



All India Institute of Medical Sciences, New Delhi

Guest Lecture on

**Opioids exacerbates dysbiosis of the gut microbiome:  
Implication in IBD and HIV disease progression**

By

**Dr. Umakant Sharma**

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Date: 4<sup>th</sup> November, 2015

Time: 3:00 PM to 4:00 PM

**Venue:**

**Conference Hall, Ground Floor, Centre for Dental Education and Research, AIIMS, New Delhi**

**Entry Free**

**All are cordially Invited**

*Please join us for tea after the lecture*

**R.S.V.P**

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## **Hydromorphone exacerbates dysbiosis of the gut microbiome in a mouse model of IBD**

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### **Abstract**

Morphine is the gold standard for moderate to severe pain management. However, attaining the required degree of analgesia often leads to tolerance involving dose escalation. A large body of studies has shown that morphine treatment can disrupt intestinal epithelial barrier and suppress immune system, which contribute to induction of sepsis. Recently, focus has shifted to the use of hydromorphone, which is considered to be more potent with fewer side effects compared to morphine. Currently, there are no studies describing the effects of hydromorphone on intestinal microbiome, gut barrier function and immunomodulation. In this study, we initially investigated the effects of analgesic doses of hydromorphone on gut microbiota, permeability, bacterial translocation and immune response. Our results show that hydromorphone, in a dose dependent manner, induced changes in microbial composition, barrier disruption and consequently increased bacterial translocation and proinflammatory cytokines. Opioid users are more susceptible for Inflammatory Bowel Disease (IBD) and its development is faster in opioid use or abuse population. Hydromorphone is prescribed to patients with IBD for pain control and associated symptoms including diarrhoea. IBD is a pathological inflammatory condition of the bowel due to gut microbial dysbiosis, barrier disruption and altered immune response. The dextran sodium sulfate (DSS)-induced colitis is widely used and well accepted murine model of IBD. In the present study, we evaluated the effect of hydromorphone on severity of IBD in DSS-induced colitis mouse model. Our results indicated that weight loss, colonoscopic score, colon length shortening, histological score, gut barrier disruption, bacterial translocation and proinflammatory cytokines were significantly greater in hydromorphone treated DSS animals when compared to all other treatment groups. IBD have been associated with alterations in the composition of intestinal flora. To expand the understanding of the pathogenesis, we have investigated the effect of hydromorphone on gut microbiota in DSS-colitis mice. The quantification of different bacterial phylum in intestinal content, their diversity and community structure were analyzed. We found that the microbiota were most profoundly altered in composition in hydromorphone treated DSS-colitis group of mice. The Firmicutes and Proteobacteria abundances were associated with disease status. Pathogenic bacteria Proteobacteria and Verrucomicrobia are increased and characterized by significant Enterobacteriaceae enrichment while Firmicutes are decreased compared with control. These data indicate the role of dysregulation of gut microbiota in acute colitis and disease severity. Increased intestinal permeability results in the invasion of normal microflora and deregulation of the immune response against indigenous microbiota, leading to faster disease development.

### **Keywords**

Inflammatory bowel diseases, Hydromorphone, Microbial dysbiosis, DSS-induced colitis mouse model