

Which anti-histamines dermatological specialists select in their therapies for common skin diseases? – A practical analysis from multiple clinics –

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In the treatment of skin diseases, antihistamines and antiallergic agents are among the most frequently used oral medications, and are available as a wide variety of products. We investigated what criteria dermatological specialists use to select antihistamines and antiallergic agents, as well as the use objectives and expected benefits. The present investigation was conducted in a total of 1,448 patients, including 336 patients with urticaria, 944 patients with eczema/dermatitis, and 199 patients with atopic dermatitis, in 6 dermatological clinics and 1 university hospital. A Case Card to record the prescription motives and clinical evaluation was used, and the results were tabulated and analyzed. As a result, it was found that the expected result was obtained in more than 80% of cases prescribed for by dermatologists based on the prescription motives for individual cases.

Key words: skin diseases, antihistamines, antiallergic agents, prescription motive, EBM

INTRODUCTION

As the concept of evidence-based medicine (EBM) becomes widespread, the evaluation of treatment based on EBM is becoming an issue. We investigated how the current treatments performed by dermatologists are evaluated. In addition, we examined the possibility of establishing more useful and safe treatment methods. As the first step, we prepared a protocol focusing on widely used drugs and frequently observed diseases. More specifically, focusing on antihistamines and antiallergic agents as the most frequently used drugs for the treatment of skin diseases, we conducted a questionnaire survey of dermatological specialists in multiple institutions using a Case Card in order to identify the motives and reasons for the selection of the drug for individual cases of skin diseases as well as the result of the use

of the drug, including whether the expected result was obtained. Furthermore, we investigated whether such a survey would be actually performable in the daily practice of practitioners. Addition of “medical practice in university hospitals” to the range of analytical items may be useful in evaluation of the actual medical practice, which may further contribute to the collaboration between hospitals and clinics, which is currently in demand.

METHODS

1) Institutions surveyed

One dermatological clinic was selected from each of six cities surrounding Tokai University Hospital, which is centrally located in Kanagawa Prefecture (Fig. 1). The requirements were as follows: the practitioner is a dermatologist certified by the Japanese Dermatological Association, has a clinical

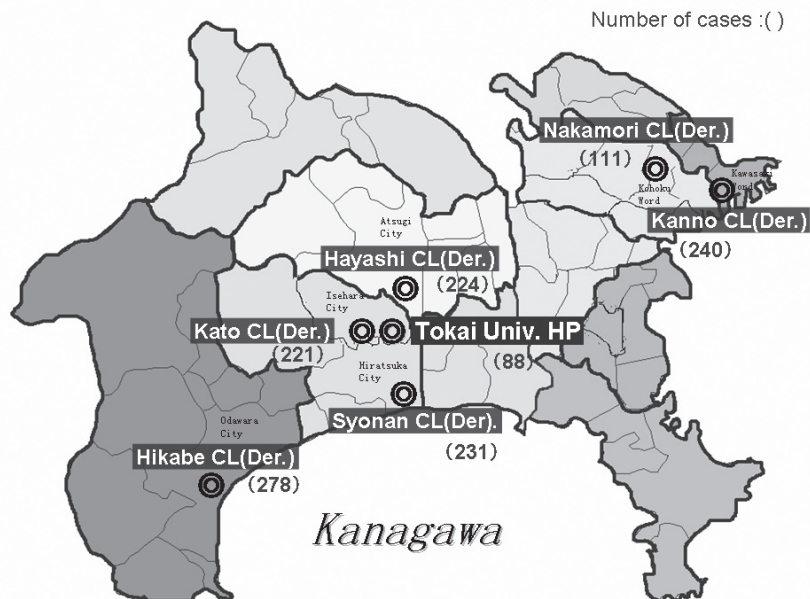


Fig. 1 Kanagawa prefecture.

experience of at least 20 years, and examines at least 100 outpatients per day. In addition, these six physicians should be graduates of different universities (However, Dr. Nakamori and Dr. Sugano are graduates of Tokai University).

2) Survey methods

(1) Case Card (Table 1)

① Patient background: Patient initials, age, sex, and the share of the health insurance were set as patient background factors, to avoid identifying the patient.

② Target diseases: The following three diseases: urticaria, eczema/dermatitis, and atopic dermatitis.

③ Prescription motives: As shown in the table, 17 items were investigated. The prescription motive in this survey means neither the characteristics/efficacy described in the product information provided by the manufacturer nor the content of research reports, but means the reason why the physician selected the antihistamine or antiallergic agent for the patient among various types of drugs.

Therefore, the prescription motive includes not only information on the mechanism of action of the drug selected, but also information on safety, dosage and administration, economic reason, and the

information dissemination activity by the MR. Multiple-choice questions were administered.

④ Drug name: 16 major drugs used in Japan were listed. "Z" was added to the drug name in the case of using a generic product.

⑤ Evaluation: At the revisit, the presence/absence of the effect or usefulness expected as the prescription motive was evaluated in five grades.

(2) Survey methods

On the same prearranged days during July to December 2000, the survey was conducted in the 6 clinics and the university hospital in all the patients for whom antihistamines or antiallergic agents were prescribed for the treatment of urticaria, eczema/dermatitis, or atopic dermatitis. A Case Card was prepared for each patient at the time of issuing the prescription, and the result was evaluated at the revisit after 2 to 4 weeks and recorded in the Case Card.

(3) Analytical method

All the Case Cards were collected from the university hospital and the 6 clinics, and the responses were simply tabulated. In addition, the relevance of the various items was analyzed and evaluated. These were analyzed by nonparametric methods. Mann-Whitney statistics were used to compare of two groups.

Table 1 Case card.

[Background]

Chart No. _____	Initial Last			First			
BirthDay / /	Age			Sex	M	F	
Patient Burden	0	1	2	3	10	Elderly	Pregnant

[Disease]

Urticaria	Eczema / Dermatitis	Atopic Dermatitis
[Prescription Motive *Chose many as you want]		[Brand Name]
Excellent antipruritic effect Additive-, synergic- effect Anticholinergic, antikinin effect Easy administration Once daily administration Easy to combine with other medication regarding number of administration Low side effect Low sedation Can sleep well High safety for elderly High safety during pregnancy High safety for pediatric High safety during lactation Low drug interaction Low drug price Big margin of drug price MR/MS enthusiasm Others ()		IPD Z Azeptin Z Atarax / P Z Alesion Z Ebastel Z Zaditen Z Zyrtec Z Zesulan/Nipolazine Z Cellect Z Tavegyl Z Daren/Remicut Z Trildan Z Polaramine Z Homoclomin Z Rizaben Z Restamine Z Others () Z

[Evaluation]

Above Expected / As Expected / Below Expected / Better before change / No Reconsultation

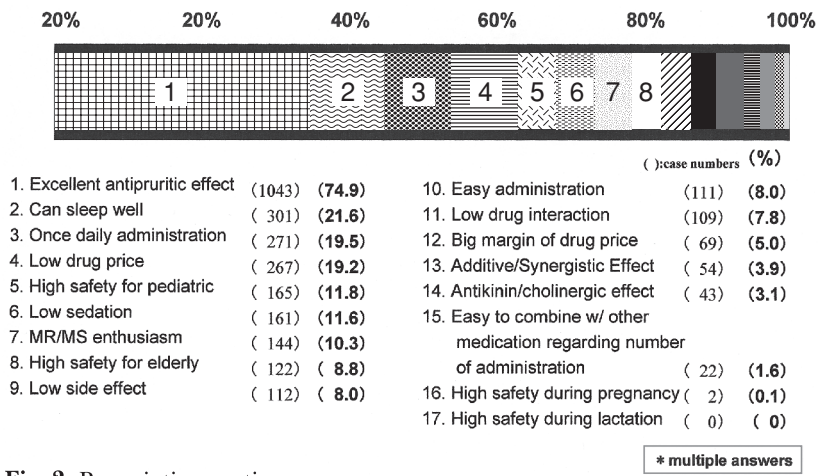


Fig. 2 Prescription motives.

Kruskal-Wallis statistics were used to compare of three groups. All tests were two-sided with significance at the 5% level.

RESULTS

A total of 1,448 cases were collected from the 7 institutions. Of these, 55 cases that had missing entries were excluded: thus, 1,393 cases were examined and analyzed. The number of patients analyzed was 346 patients

(24.8%) with urticaria, 944 patients (67.8%) with eczema/dermatitis, and 198 patients (14.2%) with atopic dermatitis.

1) Prescription motives

The most frequently observed prescription motive was “superior antipruritic effect” for 1,043 cases (74.9%), followed by “good night’s sleep” for 301 cases (21.6%), “once a day administration” for 271 cases (19.5%), “low

Table 2 Prescription motive at clinics and university hospital

Clinics		University Hospitals	
Prescription Motive	(%)	Prescription Motive	(%)
1. High antipruritic effect	78.6	Once daily administration	54.5
2. Can sleep well	22.5	Low sedation	30.7
3. Low drug price	20.5	Low drug interaction	20.5
4. Once daily administration	17.1	High antipruritic effect	19.3
5. High safety for pediatric	12.6	MR/MS enthusiasm	12.5
6. Low sedation	10.3	Can sleep well	9.1

Table 3 Prescription motive and age classification

	< 15 yrs (253)	15—65 yrs (934)	65 yrs ≤ (203)
1st	Antipruritic (77.9)	Antipruritic (74.7)	Antipruritic (71.9)
2nd	Safe for PED (62.5)	Can sleep well (23.9)	Safe for Elderly (48.8)
3rd	Easy to take (31.2)	Once Daily (23.7)	Can sleep well (27.6)
4th	Low drug price (19.8)	Low drug price (20.2)	No drug interaction (24.1)
5th	Can sleep well (8.3)	Less sedation (15.4)	Once daily (21.7)

(): Case
(): % Selected
P=0.341
P<0.001
P<0.001

drug price” for 267 cases (19.2%), “better safety profile in children” for 165 cases (11.8%), and “less likely to induce drowsiness” for 161 cases (11.6%) in this order (Fig. 2).

2) Prescription motives in the clinics and the university hospital

The most frequently observed prescription motive in the clinics was “superior antipruritic effect” (78.6%), followed by “good night’s sleep” (22.5%) and “low drug price” (20.5%). On the other hand, the most frequently observed prescription motive in the university hospital was “once a day administration” (54.5%), followed by “less likely to induce drowsiness” (30.7%) and “less incidence of adverse drug reactions” (20.5%). Thus, there were differences in the prescription motives between the clinics and the university hospital. In the clinics, “Superior antipruritic effect” (P<0.001), “good night’s sleep” (P = 0.003), “low drug price” (P<0.001), and “High safety for pediatric” (P<0.001) were significantly higher than university hospital, and in the university hospital, “once a day administration” (P<0.001), “less incidence of adverse drug reactions” (P<0.001), and “less likely to induce drowsiness” (P<0.001) were

significantly higher than clinics. But “MR/MS enthusiasm” was similar (P=0.491) (Table 2).

3) Prescription motives and age group

The patients were divided into three age groups: children aged less than 15 years, adults aged 15 to 65, and elderly people aged more than 65 years.

The results showed that the top-ranked prescription motive was the suppression of “itching” in all the age groups (children 77.9%, aged 15 to 65 years 74.7% and elderly people 71.9%). three groups were similar, P= 0.341). However, in the prescription motives ranked second and lower, differences were observed among the age group. “Safety” was the second-ranked motive for the children (62.5%) and elderly groups (48.8%). “Easiness of medication” accounted for 31.2% in the children group, whereas “less likely to induce drug interactions” accounted for 24.1% in the elderly group. “Good night’s sleep” was significantly difference among three groups (P <0.001). Moreover, children was significantly lower than aged 15 to 65 (P<0.001) and elderly group (P<0.001). But aged 15 to 65 were similar to elderly (P=0.266) (Table 3).

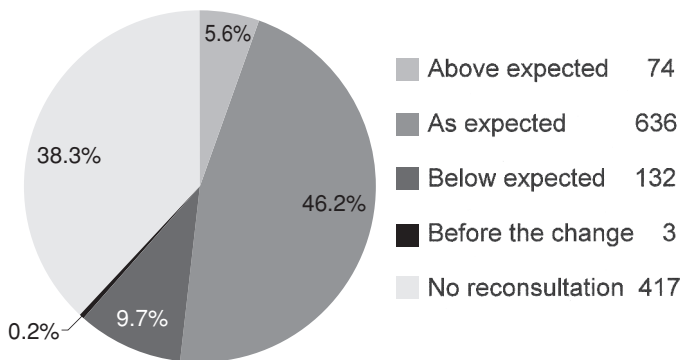


Fig. 3 Comparison in clinical effect.

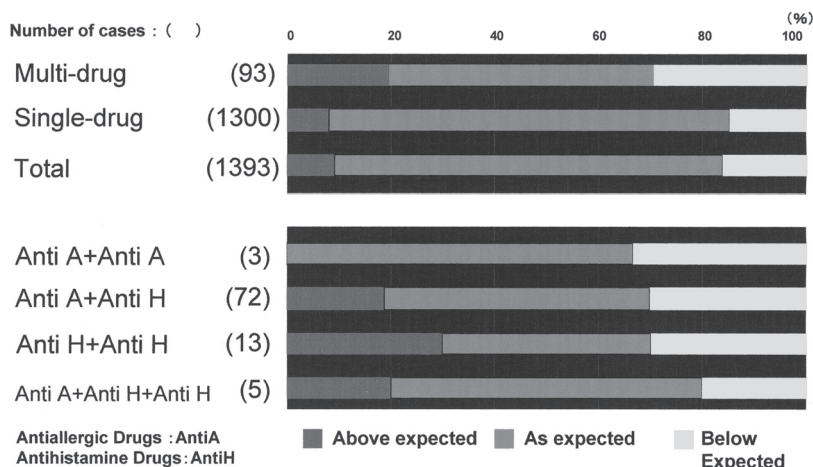


Fig. 4 Clinical effect of monotherapy and multiple drug therapy.

4) Comparison in clinical effect

At the revisit after 2 to 4 weeks, each patient was examined for whether the effect or the result expected as the prescription motive was obtained. 61.7% of the patients made the revisit.

Patients in whom “more than expected” effect as the prescription motive was observed with the selected drug (78 patients) or in whom “expected” effect was observed (643 patients) accounted for about 84.0% of 859 patients who made the revisit. “Less than expected” effect was obtained in 15.8% of the patients (Fig. 3).

5) Clinical effects of monotherapy and multiple drug therapy

The clinical effects of monotherapy and multiple drug therapy were as follows.

Monotherapy was given to 1,300 patients, whereas multiple drug therapy was given to 93 patients, which accounted for 6.7% of all patients. Regarding the clinical effect of multiple drug therapy, the number of patients with more than “as expected” effect was lower than those observed in monotherapy ($P = 0.001$) (Fig. 4).

DISCUSSION

1) Prescription motives

The top-ranked prescription motive was “superior antipruritic effect”. The majority of patients with atopic dermatitis, which is one of the target diseases in the present survey, list antipruritic effect as their reason for wanting antiallergic drugs [1]. Therefore, the reason for the prescription of antiallergic drugs in the present survey is considered

appropriate for patients. Between the report and our present survey, differences were observed in the preferable characteristics [2] of antiallergic drugs for atopic dermatitis and in the ranking of prescription motives. This may be because diseases other than atopic dermatitis were included as target diseases in our survey, and because the survey items were different. “Good night’s sleep” ranked higher than “less likely to induce drowsiness”. This result was contrary to our prediction that “less likely to induce drowsiness” would be ranked higher in the prescription motives.

2) Prescription motives in the clinics and the university hospital

The analysis of prescription motives separately for the university hospital and the clinics showed differences between these institutions. The reasons for the differences are considered as follows. For example, regarding “once a day administration”, which was the top-ranked motive in the university hospital, since patients who visit university hospitals are likely to have intractable diseases and to be adults who have jobs, priority is given to medication compliance in daily life. This reason also applies to one of the highly ranked prescription motives, “less likely to induce drowsiness”.

On the contrary, physicians in clinics select drugs that induce drowsiness and contribute to a good night’s sleep. This may be because the general practitioners give priority to patient’s complaints, such as “unable to sleep due to itching”. In fact, the rank of “less likely to induce drowsiness” in the prescription motives is lower than that in the university hospital. In other words, it is a noticeable finding that the ranking of the contradictory motives “less likely to induce drowsiness” and “good night’s sleep” is reversed between the university hospital and the clinics.

One prescription motive that was observed in the result from the clinics but not in that of the university hospital was “low drug price”. This is a logical reason for general practitioners. Since patients with intractable or chronic diseases tend to visit university hospitals, it appears less likely that the priority is given to “drug price” as the prescription motive in university hospitals. On the contrary, the “information dissemination activity by MR” was the fifth-ranked motive in the university hospital. It is not clear whether

this is attributable to a tendency to attach too much importance to data (drug information) or is simply attributable to the closeness between physicians and the MR. Taken together with the highly ranked prescription motives in the university hospital, there is a trend that physicians in university hospitals, who tend to be younger, favor drugs of which characteristics and dosage/administration are explained sufficiently.

3) Prescription motives and age group

The relationship between prescription motives and age groups was as predicted. Particularly, since elderly patients are highly likely to have various concomitant oral medications, it is considered important to pay close attention to the interactions with those drugs. On the other hand, in the adult group, “once a day administration” was the second-ranked motive, followed by “good night’s sleep”.

4) Comparison in clinical effect

“Expected” and “more than expected” effect was obtained in 84.0% of the patients. This result is considered to be similar to the finding reported [3] by Kawashima *et al.* that 65.8% of patients with atopic dermatitis in whom antiallergic drugs were prescribed were satisfied with the drugs.

5) Clinical effect of monotherapy and multiple drug therapy

The reason for the lower percentage for more than “as expected” effect in the multiple drug therapy as compared with monotherapy may be that the ratio of severe cases was higher in the patients who had multiple drug therapy. However, since the severity of the diseases was not investigated in the present survey, the survey needs to be conducted again with a different protocol to clarify the matter. Probably because the ratio of severe cases was higher in the patients who had multiple drug therapy, some cases received more than one antiallergic drug or three drugs in combination. In the present study, due to the limited sample size, the results obtained were limited. Therefore, it is considered necessary to further carry out the investigation based on drug combinations, separately for drugs with and without expected synergistic effects.

Regarding the EBM in the use of antiallergic agents, there is a report [4] on atopic dermatitis and the determination of antipruritic effect. However, although there is evidence for the use of individual drugs, there is no guideline for the selection of drugs for individual cases among multiple drugs. A number of studies [5] have been conducted based on EBM. The concept of EBM is based on “a series of action guidelines for providing medical care by taking into consideration the clinical condition specific to each patient and the sense of value of the patient, after identifying a rationale that is most reliable within the range available”. However, there is a gap between the part “a series of action guidelines for providing medical care by taking into consideration the clinical condition specific to each patient and the sense of value of the patient” and the studies actually conducted. The Consensus Group on New-generation Antihistamines (CONGA) of 2003 issued the criteria for ideal antiallergic agents [6]. However, 16 types of drug were added by the time of our present survey, and 3 types of drugs have been added to date in Japan. Therefore, the criteria cannot be used as evidence for the actual selection of drugs. The present survey revealed that the expected effect was obtained in about 84.0% of the primary physicians who prescribed drugs based on their idea according to various prescription motives. This indicates that the choice of drug prescribed by each primary physician according to various prescription motives is based on EBM.

Another objective in this survey was to prepare a certain protocol for practitioners and university hospitals in order to identify whether the survey would be actually performable in the daily practice of practitioners. The majority of cases included

in the survey were collected by practitioners. This result suggests that clinical research can be performed by involving practitioners over a short period of time. By the involvement of university hospitals in such surveys, information exchange between clinics and university hospitals is fostered, thus enhancing collaboration between hospitals and clinics.

The summary of this study was presented in the 765th and 769th Central Division Meeting of the Japanese Dermatological Association and the 18th Annual Meeting of the Japan Organization of Clinical Dermatologists.

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