The production of high dose hydrogen gas by the AMS-H-01 for treatment of disease

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Abstract

Hydrogen gas is a new and promising treatment option for a variety of diseases including stroke. Here, we introduce the AMS-H-01, a medically approved machine capable of safely producing ~66% hydrogen gas. Furthermore, we propose the significance of this machine in the future of hydrogen gas research.

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A variety of gases are under investigation for treatment of an assortment of diseases (Katz et al., 2015; Langston and Toombs, 2015; Weaver and Liu, 2015), of which, hydrogen gas has become an exciting new treatment for a range of diseases over the last nine years. Although molecular hydrogen research has demonstrated its benefits through a variety of delivery methods including inhalation, drinking hydrogen rich water, intra-peritoneal injection, and infusion of hydrogen-rich saline, inhalation of hydrogen gas has been established as the easiest and simplest route of administration (Cardinal et al., 2010; Liu et al., 2011; Xu et al., 2012; Guo et al., 2013; Homma et al., 2015; Ichihara et al., 2015; Kurokawa et al., 2015; Nakata et al., 2015; Wang et al. 2015; Zhang et al., 2015). As a biological gas, hydrogen possesses the ability to diffuse freely across biological membranes, acting in a variety of functional capacities (Huang et al., 2010). Stroke is a devastating neurological disease. A large body of research has been focus on developing new and better way to improve the overall outcomes (Cheng et al., 2015; Dock et al., 2015; Hara et al., 2015; Li et al., 2015a; Lioutas et al., 2015; Pena and Borlongan, 2015; Reuter et al., 2015; Schlunk et al., 2015; Soliman et al., 2015; Zhu et al., 2015). By inhalation, hydrogen gas is able to pass blood brain barrier effectively, leading to improved neurological deficits in variety of stroke models (Ohsawa et al., 2007; Chen et al., 2010; Lekic et al., 2011; Zhan et al., 2012).

Previous investigators studying the treatment effect of hydrogen gas have typically used a bottled hydrogen gas mixture. Due to the explosive safety concern that flammable gas contained in the mixed gas cannot exceed one third of the lower explosion limit (4%), these preclinical studies were able to administer a maximum dose of 2.9% hydrogen gas (Ohsawa et al., 2007; Eckermann et al., 2012; Hardeland, 2012; Matheson Gas, 2001). At these concentrations, significant dose-dependent benefits have been observed. Investigators testing the therapeutic effect of low dose hydrogen gas have proposed multiple mechanisms of protection, including radical scavenging, anti-inflammatory effects, and anti-apoptotic effects (Li et al., 2012, 2015b; Zhan et al., 2012; Fujii et al., 2013; Kawamura et al., 2013; Yonamine et al., 2013; Kikkawa et al., 2014; Liu et al., 2014; Homma et al., 2015; Jing et al., 2015; Shi et al., 2015).

Recently, investigators have begun to evaluate the efficacy of high dose hydrogen for disease treatment. Asclepius Meditec Co. Ltd., Shanghai, China, has now developed a hydrogen-oxygen nebulizer machine (AMS-H-01), the only hydrogen inhalation device having met "Medical Device III" requirements (Soliman et al., 2015) and suitable for human (**Figure 1**) and animal (**Figure 2**) applications (Asclepius Meditec Co. Ltd., 2016a). Using a standard wall power outlet and having the form factor of a desktop

Figure 1: The AMS-H-01 is equipped with a nasal breathing mask for human treatment by inhalation.

Figure 2: The AMS-H-01 is equipped for animal treatment.
Note: The larger container is used to hold animals during treatment sessions; while, the smaller box is used for moisture and carbon dioxide removal.

computer, the AMS-H-01 impressively produces a ~66% hydrogen gas mixture in real time at a rate of 2–3 L/min. Through a unique water electrolysis method (Asclepius Meditec Co. Ltd., 2016b), the AMS-H-01 splits molecular water into its stoichiometric 2:1 hydrogen to oxygen ratio, explaining the ~66.6% hydrogen and ~33.3% oxygen gas mixture produced by the machine. The AMS-H-01 was created using multiple patents, and strict testing was required for medical approval. Other devices may be able to produce a similar concentration of hydrogen gas but have not met "Medical Device III" requirements (Asclepius Meditec Co. Ltd., 2016b).

Importantly, the AMS-H-01 was designed with an emphasis on safety. Its design prevents formation of a hydrogen and oxygen gas cavity during the electrolysis process. Prevention of gas accumulation as well as an atomization process that occurs in combination with water allows the AMS-H-01 to avoid spontaneous combustion (Asclepius Meditec Co. Ltd., 2016b).

Since the benefits of low dose hydrogen gas have already been supported in literature, we hypothesize that high dose hydrogen gas will demonstrate greater treatment efficacy than low dose hydrogen gas. However, this hypothesis needs to be supported by future studies using AMS-H-01 or an alternate machine capable of producing high dose hydrogen. Optimistically, if high dose hydrogen gas is shown to be beneficial, we predict that human clinical trials will proceed quite rapidly due to the ease of hydrogen gas administration in a clinical setting.

Author contributions
RC conceived, collected the information/figures/references, and drafted the manuscript. LH participated in the manuscript drafting and editing, as well as gathering the references. JZ is the corresponding author, and participated in conceiving and revising of the manuscript. All authors read and approved the final manuscript.

Conflicts of interest
None.

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