



Original Article

Changes in IL-4 and IL-13 expression in allergic-rhinitis treated with hydrogen-rich saline in guinea-pig model

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Abstract

Background

Medical gas hydrogen (H₂) has a special role in airway inflammation; however, the effect of H₂ on allergic rhinitis (AR) remains unclear. This study explored the possible roles of H₂ on the pathogenesis of AR and observed the influences of H₂ on cytokines IL-4 and IL-13.

Methods

An AR guinea pig model was established by nasal ovalbumin sensitisation. Eighteen guinea pigs were divided into three groups, namely, saline control, AR-sensitised, and hydrogen-rich saline (HRS)-treated groups, with each group having six guinea pigs. The frequencies of sneezing and scratching were recorded. The IgE level and cytokine (IL-4 and IL-13) levels in the serum were measured. The expression levels of IL-4 and IL-13 mRNA and protein in the nasal mucosa were also determined by real-time reverse transcriptase–polymerase chain reaction and Western blot. We also observed the infiltration of cytokine (IL-4 and IL-13) in nasal mucosa by immunofluorescence.

Results

The frequencies of sneezing and scratching, as well as the levels of IgE, IL-4, and IL-13, in the serum were higher in the AR group than in the control group ($p < 0.01$), whereas all these parameters were decreased significantly after HRS treatment ($p < 0.05$). The expression levels of IL-4 and IL-13 mRNA and protein in the nasal mucosa were also lower in guinea pigs treated with HRS than those in the AR group ($p < 0.05$).

Conclusions

HRS could affect anti-inflammation in AR and decreased the expression of IL-4 and IL-13.

Introduction

Rhinitis, especially allergic rhinitis (AR), is a major health problem. Several treatments are available for this condition, but none is ideal. Recent studies have shown that gas signal messengers, such as nitric oxide (NO), carbon monoxide (CO), and hydrogen sulphide (H₂S), play important regulatory roles in allergy medicine, which is a rapidly emerging field.^{1, 2}

Molecular hydrogen as an antioxidant possesses protective and therapeutic values because of its ability to selectively reduce cytotoxic reactive oxygen species (ROS). In 2007, Ohsawa et al.³ reported that 2% hydrogen can effectively remove free radicals and evidently reduce cerebral ischaemia–reperfusion (I/R) injury. They found that the treatment effect of hydrogen on cerebral I/R injury is attributed to its ability to diffuse rapidly across membranes, and hydrogen could reach and react with cytotoxic ROS and thus protect against oxidative damage in inflammation. Signal messengers, such as NO, CO, H₂S, and hydrogen (H₂), are also considered to play an important role in the inflammatory processes of the upper and lower respiratory tract physiology.^{4, 5} However, the role of H₂ in AR has neither been elucidated nor reported in previous studies.

AR is a chronic inflammatory disorder of the nasal airways with Th1/Th2 imbalance. IL-4 and IL-13 are immunoregulatory cytokines that are predominantly secreted by activated Th2 cells. Over the past several years, IL4 and IL-13 have been generally acknowledged as key mediators in the pathogenesis of AR, and they directly influence Th2 cell maturation and drift. IL-4 and IL-13 share the same receptor subunit and play pivotal roles in IgE-dependent inflammatory reactions, as well as acting on B cells to induce IgE production. IL-13 is implicated in various allergic responses, including airway hypersensitivity, mucus hypersecretion, AR, and asthma.^{6, 7}

To clarify the role of H₂ in the pathogenesis of AR, we used hydrogen-rich saline (HRS) instead of H₂ for the treatment of guinea pigs because H₂ cannot be controlled. The clinical symptoms of animals, including sneezing and nose rubbing, and IgE were studied as inflammation markers. The expression levels of IL-4 and IL-13 in the serum and nasal mucosa were also studied by ELISA, real-time reverse transcriptase–polymerase chain reaction (RT–PCR), and Western blot to reveal the influence of H₂ on Th2 cytokine in AR.

Section snippets

Material and animal models

High-purity H₂ gas was dissolved in saline for 6h at 0.4MPa to reach a supersaturated level, and gas chromatography was conducted to measure the actual concentration of hydrogen saline.⁸ The HRS was stored at atmospheric pressure and 4°C in an aluminium bag with no dead volume. HRS was freshly prepared every week to ensure that the concentration was always higher than 0.6mmol/L. Gas

chromatography (Biogas Analyzer Systems-1000; Mitleben, Japan) was performed to confirm the hydrogen content in...

Frequencies of scratching and sneezing and IgE level in serum

The frequencies of scratching and sneezing are shown in Fig. 1. The frequencies of scratching and sneezing in the AR-sensitised group were significantly increased compared with the control group ($p < 0.05$). In the HRS-treated group, the frequencies of scratching and sneezing decreased significantly compared with those of the AR-sensitised group ($p < 0.05$). The level of IgE in the AR-sensitised group was higher than that in the control group ($p < 0.01$). After HRS treatment, the IgE content in the...

Discussion

The current study is the first to show the anti-inflammation effect of hydrogen on AR-sensitised guinea pigs. Previous studies showed that gaseous transmitters, such as NO, CO, and H₂S, play important roles in the pathogenesis of AR.^{10, 11} Hydrogen, which is a colourless gas with the lightest element, is increasingly recognised as a new member of the growing family of “gasotransmitters”. In 2007, researchers from Japan reported that hydrogen gas possesses antioxidant and anti-apoptotic...

Conclusions

The results demonstrated that HRS could attenuate AR inflammation by possibly inhibiting the expression of IL-4 and IL-13. However, additional investigations should be conducted to identify the underlying mechanisms of the signalling pathways involved in HRS anti-AR inflammation in the future....

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study....

Right to privacy and informed consent

The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document....

Protection of human subjects and animals in research

The authors declare that the procedures followed were ...

Conflict of interest

The authors declare no conflict of interest in the publication of this paper....

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