

## Department of Dentistry

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Katsuhiko Hayashi, *Professor*  
Shigeru Suzuki, *Associate Professor*

Akihiro Ikai, *Professor*

### General Summary

1. Clinical investigation of patients with medication- related osteonecrosis of the jaw in our department
2. TNF $\alpha$ R-P2X3R mechanisms in trigeminal ganglion neurons are involved in orofacial neuralgia associated with macrophage infiltration in the rat model of trigeminal nerve compression
3. The effect and problem of perioperative oral functional management for the treatment of otorhinolaryngologic neoplas

### Research Activities

*Clinical investigation of patients with medication- related osteonecrosis of the jaw in our department*

Bisphosphonate preparations are used for the prevention and treatment of bone related events such as bone metastasis of solid cancer, paraneoplastic hypercalcemia, multiple myeloma, and bone metabolism diseases such as osteoporosis. However, the bisphosphonate-related osteonecrosis of the jaw (BRONJ), which is an adverse event, is refractory to treatment for scratching of necrotic tissue and antibiotics therapy etc. Recently, osteonecrosis of jaw associated with novel therapeutic agents such as anti-RANKL antibody preparation (denosumab) and angiogenesis inhibitor (bevacizumab, sunitinib), which have different mechanisms of action from BP preparations, have also been reported, that is commonly referred to as Medication-Related osteonecrosis of the jaw (MRONJ).

The subjects were 24 patients diagnosed as MRONJ after seeing Department of Dentistry, Jikei University School of Medicine from January 2014 to January 2016. Among the 24 cases, the primary disease was breast cancer and prostate cancer with each 14 patients. In the administration route, 18 with injections and 6 with oral drugs were administered, among them 7 cases of new therapeutic agent only administration. By site, there were 20 cases of mandible and 4 cases of maxilla, almost all cases of chemotherapy, steroid therapy, or diabetes among risk factors were recognized. In stage classification, 4 cases of I, 14 cases of II, 6 cases of III. There were 14 cases of spontaneous onset and 10 cases after surgical treatment as a trigger for onset. It was suggested that with patients receiving bone resorption suppressive drugs or angiogenesis inhibitors, surgical invasion to the jawbone or bacterial infection may deeply involve in the onset of MRONJ.

*TNF $\alpha$ R-P2X3R mechanisms in trigeminal ganglion neurons are involved in orofacial neuralgia associated with macrophage infiltration in the rat model of trigeminal nerve compression*

Trigeminal neuralgia is characteristic disease accompanying sharp pain and is triggered

by well-recognized motions such as speaking. Some previous studies have reported that demyelination of the trigeminal nerve at the root entry zone is the possible mechanism underlying trigeminal neuralgia. However, the precise underlying mechanisms are not entirely understood.

Male Sprague-Dawley rats (180–200 g) were used in this study. We developed the trigeminal nerve decompression (TNC) model by placing the glass rod on the trigeminal root, and TNF $\alpha$ , TNF $\alpha$ R, P2X3R expression and macrophage infiltration were studied immunohistochemically in the trigeminal ganglion (TG), and also studied the head-withdrawal threshold (HWT) to mechanical stimulation of the whisker pad skin.

After decompression of the trigeminal nerve, mechanical HWT was significantly decreased in TNC rats compared with sham rats. The number of P2X3R-immunoreactive (IR) and TNF $\alpha$ R-IR neurons innervating whisker pad skin, and neurons encircled with ibal1-positive cells was significantly increased in TNC rats compared with sham rats. TNF $\alpha$  was also expressed in ibal1-IR cells. Furthermore, the decreased HWT was significantly recovered following local injection of P2X3R antagonist.

The trigeminal nerve decompression could be a reliable model of trigeminal neuralgia, and the present results suggest that TNF $\alpha$ R-P2X3R signaling associated with TNF $\alpha$  release from activated macrophage is involved in trigeminal neuralgia.

#### *The effect and problem of perioperative oral functional management for the treatment of otorhinolaryngologic neoplas*

The aim of perioperative oral functional management for the treatment of otorhinolaryngologic neoplasm is to prevent complications including surgical site infections and postoperative pneumonia in patients undergoing surgery, and to reduce oral complications such as oral mucositis by chemotherapy or radiotherapy. This oral management is supportive therapy that is required to secure quality cancer treatment.

In our department, approximately 600 cases a year were referred for perioperative oral functional management from medical departments at the hospital such as otorhinolaryngology, cardiac surgery, hematology, and respiratory medicine. Requests from otolaryngology accounted for 25% of those cases. To provide enough preoperative oral management in these cases, cooperation should be facilitated between medicine and dentistry in-hospital and early dental intervention should be encouraged. Furthermore, regional cooperation between hospitals and dental clinics is important to continue oral management after the perioperative period. A multidisciplinary approach is increasingly emphasized during the perioperative period in the medical profession.

#### **Publications**

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