

## Short Communication

# Hydrogen Gas Inhalation for Treatment of Advanced Carcinoma

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Therapeutic effects of hydrogen gas for a wide range of disease categories and disease models have been investigated thoroughly and the positive effects were reported since 2007, when Ohsawa et al. showed that inhalation of hydrogen gas can protect the brain against I/R injury and stroke (Nat Med 2007). Hydrogen (H<sub>2</sub>) as a potent antioxidant and anti-inflammatory agent, potentially anticancer-like activities have been suggested (Dole et al. Science 1975). Recent experimental study demonstrates that inhalation of 66.7% molecular hydrogen has an inhibitory effect on lung and ovarian cancer growth and suppresses the proliferation of CSCs-like cells and angiogenesis, which may contribute to its anti-tumor effects (Wang et al. Biomed Pharmacother 2018; Shang et al. Transl Cancer Res 2018). Here we report a 72-year-old woman with advanced gallbladder poorly differentiated adenocarcinoma confirmed pathologically at stage IV (TNM stage T4N1aM0) with massive intrahepatic and the lymph node metastases in hilar area and around the head of the pancreas, and involvement of duodenum, causing upper gastrointestinal obstruction. The patient was extremely exhausted, accompanied by severe anemia and hypoalbuminemia (ZPS 4/5). In the past history, patients with rheumatic heart disease, has recent cardiac dysfunction; fasting blood glucose was increased for a long time, up to 22mmol/L. Blood tumor markers CA19-9, Alpha-Fetoprotein

(AFP) and Carcinoembryonic Antigen (CEA) were all elevated. In addition to receiving symptomatic and supportive care, any conventional “anti-cancer” treatment cannot be used. The patient volunteered to receive hydrogen gas therapy only, inhaled hydrogen (66%) (Hydrogen-oxygen atomizer AMS-H-01, Shanghai Asclepius, China), through a nasal cannula gas flow 3000ml/min. The daily inhalation time was 2 h initially, gradually increased to 6h/d after one month. Within 1 month after treatment, gallbladder and liver tumors enlarged, CA19-9, AFP and CEA levels were increased, but patients felt better, peripheral blood red blood cells, hemoglobin and albumin were all increased. After continuing to inhale hydrogen for 2 months, the patient’s vomiting number was gradually decreased, the gastroduodenal tube was removed. After 3 months, the patient’s performance has markedly improved. The tumor markers completely fell to the normal reference range, and CT showed more than 50% reduction in gallbladder tumors and multiple intrahepatic and hilar metastases (defined as partial remission PR on RECIST). Blood sugar drops to normal when insulin was no longer used. So far, the patient is in a state of continuous remission up to 10 months and is in the process of further improvement (ZPS 1-0/5). This is the first report of longer-term remission after hydrogen inhalation in patients with advanced and metastatic gallbladder cancer. Of particular interest is the discovery of a “false progression” in the tumor at the beginning of hydrogen inhalation and then continuous improvement showing a pattern very similar to the pseudoprogression - alleviation pattern that occurred after PD-1 antibody treatment. Studies have shown that hydrogen gas can inhibit the expression of PD-1 in CD8 T cells and restore exhausted T cell activity (Akagi et al. Oncol Rep 2019). It is speculated that the improvement after hydrogen inhalation in this case may be related to the immunomodulatory effects of the gas, in addition to the generally recognized selective anti-oxidation and anti-inflammation.