学位の種類	博士（医学）
報告番号	甲第１４０５号
学位記番号	第１０１０号
氏名	廣瀬 泰彦
授与年月日	平成 26 年 3 月 25 日
学位論文の題名	Oxygen nano-bubble water reduces calcium oxalate deposits and tubular cell injury in ethylene glycol-treated rat kidney （酸素ナノバブル水はエチレングリコール投与ラットの腎においてシュウ酸カルシウムの沈着と腎尿細管細胞障害を減少させる） Urolithiasis: Volume 41, Issue 4 (2013), Page 279-294
論文審査担当者	主査：　高橋 智 副査：　大手 信之，郡 健二郎

Oxygen nano-bubble water reduces renal calcium oxalate deposits and renal tubular cell injury in a hyperoxaluric rat model

【Introduction】Renal tubular cell injury induced by oxalate is thought to be the initial trigger of renal calcium oxalate deposition. The subsequent inflammation and retention of crystals in the renal tubules play an important role in kidney stone disease [1]. Water including oxygen nano-bubbles (nanometer-sized bubbles generated from oxygen microbubbles; ONB water) has anti-inflammatory effects [2), 3)]. Therefore, we investigated the inhibitory effects of ONB water using kidney stone forming rats induced by ethylene glycol (EG) and vitamin D_3-treatment. 【Methods】 We examined crystal formation using Pizzolato staining and polarized light optical microscopy. We also evaluated cell injury via urinary excretion of *N*-acetyl-β-D-glucosaminidase (NAG). Renal expression of inflammation-related genes and an oxidative stress related gene were examined by quantitative reverse transcriptase polymerase chain reaction. Renal expression of osteopontin (OPN), monocyte chemoattractant protein-1 (MCP-1), and superoxide dismutase-1 (SOD-1) proteins and

oxidation products and the crystal binding molecule hyaluronic acid (HA) were examined by immunohistochemistry. 【Results】In this model rat, drinking ONB water decreased urinary excretion of NAG and renal expression of MCP-1, OPN, and HA significantly. Sequentially, the area of renal calcium oxalate depositions decreased, and urinary calcium excretion increased. 【Conclusion 】ONB water suppressed renal calcium oxalate deposition through renal tubular cell protection and anti-inflammatory and antioxidant effects in this model rat.

1. Hirose M, Tozawa K, Okada A, *et al*. Gyloxylate induces renal tubular cell injury and microstructural change in experimental mouse. *Urol Res* 2008; **36**: 139–147.
2. Chiba K, Takahashi M. Oxygen nano-bubble water production method. JP, 4080440. 2008-02-15
3. Takahashi M. Tiny bubbles for industry and science. *J Multiphase Flow* 2004; **18**: 324–331 (in Japanese).