Is there a link between oral microbiome and chronic liver diseases

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Abstract

Background: The oral cavity is a large reservoir of bacteria of more than 700 species or phylotypes and is strongly relevant to host health and disease. The oral microbiota plays an important role for keeping our health by creating a protective layer in the mouth which stops colonization by pathogens. If the microbial composition is disturbed, the oral microbiota may encourage a state of disease in the oral or extra-oral tissues such as the liver. Evidence suggests that a link exists between dysbiotic oral microbiome and liver disease through oral-liver-gut axis. Dysbiosis, defined as a pathological change in the microbiome, has a variable effect on the compensated and decompensated liver cirrhosis.

Development and composition of the oral microbiome:

The oral cavity of neonates is a sterile area that is rapidly inoculated with different microorganisms from the first feedings to begin acquiring resident oral microbiota. Initial colonization occurs rapidly after birth and first colonizers are called the pioneer species including streptococcus salivarius, followed in the first year of life by different aerobes streptococcus, neisseria, actinomyces, lactobacillus and veillonella. Once tooth eruption begins, gingival cervices exist for periodontal microbial colonization and more nonshedding surfaces become available for bacterial colonization.

Bacteria from different groups adhere not only to oral mucosa and tooth but also to each other forming a diverse community, allowing changes in local microbial environment and initiating first steps in oral diseases. This adhesion is achieved by adhesion receptor binding that attach to receptors on host cells or bacteria including pili, cellular transporters and extracellular matrix proteins.

Human microbiome consists of core microbiome representing predominant species existing in different body areas under healthy conditions, and variable microbiome that evolves in response to changes in individual lifestyle or genetic determinants and is unique for each individual. About 700 different species of prokaryotes belonging to 12 different phyla have been detected in the oral cavity; The 12 phyla are Firmicutes.

Although bacteria is the main constituent of oral microbiome and its role is well established in development of many diseases, other organisms share in the oral microbiome like virome and mycobiome with less characterized role. Commonest oral fungi is candida species that is associated with oral candidiasis, while common virome include Epstein-Barr virus and Cytomegalovirus that are linked to oral diseases like periodontitis. Finally two species of protozoa are found in the oral cavity as normal microbiome: entamoeba gingivalis and trichomonas tenax, these two organisms are considered harmless saprophytes and their increased numbers in oral cavity is linked to increased amounts of food debris and bacteria and poor dental hygiene.

Oral microbiome link to health and diseases:

Commensal microbiota play pivotal role in maintaining oral and systemic health; as local and systemic immunity develop in response to interaction between host immune system and commensal flora. Presence of oral microbiota in the mouth cavity prevents...
Oral microbiome link to liver diseases:
Up to 1.5 L of saliva is swallowed daily, and despite acidic media in the stomach presence of oral bacteria in the gut is common. This results in changes in the composition of gut microbiota leading to increased gut permeability, translocation, endotoxemia and systemic inflammation. The link between oral cavity, gut and liver is known as the oral-gut-liver axis and play an important role in development and pathogenesis of many liver diseases. Migration of oral bacteria (e.g. Porphyromonas gingivalis) and other products (e.g.: lipopolysaccharides: LPS, peptidoglycans and bacterial DNA) into systemic circulation is associated with activation of innate immune response. These pathogen associated molecular patterns (PAMPs) activates toll like receptor 4 (TLR4) that activates T cells and neutrophils to produce proinflammatory cytokines and reactive oxygen species. Such response may enhance liver inflammation, fibrosis and progression of portal hypertension.

Bacterial translocation and endotoxemia can directly cause hepatocyte death and deterioration of previously stable liver cirrhosis. Oral microbiome evaluation may also have a potential diagnostic value in patients with liver cirrhosis as evaluation of salivary samples showed increased Enterococcaceae and Enterobacteriaceae in cirrhotic patients, while tongue coat samples in cirrhotic patients showed higher levels of Fusobacterium and Oribacterium compared to healthy individuals.

Abdel Naser et al. studied the effect of chronic hepatitis C virus (HCV) infection on oral microbiome and revealed that those patients had significant microbial diversity compared to healthy subjects and certain bacterial species were found to be increased in the microbiome of chronic HCV patients like streptococcus perioris, streptococcus mitis and Granulicatella elegans, these species are associated with enhanced pro-inflammatory pathways and inhibition of anti-inflammatory pathways. Furthermore, chronic HCV patients successfully treated with direct acting antivirals (DAAs) had a microbial profile largely similar to healthy individuals but not identical to them. Such shift in oral microbiome profile in chronic HCV patients may be attributed to HCV infected B-lymphocytes that secrete lower levels of IgA leading to oral microbial dysbiosis. On the other hand, hepatitis B virus (HBV) induced chronic liver diseases is associated with lower oral microbial diversity with elevated Firmicutes/Bacteroides ratio. Other bacterial species that increased in HBV infection include fusobacterium, parvimonas, eubacterium and treponemamay pass to the gut as opportunistic pathogen and contributes to gut dysbiosis.

In autoimmune hepatitis patients (AIH) oral microbiome showed increases in veillonella dispar, moreover it was associated with disease severity suggesting that it may be associated with lipopolysaccharide synthesis and metabolism of amino acids, this increase correlated positively with pro-inflammatory cytokines like interleukin 6 and 12 (IL-6 & IL-12) Primary biliary cholangitis (PBC) patients hadsignificant changes in some species compared to healthy subjects. haemophilus, veillonella, clostridium, lactobacillus, streptococcus and klebsiella showed increased abundance, whereas bacteroides, sutterella and faecalibacterium were decreased.

Conclusion
There is growing evidence that oral dysbiosis plays a role in the pathogenesis of liver disease and contributes to the overall systemic inflammatory milieu. Consequently, having a better understanding of the oral-gut-liver represents an exciting new research frontier. The oral cavity has potential to be considered an additional factor in future discussions on the impact of microbiota on cirrhosis-associated complications.

References