 10.1093/jinfdis/jiq061]

Tjalsma H, Boleij A, Marchesi JR, Dutilh BE. A bacterial driver-passenger model for colorectal cancer: beyond the usual suspects. Nat Rev Microbial 2012; 10: 575-582 [PMID: 22728587 DOI: 10.1038/nrmicro2819]

Liong MT. Roles of probiotics and prebiotics in colon cancer prevention: Postulated mechanisms and in-vivo evidence. Int J Mol Sci 2008; 9: 854-863 [PMID: 19325789 DOI: 10.3390/ijms9050854]

Henao-Mejia J, Elinav E, Thaiss CA, Flavell RA. The intestinal microbiota in chronic liver disease. Adv Immunol 2013; 117: 73-97 [PMID: 23611286 DOI: 10.1016/B978-0-12-405524-9.00003-7]

Wang Y, Liu Y, Sidhu A, Ma Z, McClain C, Feng W. Lactobacillus rhamnosus GG culture supernatant ameliorates acute alcohol-induced intestinal permeability and liver injury. Am J Physiol Gastrointest Liver Physiol 2012; 303: G32-G41 [PMID: 22538402 DOI: 10.1080/07315724.2012.1072004]

Cope K, Risby T, Diehl AM. Increased gastrointestinal ethanol production in obese mice: implications for fatty liver disease pathogenesis. Gastroenterology 2000; 119: 1340-1347 [PMID: 11054393 DOI: 10.1053/gast.2000.19267]

Wigg AJ, Roberts-Thomson IC, Dymock RB, McCarthy PJ, Grose RH, Cummins AG. The role of small intestinal bacterial overgrowth, intestinal permeability, endotoxaemia, and tumour necrosis factor alpha in the pathogenesis of non-alcoholic steatohepatitis. Gut 2001; 48: 206-211 [PMID: 11156641 DOI: 10.1136/gut.48.2.206]

Farhadi A, Gundlapalli S, Shaikh M, Frantzides C, Harrell L, Kwasy MM, Keshavarzian A. Susceptibility to gut leakiness: a possible mechanism for endotoxaemia in non-alcoholic steatohepatitis. Liver Int 2008; 28: 1026-1033 [PMID: 18397235 DOI: 10.1111/j.1478-3231.2008.01723.x]

Poritz LS, Garver KJ, Tilberg AF, Kolun WA. Tumor necrosis factor alpha disrupts tight junction assembly. J Surg Res 2004; 116: 14-18 [PMID: 14733244 DOI: 10.1016/S0022-4804(03)00311-1]

Wu ZW, Ling ZY, Lu HF, Zuo J, Shen GF, Zheng SS, Li LJ. Changes of gut bacteria and immune parameters in liver transplant recipients. Hepatobilary Pancreat Dis Int 2012; 11: 40-50 [PMID: 22251469]

Dapito DH, Mencin A, Gwak GY, Pradere JP, Jang MK, Mederacke I, Caviglia JM, Khiabanian H, Adeyemi A, Bataller R, Lefkowitch JH, Bower M, Friedman R, Sartor RB, Rabbadan R, Schwabe RF. Promotion of hepatocellular carcinoma by the intestinal microbiota and TLR4. Cancer Cell 2012; 21: 504-516 [PMID: 22516259 DOI: 10.1016/j.ccr.2012.02.007]

P- Reviewer: Czubkowski P, Gobejishvili L S- Editor: Qi Y L- Editor: Roemmele A E- Editor: Zhang FF
