Allergology International 65 (2016) 483–486

Contents lists available at ScienceDirect

Allergology International

journal homepage: http://www.elsevier.com/locate/alit

Letter to the Editor

Prescription of adrenaline auto-injectors to 1145 Japanese outdoor workers in 2015

Dear Editor,

In Japan annually, approximately 20 people die of anaphylaxis caused by Hymenoptera stings.[1] In particular, forestry and field workers are at high risk of Hymenoptera stings and may develop occupation-related allergies after being stung. Previously, we reported that 30–40% of Japanese forestry and field workers had specific (s)IgE to Hymenoptera venom.[2] To prevent anaphylactic shock caused by Hymenoptera stings, administration of adrenaline is very important.[3] However, there are few surveys of Hymenoptera stings in the occupational setting and prescription of adrenaline injectors to affected workers. We surveyed outdoor workers in Japan to examine the rate of prescription of adrenaline auto-injectors.

A total of 1332 (1257 men, 75 woman) participants took part in this study (Table 1). Forestry workers (FWs) and building contractors (BCs) were staff members of a private forest owners' cooperative and a private building industry cooperative, respectively, in Tochigi prefecture, Japan, and electrical facility field workers (EFFWs) were employed by Tochidenko, Tochigi, Japan. The main work of FWs is forestation, which includes weeding, planting, and felling of trees, and these workers are frequently exposed to Hymenoptera stings. EFFWs and BCs also usually work outdoors and are at a high risk of Hymenoptera stings. Office workers (OWs) who work in the same area were also recruited. All participants completed questionnaires and underwent peripheral blood tests between September and November 2015. Fifteen volunteers (13 men, 2 women; mean age, 31.5 ± 3.8 years; range, 26–48 years) who had never experienced a Hymenoptera sting were enrolled as controls. This study was approved as No1525 and No1526 in authorization number by the Dokkyo Medical University Koshigaya Hospital Research Ethics Committee, and written informed consent was obtained from each participant prior to enrollment.

A questionnaire on the following items was administered by an allergist: age, sex, experience of a Hymenoptera sting (yes or no) and systemic reactions (yes or no) to a Hymenoptera sting according to Mueller grade[4] (either grade I to IV), prescription (yes, unknown, or no) and carrying (usually, sometimes, or rarely) of an adrenaline auto-injector, and occupation. In addition, a 10-mL peripheral blood sample was taken from each participant. Serum was immediately extracted and sIgE antibody to Hymenoptera venom was measured. The measurement of sIgE to wasp, hornet, and honey bee venom was determined by Sanritsu Corporation, Chiba, Japan. Detection of sIgE by AlaSTAT 3g Allergy (AlaSTAT), a chemiluminescent enzyme immunoassay (CLEIA), was expressible in quantitative units (IU_A/mL) and has a working range of 0.1–500 IU_A/mL. The interpretations of positive results for AlaSTAT are based on values ≥ 0.1 IU_A/mL as described previously.[5,6]

Data are presented as mean ± standard deviation (S.D). The χ^2 test, which assessed differences in bivariate analysis and by single logistic regression, was tested for independence and odds ratios (ORs) with 95% confidence intervals (95%CI) in prescription and carrying auto-injector with positive results for sIgE to either Hymenoptera venom between FWs and the other workers. *P* values of less than 0.05 were considered to indicate statistical significance. Statistical analyses were performed with JMP software (Version 7.4 for MAC, SAS Institute, Cary, NC, USA).

Table 1 summarizes the characteristics of the FWs, BCs, EFFWs, and OWs. sIgE to hornet, wasp, and honey bee venom was ≥0.1 IU_A/mL in 169 (44.5%), 189 (49.7%), and 43 (11.3%) FWs; 92 (16.5%), 114 (20.5%), and 33 (5.9%) BCs; 25 (12.0%), 36 (17.2%), and 8 (3.8%) EFFWs; and 19 (10.2%), 23 (12.3%), and 7 (3.7%) OWs, respectively. Positive results of sIgE (≥0.1 IU_A/mL) to either Hymenoptera venom were seen in 214 (56.3%) FWs, 143 (25.7%) BCs, 45 (21.5%) EFFWs, and 27 (14.4%) OWs. All 15 controls had negative results for sIgE to each Hymenoptera venom. In addition, 87 (22.9%) FWs, 18 (3.2%) BCs, 16 (7.7%) EFFWs, and 2 (1.1%) OWs had received a prescription for an adrenaline auto-injector. And 312 (82.1%) FWs, 318 (57.2%) BCs, 125 (59.8%) EFFWs, and 86 (46.0%) OWs had experienced a Hymenoptera sting. In the subjects had experienced a Hymenoptera sting, the systemic reactions or the positive results of either venom-sIgE were seen in 58 (18.6%) or 196 (62.8%) FWs, 39 (12.3%) or 110 (34.6%) BCs, 12 (9.6%) or 37 (29.6%) EFFWs, and 3 (3.5%) or 18 (20.9%) OWs, respectively.

Figure 1A shows the occupational setting and prescription of adrenaline auto-injector. In workers with a positive result of sIgE Ab to either Hymenoptera venom, the prescription of adrenaline auto-injector was given to 71 out of 214 (33.2%) FWs, 9 of 143 (6.3%) BCs, 7 of 45 (15.6%) EFFWs, and 2 out of 27 (7.4%) OWs. The number of FWs, BCs, EFFWs, and OWs who carry their auto-injectors were 37 (52.1%), 7 (77.8%), 5 (71.4%), and 1 (50.0%), respectively. The ORs for the prescription of adrenaline auto-injector to workers with positive results of sIgE to either Hymenoptera venom, relative to FWs, were as follows; in EFFWs, OR 0.469 (95%CI, 0.231–0.951); in BCs, OR 0.190 (95%CI, 0.098–0.367); in OWs, OR 0.223 (95%CI, 0.058–0.859). The prescription of adrenaline auto-injector to workers with positive results of sIgE to Hymenoptera venom was significantly ($P < 0.0001$, respectively) greater for FWs than other outdoor

Peer review under responsibility of Japanese Society of Allergology.

http://dx.doi.org/10.1016/j.alit.2016.04.005

Table 1
Subject characteristics (n = 1332).

Occupation (n)	Total (1332)	FWs (380)	EFFWs (209)	BCs (556)	OWs (187)
Sex (n)					
Male (%)	1257 (94.4)	374 (98.4)	207 (99.0)	549 (98.7)	127 (67.9)
Female (%)	75 (5.6)	6 (1.6)	2 (1.0)	7 (1.3)	60 (32.1)
Age (years)					
10–19	26 (2)	4 (1.1)	8 (3.8)	14 (2.5)	0 (0.0)
20–29	157 (11.8)	42 (11.1)	37 (17.7)	56 (10.1)	22 (11.8)
30–39	267 (20.0)	86 (22.6)	43 (20.6)	112 (20.1)	26 (13.9)
40–49	306 (23.0)	100 (26.3)	45 (21.5)	126 (22.7)	35 (18.7)
50–19	287 (21.5)	66 (17.4)	48 (23.0)	109 (19.6)	64 (34.2)
60–69	244 (18.3)	68 (17.9)	24 (11.5)	121 (21.8)	31 (16.6)
≥70	45 (3.4)	14 (3.7)	4 (1.9)	18 (3.2)	9 (4.8)
Wasp-sIgE (n, mean±SD)	1.24±4.89	2.25±5.98	0.67±2.62	0.92±4.12	0.78±6.08
Negative (%)	970 (72.8)	191 (50.3)	173 (82.8)	442 (79.5)	164 (87.8)
Positive (%)	362 (27.2)	189 (49.7)	36 (17.2)	114 (20.5)	23 (12.3)
Hornet-sIgE (n, mean±SD)	0.99±4.87	2.12±6.77	0.22±0.37	0.72±4.79	0.37±1.94
Negative (%)	1027 (77.1)	211 (55.5)	184 (88.0)	464 (83.5)	168 (89.8)
Positive (%)	305 (22.9)	169 (44.5)	25 (12.0)	92 (16.5)	19 (10.2)
Hony-bee sIgE (n, mean±SD)	0.28±1.51	0.35±1.32	0.15±0.39	0.32±2.1	0.15±0.30
Negative (%)	1241 (93.2)	337 (88.7)	201 (96.2)	523 (94.1)	180 (96.3)
Positive (%)	91 (6.8)	43 (11.3)	8 (3.8)	33 (5.9)	7 (3.7)
Either venom-sIgE (n)					
Negative (%)	903 (67.8)	166 (43.7)	164 (78.5)	413 (74.3)	160 (85.6)
Positive (%)	429 (32.2)	214 (56.3)	45 (21.5)	143 (25.7)	27 (14.4)
Prescriotion of adrenaline (n)					
Yes (%)	123 (9.2)	87 (22.9)	16 (7.7)	18 (3.2)	2 (1.1)
No (%)	1098 (82.4)	277 (72.9)	165 (78.9)	483 (86.9)	173 (92.5)
Unknown (%)	111 (8.3)	16 (4.2)	28 (13.4)	55 (9.9)	12 (6.4)
Experience of Hymenoptera stings (n)					
Yes (%)	841 (63.1)	312 (82.1)	125 (59.8)	318 (57.2)	86 (46.0)
No (%)	491 (36.9)	68 (17.9)	84 (40.2)	238 (42.8)	101 (54.0)
Out of subjects who had experienced a Hymenoptera sting					
Systemic reaction (n)					
Yes (%)	112 (13.3)	58 (18.6)	12 (9.6)	39 (12.3)	3 (3.5)
No (%)	729 (86.7)	254 (81.4)	113 (90.4)	279 (87.7)	83 (96.5)
Either venom-sIgE (n)					
Negative (%)	480 (57.1)	116 (37.2)	88 (70.4)	208 (65.4)	68 (79.1)
Positive (%)	361 (42.9)	196 (62.8)	37 (29.6)	110 (34.6)	18 (20.9)

FWs, forestry workers; BCs, building contractors; EFFWs, electrical facility field workers; OWs, office workers; n, numbers; sIgE, specific IgE.
Levels of sIgE (IUA/mL) are presented as mean±standard deviation (SD).
The interpretations of positive results are based on values ≥0.1 IUA/mL.
The interpretations of negative results are based on values <0.1 IUA/mL.

workers or OWs. In addition, Figure 1B shows prescription of adrenaline auto-injector in 58 FWs, 39 BCs, 12 EFFWs, and 3 OWs who had experienced systemic reactions to a Hymenoptera sting with the result of sIgE to either Hymenoptera venom. The prescription of adrenaline auto-injector in subjects with a positive result of sIgE to either Hymenoptera venom was given to 28 out of 49 (57.1%) FWs, 7 of 31 (22.6%) BCs, 2 of 4 (50.0%) EFFWs, and 1 out of 3 (33.3%) OWs. The results indicate that workers in the private forest owners' cooperative were more likely to be prescribed an adrenaline auto-injector compared with other workers. However, several investigators have reported that patients with recent severe reactions and positive venom skin test, which is an economic method to demonstrate sIgE to Hymenoptera venom,[7] might have a 10–17% chance of a systemic reaction to their next sting.[8,9] Furthermore, patients with recent severe reactions and positive venom skin test results might have a 40–70% chance of systemic reaction to their next sting.[8] Thus, the prescription of an adrenaline auto-injector to outdoor workers might be considered to be few. On the other hand, sIgE levels decline over several years if a person does not experience a subsequent Hymenoptera sting and disappearance of sIgE levels is thought to occur immediately after stings.[9,10] Thus, if results of sIgE to Hymenoptera venom immediately after Hymenoptera stings are negative, they need to be re-measured after a few weeks. Moreover, subjects who had experienced an anaphylactic reaction due to Hymenoptera stings require the prescription of an adrenaline auto-injector. In addition, although there was no significant differences in usually carrying their auto-injector, compare with the percentage of the other workers ($P = 0.84$ to EFFWs, $P = 0.54$ to BCs, and $P = 0.60$ to OWs), that of FWs tended to be less (data not shown). The results indicate that FWs who had never experienced systemic anaphylactic reactions despite the frequency of Hymenoptera stings might not consider the importance of carrying the auto-injector.

In conclusion, the prescription of adrenaline auto-injector to Japanese outdoor workers who had a positive result of sIgE to either Hymenoptera venom was approximately 6–33%. In addition, the prescription of adrenaline auto-injector in these workers who had experienced systemic reactions to a Hymenoptera sting with a positive result of sIgE to either Hymenoptera venom was approximately 23–57%. The percentage of outdoor workers who usually carry their auto-injector during work was approximately 52–78%. This study suggests that the owners of the cooperative need to think about the prescription of adrenaline auto-injector for outdoor workers who was positive results, including a part of negative results, for sIgE Ab to Hymenoptera venom. In addition, outdoor workers should be educated about usually carrying an adrenalin auto-injector.

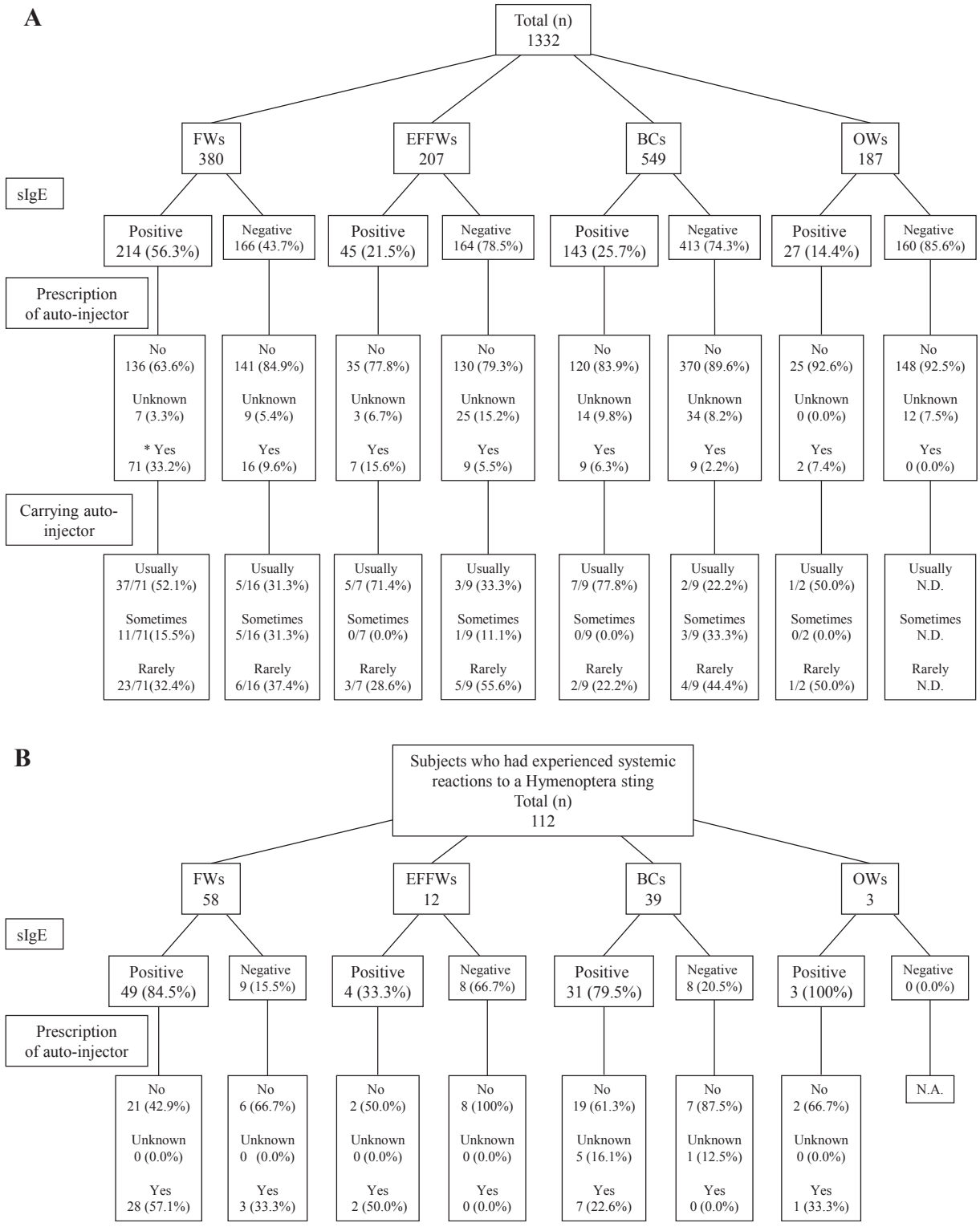

Fig. 1. A. Prescription and carrying of adrenaline injector by FWs, BCs, EFFWs, and OWs with a positive result of sIgE to either Hymenoptera venom in this study. *$P < 0.0001$, compared with prescription of adrenaline auto-injector to EFFWs, BCs, or OWs. N.D., not done. **B.** Prescription of adrenaline auto-injector by FWs, BCs, EFFWs, and OWs who had experienced systemic reactions to a Hymenoptera sting with the result of sIgE to either Hymenoptera venom in this study. N.A., not applicable.

Conflict of interest

The authors have no conflict of interest to declare.

Masamitsu Tatewaki [a,f], Hirokuni Hirata [a,*,f], Yoshihiko Ikeno [b], Ikuo Akutsu [b], Seiko Sekiguchi [a], Natsumi Suzuki [a], Kumiya Sugiyama [a], Masafumi Arima [c], Kazuhiro Kurasawa [c], Takeshi Fukuda [d], Daisuke Shima [e], Yasutsugu Fukushima [a]

[a] *Department of Respiratory Medicine and Clinical Immunology, Dokkyo Medical University Koshigaya Hospital, Saitama, Japan*
[b] *Department of Rheumatology, Nasu Red Cross Hospital, Tochigi, Japan*
[c] *Department of Rheumatology, Dokkyo Medical University, Tochigi, Japan*
[d] *Dokkyo Medical University, Tochigi, Japan*
[e] *Medical Affairs, Global Established Pharma Business, Pfizer Japan, Tokyo, Japan*

* Corresponding author. Department of Respiratory Medicine and Clinical Immunology, Dokkyo Medical University Koshigaya Hospital, 2-1-50 Minamikoshigaya, Koshigaya-shi, Saitama 343-8555, Japan.
E-mail address: hirokuni@dokkyomed.ac.jp (H. Hirata).

References

1. *[Demographic Survey in Japan]*. Ministry of Health, Labour and Welfare, Japan, 2013 (in Japanese).
2. Hayashi Y, Hirata H, Watanabe M, Yoshida N, Yokoyama T, Murayama Y, et al. Epidemiologic investigation of hornet and paper wasp stings in forest workers and electrical facility field workers in Japan. *Allergol Int* 2014;**63**:21–6.
3. Barnard JH. Nonfatal results in third-degree anaphylaxis from hymenoptera stings. *J Allergy* 1970;**45**:92–6.
4. Mueller HL. Diagnosis and treatment of insect sensitivity. *J Asthma Res* 1966;**3**:331–3.
5. Watanabe M, Hirata H, Arima M, Hayashi Y, Chibana K, Yoshida N, et al. Measurement of Hymenoptera venom specific IgE by the IMMULITE 3gAllergy in subjects with negative or positive results by ImmunoCAP. *Asia Pac Allergy* 2012;**2**:195–202.
6. Izuhara K, Kawasaki S, Tanaka S. [Clinical validation of the IMMULITE 3gAllergy]. *Rinsho Meneki Arerugika* 2013;**59**:696–703 (in Japanese).
7. Krishna MT, Ewan PW, Diwakar L, Durham SR, Frew AJ, Leech SC, et al. Diagnosis and management of hymenoptera venom allergy. *Clin Exp Allergy* 2011;**41**:1201–20.
8. Golden DB, Marsh DG, Freidhoff LR, Kwiterovich KA, Addison B, Kagey-Sobotka A, et al. Natural history of Hymenoptera venom sensitivity in adults. *J Allergy Clin Immunol* 1997;**100**:760–6.
9. Golden DB, Tracy JM, Freeman TM, Hoffman DR, Insect Committee of the American Academy of Allergy, Asthma and Immunology. Negative venom skin test results in patients with histories of systemic reaction to a sting. *J Allergy Clin Immunol* 2003;**112**:495–8.
10. Hayashi Y, Hirata H, Watanabe M, Yoshida N, Yokoyama T, Kakuta T, et al. Usefulness of specific-IgG4 to Hymenoptera venom in the natural history of hymenoptera stings. *J Investig Allergol Clin Immunol* 2014;**24**:192–4.

Received 2 March 2016
Received in revised form 11 April 2016
Accepted 12 April 2016
Available online 17 May 2016

[f] Dr. Tatewaki and Dr. Hirata contributed equally to this work.