Oxyhydrogen Generator For Management Of COVID 19

INTRODUCTION

Hydrogen gas is said to be a new and promising treatment option for variety of diseases. Its applications range from acute illness such as ischaemia–reperfusion injury, shock and damage healing to chronic illness such as metabolic syndrome, rheumatoid arthritis, and neurodegenerative diseases.[1] There is a growing evidence obtained by animal model experiments on molecular hydrogen (H_2) as antioxidant, anti-inflammatory, antiapoptotic and antiallergic.[2-9] The claimed benefits were demonstrated through various delivery methods including drinking hydrogen rich water, intra-peritoneal injection, infusion of hydrogen-rich saline and inhalation.[5, 6, 10-13] However, inhalation of hydrogen gas has been established as the easiest and simplest route of administration. It also allows monitoring of the dose of hydrogen. As a biological gas, hydrogen has the ability to diffuse freely across biological membranes, acting in various functional capacities.[14, 15]

Oxyhydrogen generator is commonly used for engineering applications, transportation as well as for fuel and power generation (for domestic use such as cooking or industry applications such as welding and cutting).[16] In recent years, alongside with the discovery of health and wellness benefits of molecular hydrogen, it has been developed as hydrogen inhalation device for health. The device produces hydrogen (~66%) and oxygen (~33%) gas mixture through water electrolysis method at a rate of 2-3L/min. The electrolysis process splits molecular water into its stoichiometric 2:1 hydrogen to oxygen ratio. The standard specification of the device comprises of an electrolysis unit (at least one positive and one negative plate), a filter unit and a control unit. The control unit is used for adjusting voltage of the positive plate and the negative plate to change the proportion of the produced hydrogen to the produced oxygen.[17, 18]

Figure 1: The AMS-H-01 oxyhydrogen generator is highly portable, equipped with a nasal breathing mask for human treatment by inhalation[18]

In the ongoing epidemic of coronavirus disease 2019 (COVID-19), the use of inhalational hydrogen (H2/O2: 66.6%/33.3%) among suitable patients (criteria not specified) has been included in the national treatment protocol for coronavirus pneumonia in China.[19] The inhalational hydrogen is claimed to be beneficial in two ways;

1. As a therapeutic antioxidant

One of the major mechanisms the COVID-19 virus causes illness is by oxidative stress, producing breakdown products of oxygen including superoxide radical, hydrogen peroxide and hydroxyl radical, which are referred collectively as reactive oxygen species (ROS). These unstable radicals cause damage to various molecules in the body such as fats (lipid peroxidation and cell membrane damage), DNA (genetic malformations) and proteins (enzyme damage). In acute viral-induced oxidative stress, this process is accelerated and may overwhelm the innate ROS detoxification system causing both cellular and organ damage and potential failure.[20, 21] Hydrogen (H_2) eliminates free radicals by acting as specific scavenger of highly active oxidants, hydroxyl radical (OH) and peroxynitrite ($ONOO^-$). It also indirectly reduces oxidative stress by regulating the expression of various genes.[22, 23]

2. As an anti-inflammation

Viral infection is capable of producing an excessive immune reaction in the host by stimulating massive release of cytokines. Unfortunately, at higher levels these same cytokines, in what is sometimes called 'cytokine storm', may cause increased inflammation in the tissues. Dysregulation of immune responses following hyper-inflammation and cytokine storm, may lead to multiple organ failure, pulmonary tissue damage (diffuse alveolar damage with inflammatory infiltration and oedema, interstitial fibrosis) and reduced lung capacity which is well-known in patients with COVID-19 infection.[20,21] Hydrogen (H_2) inhibits oxidative stress-induced inflammatory tissue damage via downregulation of pro-inflammatory and inflammatory cytokines. [22, 23]

EVIDENCE on EFFECTIVENESS and SAFETY

Effectiveness

Based on extensive search through available scientific databases (Ovid MEDLINE, Cochrane Database, PubMed) and Google search engine, there was no retrievable evidence on the effectiveness of inhalational hydrogen using oxyhydrogen generator in the management of COVID-19. However, there was an anecdotal evidence of improvement in respiratory symptoms following the use of oxyhydrogen inhalation device which generated hydrogen oxygen gas mixture in 2:1 ratio (H2/O2: 66.6%/33.3%). No duration or frequency of usage was specified. The testimonies were given by Covid-19 patients in Wuhan Hanyang Hospital (one patient) and Guangzhou Hospital (three patients), China. They described a reduction in chest discomfort and breathlessness as well as resolution of cough symptom (one patient). There was also a testimony by a respiratory physician who involved in managing Covid-19 patients in Wuhan, China. He observed an improvement in dyspnoiec symptom among his patients which he believed was due to the reduction in airway resistance by inhalational hydrogen.[23, 24]

Zhang N et al. (2018) investigated the effect of inhalational hydrogen gas (H2/O2: 67%/33.3%) produced by the AMS-H-01 oxyhydrogen generator on the lung with increase airway resistance, inflammatory pulmonary infiltration and mucos plug formation using asthmatic mice model. The hydrogen gas was administered for 60 minutes once a day for seven consecutive days. It was shown that the hydrogen gas reduced lung resistance [3.53 ± 1.9 cm/H2O/ml/s (pre); 2.052 ± 1.2 cm/H2O/ml/s (post), $p < 0.05$] as well as the accumulation of inflammatory cells [3.22 ± 0.67 (pre); 2.22 ± 0.67(post), $p< 0.01$] and epithelial goblet cell hyperplasia [4.00 ± 0.81 (pre); 2.9 ± 0.73 (post), $p < 0.01$] which led to the reduction in mucus production. There was also significant reduction in inflammatory cytokines present in bronchoalveolar lavage fluid from asthmatic mice model. [IL-4 : 42.11 ± 24.31(pre); 18.91 ± 10.66 pg/ml(post), $p < 0.05$), IL-13: 68.04 ± 35.26 pg/ml (pre);

32.57 ± 4.43 pg/ml (post), $p < 0.05$), TNF-α: 38.62 ± 14.12 pg/ml (pre); 26.12 ± 5.59 pg/ml (post), $p < 0.05$), CXCL15: 141.4 ± 40.75 pg/ml(pre); 106.3 ± 40.75 pg/ml(post), $p < 0.05$] A significant reduction was seen in the oxidative stress index measured by the levels of superoxide dismutase (SOD), malondialdehyde (MDA) and myeloperoxidase (MPO) [Reduction in level of MDA (5.37nmol/mg to 1.82 nmol/mg, $p < 0.05$) and MPO (1.51 U/g to 1.11U/g, $p < 0.05$), increased in SOD activity (16.98 U/mg to 20.92U/mg)]. [25]

Safety

There was no retrievable evidence on the safety of using oxyhydrogen generator for hydrogen gas therapy among COVID-19 patients. However, the use of inhalational hydrogen gas produced by AMS-H-01 oxyhydrogen generator among patients with tracheal stenosis in one experimental study, reported no adverse reaction or inhalation related discomfort occurred.[26]

Previous preclinical studies highlighted explosive safety concern whereby flammable gas contained in the mixed gas cannot exceed one third of the lower explosion limit (4%) and these studies were able to administer a maximum dose of 2.9% hydrogen gas.[27-29]

Cost

The market price of similar hydrogen inhalational device is approximately RM14,000.[30]

CONCLUSION

Based on anecdotal claims and animal study finding, inhalation of hydrogen gas produced by oxyhydrogen generator/machine may play a role in reducing airway inflammation and improving lung function in patient with COVID-19. These therapeutic effects may be involved with correcting the oxidative/antioxidative imbalance and suppressing inflammatory mediators. However, more clinical trials are needed to prove the clinical safety of its use and the therapeutic effects of hydrogen gas at the bedside.

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Based on available evidence up to 9 April 2020

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