TANG [HUMANITAS MEDICINE]

Original Article

A comparison study of the effects of loratadine-pharmacopuncture and loratadine-oral administration based on traditional Korean medicine theory on anaphylactic reaction in mice

Hyun-Min Kim, Hyun-Min Kim, Min-Jung Lee, Min-Gi Cho, Deok Kang, Yu-Kyung Kim, Changmin Kim, Do-Hyun Kang, Si-Hwa Jeong, Ik-Gyun Ahn, Jun-Hyeok Hwang, Jae-Hyun Kim, Hyun-Jin Lee, Jun-Yeong Jang, Ho-Jung Park, Sin woo Kang, Jieun Youm, Seung-won Baek, Eu Jin Kim, Moon-Kou Shin, Chan Park, Chang-Bin Son, Tae-Bin Yim, Jung Hyun Lim, Sung-eun Hong, Jun-Hyuk Choi, Jun-Dong Kim, Dong-ju Yoon, Dong-Min Lee, Soo-Min Yu, Ye-Im Hong, Yeong-Seok Lee, Bon-Cheol Koo, Hyoung-Jun Park, Chae-Yoon Uem, Min-Jeong Kim, Jayoung Oh, Nam-Gyeong Park, Eun-Jong Kim, Whi-Sung Cho, Ho-Sung Lee, Tae-oh Kim, Cheol Yoon, Sung-Keun Kwon, Dong-Hyeon Jeong, Changwon Lee, Sang-Yeol Yu, Chae-won Shon, Gyu-Ri Jeon, Yang-Seok Hong, Ho-Seon Song, Kyung-jin Bae, Yu-Jin Son, Sung-Gyu Hong, Hwa-Pyeong Kim, Gi-Moon Song, Tae-Ha Kim, Hwi-Kyung Kim, Min-woo Jung, Kyung-Bok Park, Young-Gil Song, Tae-Woon Min, Soo-Ho Jeong, Seung-Jae Han, Yoon-Jae Won, Ju-Eun Lee, Tae-Hun Kim, Myung-Chul Cha, Su-Jin Suhl, Cho-Hyun Hwang, Do-Won Lee, Yun-Ha Kim, Ye-Ji Kim, Woo-hyun Kim, Jae-Ho Kim, Yun-Jae Cho, Hye-Jin Lee, Han-Young Lee, Soon-seok Oh, Myung-Sun Kim, Woo-Lim Jeong, Won-Jung Ha, Han-Sol Lee, Lurie Lee, Seo-Jung Ha, Yohwan Kim, Jeong-Weon Huh, Da-Kyung Choi, Sang-Ha Park, Jun-Hyuk Shin, Han-Jung Huh, In-Hu Bae, Han-Lim Lee, Soo-Jong Kim, Won-Jun Lee, Noo-Ri Choi, Jina Jung, Da-Eun Jung, Jee-Hyun Park, Seung-hyun Hong, Hye-jin Jun, Phil-Dong Moon*

Department of Pharmacology, College of Korean Medicine, Kyung Hee University, Dongdaemun-Gu, Seoul 02447, Republic of Korea

ABSTRACT

Pharmacopuncture, or herbal acupuncture, is a new form of therapy derived from combinations of two traditional therapeutic methods, herbal medicine and acupuncture therapy. To compare the efficacy between loratadine-pharmacopuncture (LP) and loratadine-oral administration (LO), the effect of loratadine was investigated in murine models. Anti-anaphylactic effects of loratadine treatments were investigated in compound 48/80-induced systemic anaphylactic reaction and passive cutaneous anaphylaxis (PCA). LP treatment significantly inhibited the compound 48/80-induced systemic anaphylactic reaction and PCA. The effect between LP and LO were on a similar level. These results indicate that LP can be used as an alternative method for LO in case of emergency.

Keywords loratadine-pharmacopuncture, systemic anaphylactic reaction, passive cutaneous anaphylaxis

INTRODUCTION

Pharmacopuncture, or herbal acupuncture, is a new form of therapy derived from combinations of two traditional therapeutic methods, herbal medicine and acupuncture therapy. Pharmacopuncture is mainly categorized depending on the medicinal materials used. There are four main categories: meridian-field pharmacopuncture, eight-principle pharmacopuncture, bee-venom pharmacopuncture, and single-compound pharmacopuncture. Among them, single-compound pharmacopuncture uses extracts from medicinal materials such as Hominus placenta, Scolopendrid, wild ginseng and ginger (Kim and Kang, 2010). Single-compound pharmacopuncture traditionally has used eastern medicinal materials; however, we used western medicinal material in this study. We used the principle of pharmacopuncture treatment, but selected a material from western medicinal materials that work fast. Loratadine (LOR) is an active component of the second generation of selective antihistaminic pharmaceutical usually known as Claritin (Armaković et al., 2016). LOR is an important active pharmaceutical ingredient used in a wide variety of prescription and over-the-counter products for the treatment and relief of allergy symptoms (Lu et al., 2010). Kreutner et al. (1987) reported that LOR exerts anti-allergic activity. LOR showed inhibitory effects in the treatment of allergic rhinitis (Katelaris, 1990) and asthma (Town and Holgate, 1990). Thus, here we compared the efficacy between loratadine-pharmacopuncture (LP) and loratadine-oral administration (LO) in mice.

ST36 is a specific acupoint located on the stomach meridian (足陽明胃經) and known to strengthen the Qi, not only the stomach Qi, even though this acupoint belongs to the stomach meridian but also the general Qi in the whole body. ST36 is one of the most frequently used acupoints that can be stimulated through needles or “moxibustion” to balance and harmonize Yin and Yang by improving the flow of Qi along the meridians. For this reason, ST36 is the target to treat various diseases in the gastrointestinal tract as well as general

*Correspondence: Phil-Dong Moon
E-mail: pdmoon@khu.ac.kr
Received February 12, 2018; **Accepted** February 23, 2018; **Published** February 28, 2018
doi: http://dx.doi.org/10.5667/tang.2018.0003

Table 1. Effect of LP or LO on compound 48/80-induced systemic anaphylactic reaction in mice

Treatment [a]	Compound 48/80 (8 mg/kg)[b]	Mortality (%)[c]
None (saline)	+	100.00 ± 0.00
LP (0.1 mg/kg)	+	75.00 ± 14.43
LP (1 mg/kg)	+	41.67 ± 8.33*
LP (10 mg/kg)	+	25.00 ± 14.43*
LO (0.1 mg/kg)	+	75.00 ± 14.43
LO (1 mg/kg)	+	58.33 ± 8.33
LO (10 mg/kg)	+	25.00 ± 14.43*

[a]The groups of mice (n = 4/group) were pretreated with LOR 1 h before the compound 48/80 injection.
[b]The compound 48/80 solution was intraperitoneally given to the groups of mice.
[c]Mortality (%) is presented as the 'number of dead mice × 100 / Total number of experimental mice'. Each datum represents the mean ± S.E.M. of three independent experiments. *p < 0.05; significantly different from the control value.

symptoms in the whole body (Hu et al., 2013).

Mast cells release preformed and newly synthesized mediators such as histamine, proteases, leukotrienes, and prostaglandins (Moon et al., 2014) Among them, histamine is regarded as a principal mediator of allergic reaction (Kim et al., 2017). Compound 48/80 is well-known histamine releaser (Kim et al., 2003).

The secretory responses of mast cells can be induced by aggregation of their cell surface-specific receptors for immunoglobulin E (IgE) by the corresponding antigen (Alber et al., 1991; Hong et al., 2003; Metzger et al., 1986). It has been established that the anti-IgE antibody induces passive cutaneous anaphylaxis (PCA) as a typical in vivo model for immediate-type hypersensitivity reactions in anaphylactic reactions. In the present study, we used murine in vivo model to compare the efficacy between LP and LP.

MATERIALS AND METHODS

Materials

Compound 48/80, anti-dinitrophenyl (DNP) IgE antibody, DNP-human serum albumin (HSA), and Evans blue were purchased from Sigma Chemical Co. (St. Louis, MO, USA). Claritin (LOR) was purchased from Kyung Hee Jeong Mun drug store (Seoul, Republic of Korea).

Animals

Male ICR mice (4 weeks old) were purchased from the Dae-Han Experimental Animal Center (Eumsung, Republic of Korea), and the animals were maintained at the College of Korean Medicine, Kyung Hee University. The mice were housed five to ten per cage in a laminar air-flow room maintained at a temperature of 22 ± 1°C and relative humidity of 55 ± 1% throughout the study. The research was conducted in accordance with the internationally accepted principles for laboratory animal use and care as found in the US guidelines (NIH publication #85-23, revised in 1985) and Kyung Hee University (No. KHUASP(SE)-15-118).

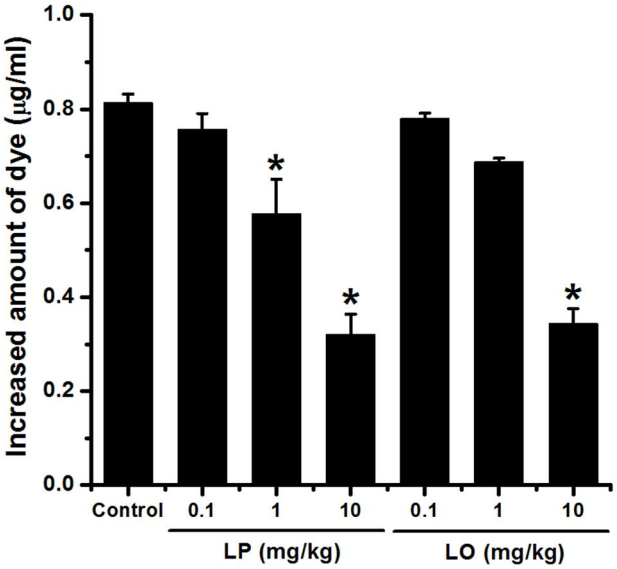

Fig. 1. Effect of LP or LO on 48 h PCA in mice. The groups of mice (n = 4/group) were pretreated with LOR 1 h before antigen (DNP-HSA) injection. Each datum represents the mean ± S.E.M. of three independent experiments. *p < 0.05; significantly different from the control value.

LOR treatment

Mice were divided randomly into 'LP', 'LO' and 'Control' groups. The concentration of LOR injected each mouse of LP group was 10 times higher than LO group, but 10 times less in volume. The Zusanli acupoint (ST36) is located 5 mm below and lateral to the anterior tubercle of the tibia. LOR (0.1 to 10 mg/kg) was injected into ST36 acupoint of each mouse (LP group) using a microsyringe with a 29-gauge hypodermic needle and administered orally with sonde in LO group.

Compound 48/80-induced systemic anaphylactic reaction

To assess compound 48/80-induced systemic anaphylactic reaction, a murine model was used, as previously described (Kim et al., 2013).

PCA reaction

To measure PCA reaction, a murine model was used, as previously described (Kim et al., 2013).

Statistical analysis

SPSS software (version 23.0, SPSS Inc, Chicago, IL, USA) was used to analysis the results statistically. Our results are expressed as the mean standard error of the mean (S.E.M.). The statistical evaluation of the results was performed by an independent t-test and an ANOVA with a Tukey post hoc test. The results were considered significant at a value of $p < 0.05$.

RESULTS

Comparison of the effects between LP and LO on compound 48/80-induced systemic anaphylaxis

To compare the contribution between LP and LO in anaphylactic reaction, we first used the in vivo model of systemic anaphylaxis. As shown in Table 1, an oral administration of saline as a control induced 100% of fatal reaction. When the LOR (10 mg/kg) was treated to the mouse 1 h before compound 48/80 injection, the mortality was significantly reduced at both groups (Table 1, $p < 0.05$).

However, the effect of LP was better than LO in the concentration of 1 mg/kg (Table 1, $p < 0.05$).

Comparison of the effects between LP and LO on PCA

PCA is one of the most important in vivo models of anaphylaxis in local allergic reactions (Wershil et al., 1987). When the LOR was treated to the mouse, the PCA reaction was inhibited (Fig. 1). The best result was obtained at LP group.

DISCUSSION

Allergic reactions are associated with the activation of mast cells and the release of inflammatory mediators. In most cases, this process relies on signaling through the FcεRI-IgE complex (Liew et al., 2010). However, it has been shown that other substances, including compound 48/80, can directly activate mast cells, thus inducing degranulation. Compound 48/80 is known to trigger mast cell activation by binding to G proteins in the cytoplasm and initiating biochemical cascades that result in the release of inflammatory mediators (Tatemoto et al., 2006). Our results showed that the LP treatment inhibited the compound 48/80-induced systemic anaphylactic reaction (Table 1). Thus, we could presuppose that LP treatment regulates the degranulation and release of inflammatory mediators from mast cells induced by compound 48/80.

Mast cells are bone marrow-derived white blood cells with prominent roles in allergic response and anaphylaxis. Allergy and anaphylaxis begin with sensitization of mast cells through the binding of an antigen-specific IgE to FcεRI receptors on the mast cell surface. Subsequent cross-linking of FcεRI receptors by antigen binding to IgE stimulates the release of pro-inflammatory mediators, including histamine and β-hexosaminidase, from storage sites in cytoplasmic granules (Chen et al., 2010; Han et al., 2009; Kopeć et al., 2006; Tiwari et al., 2008). Our results showed that the LP treatment inhibited PCA (Fig. 1). It is conceivable that the LP treatment inhibits the immediate type allergic reactions, probably through interference with the degranulation system.

In conclusion, the present findings suggest that the LP treatment has a potential as a new method to administer a drug to human who are difficult to take a drug orally.

ACKNOWLEDGEMENTS

This work was supported by Kyung Hee University.

CONFLICT OF INTEREST

The authors declare that there was no conflict of interest.

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