Acceptability and Long-Term Compliance with Drug Treatment for Hypercholesterolemia in Japanese Male Workers: II. Long-Term Compliance with Drug Treatment

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Abstract: Acceptability and Long-Term Compliance with Drug Treatment for Hypercholesterolemia in Japanese Male Workers: II. Long-Term Compliance with Drug Treatment: Masayuki TATEMACHI, *et al.* Department of Environmental and Occupational Health, Toho University School of Medicine—We undertook a prospective study to assess the long-term compliance of Japanese male workers with drug treatment for hypercholesterolemia. In workers who accepted treatment with simvastatin, an HMG-CoA reductase inhibitor, compliance was monitored every 6 months with an interview. Factors affecting compliance were identified by using the background characteristics of subjects and a self-administered questionnaire on their type of job, job style, private lifestyle and psychological status at work. Mean (SD) follow-up periods were 21.5 (10.6) months for 640 workers, and 240 noncompliant (< 75 % of prescription) subjects were found. Of these 240, 23 (9.6%) were restored to be finally compliant at the last follow-up (re-compliant). We assessed the time-course rate of compliant subjects and factors affecting drug compliance using Cox proportional hazard model by setting occurrence of a noncompliant attitude to an endpoint. The cumulative compliance rate at 36 months was 0.508 when excluding 23 re-compliant subjects and 0.529 when considering them as compliant. Multivariate analysis showed that age and present

medical illness with hypertension (HT) in background characteristics of subjects and the habit of having breakfast daily in factors related to private-lifestyle were significantly associated with compliance. Baseline lipid profiles and work related issues were not associated with compliance. The occurrence rate of side effects did was similar in compliant and noncompliant workers. In this study, even though considering the re-compliant subjects, the rate of compliant subjects over a 3-yr period was considerably low (around 50%). The factors related to compliance were age, present illness with HT and the habit of having breakfast daily.
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In treating chronic disease such as hypercholesterolemia, patients' noncompliance with both lifestyle modification and drug treatment is a major problem¹⁾. Although drug treatment for hypercholesterolemia has proved to be effective for both primary and secondary prevention of ischemic heart disease (IHD) in several trials^{2–4)}, noncompliance, in clinical practice, with those treatments for lowering serum cholesterol is a major problem in treating hypercholesterolemia as described in major clinical trials in which the rate of noncompliance was reported to be 15.6 to 23.5%⁵⁾.

Previous reports showed that drug compliance generally depends on side effects, particularly in gastrointestinal symptoms¹⁾. Nevertheless, in drug treatment for patients with hypercholesterolemia with

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HMG-CoA reductase inhibitors, having less gastrointestinal side effects, difficulties in complete patient compliance are reported, most likely because the patients, being without symptom, feel no necessity and no motivation for treatment^{6,7}.

In the workplace, management for hypercholesterolemia has a high priority because more than 24.7 % of workers have hypercholesterolemia in the middle-age population⁸. In our preliminary study, the distribution of the serum total cholesterol level of those workers was in the range requiring drug therapy as recommended in the guideline of the Japan Arteriosclerosis Society⁹. We believe that improving compliance with drug treatment is an important issue, and identifying affecting factors associated with jobs is crucial in health care of the workplace. We therefore conducted a prospective study. The profiles of participants were described in detail in part I of this study¹⁰. Briefly, we recommended a treatment with simvastatin, an HMG-CoA reductase inhibitor, in addition to a diet-based treatment program, for all eligible workers, with hypercholesterolemia diagnosed in a legally required medical check-up, and who had not been improved after a 3-month diet therapy. Subsequently, according to each individual preference, subjects were divided to two groups; a group accepting drug treatment (DT) and a group rejecting it. And then we followed them up for three years. This paper describes the long-term compliance of patients with simvastatin treatment, as well as factors affecting treatment compliance using baseline and follow-up data.

Methods

Subjects and methods

The subjects and study design were described in part I of this study¹⁰ and methods for measuring relevant factors are described in this paper. In this study, 15 subjects who had taken cholesterol-lowering drug before this study were also included in addition to the 656 subjects described in part I¹⁰.

Treatment with drugs and health guidance

Subjects in the drug treatment group (DT) received dietary advice from an industrial physician or nurse, or from both for more than 15 min every 6 months, using standardized information brochure¹¹. Health guidance consisted of explaining the relationship between hypercholesterolemia and IHD, and the necessity of lipid lowering treatment as well as other risk factors for IHD which included hypertension, diabetes mellitus, family history, obesity and smoking. The health professional then recommended an ideal diet according to the standardized method. Finally, the health professional cautioned against inappropriate lifestyle factors for each worker by reviewing the worker's lifestyle, and recommended some steps for improvement.

Patients in the DT received simvastatin 5 mg once daily. If the serum TC level did not decrease to the target level described below, the dose of simvastatin was increased to 10 mg, and if necessary, another drug was added after a 1-month evaluation. The targeted level for total cholesterol was less than 220 mg/dl in patients without risk factors for IHD and less than 200 mg/dl in patients with risk factors for IHD according to the JAS guidelines.

Follow-up

Industrial physicians followed up subjects every 3 months, performed blood tests to determine lipid profiles and to survey side effects. They gave health guidance with a standardized information brochure as described above every 6 months and collected the data. The visits were left as the participants' responsibility and no additional approach from professionals was started if participants ignored periodical visits.

Drug compliance

Investigators classified drug compliance in data from interviews into 4 grades: always took the drug according to the prescription (complete); occasionally forgot to take the drug (good); frequently forgot to take the drug (poor); and always forgot to take the drug (very poor). The criteria referring to these grades were as follows: complete, $\geq 90\%$ use of the prescription; good, $\geq 75\%$ and $< 90\%$ use of the prescription; poor, $\geq 25\%$ and $< 75\%$ use of the prescription; and very poor, $< 25\%$ use of the prescription. The data on compliance and serum chemistry were collected at 1, 3, 6, 12, 24, 30 and 36 months after the start of treatment.

Job profiles and lifestyle

Job profiles and private lifestyle, including type of job, work shift, work overtime, commuting time, marital status, living style, frequency of having breakfast, frequency of eating dinner out, frequency of exercise, sleep time, smoking habit, alcohol consumption, and stress level, were determined by a self-administered questionnaire. Alcohol consumption was calculated by multiplying the typical amount of ethanol (g) consumed in a day by the frequency of drinking in a week. Stress level was classified into 11 grades, with 0=low and 10=high.

Quality control for laboratory data

For the purpose of quality control in conducting a multi-centered study, we chose the laboratories that participated in Zenkoku Roudou Dantai Rengou-Kai or certified by quality control programs, with Clinical Examination Quality Control Investigation conducted by the Japanese Medical Association. In addition, we confirmed the use of the compatible assay methods and international unit for GOT, GPT and γ -GTP concentrations among laboratories.

Statistical Analysis

The statistical analysis was performed using SPSS software (SPSS Japan, Inc., Tokyo). The rate of compliant subjects was estimated and factors affecting compliance were identified by using Cox proportional hazard model.

Results

Compliance with drug treatment

In this study, the 671 subjects included 656 who accepted drug treatment (DT group) in part I of this study [10], and 15 who had taken cholesterol-lowering drugs before this study and were not included in part I. Out of 671 subjects, 31 subjects were excluded because 25 had no follow-up data (rejected participation in this part II study), and 6 had no information about compliance. Thus, we analyzed data on 640 workers who were followed up once or more than once. Mean (SD) follow-up periods were 21.5 (10.6) months. The numbers of subjects who were followed up for <1y, 1y≤ and <2y, and ≥ 2y were 86, 209 and 345, respectively. There were no significant differences in background characteristics such as age, lipid profiles, present illnesses, work-related factors, or private-lifestyle among subjects with different follow-up periods (data not shown). There were significant differences in mean follow-up periods among 28 institutions, but not among sectors or locations of industries.

Drug compliance clearly affected the serum lipid profile. Subjects having better compliance (complete or good with an interview) had more reduction, particularly in the serum total cholesterol (TC) level and in the low-density lipoprotein cholesterol (LDL-C) than poor compliance subjects (poor or very poor with an interview) (Fig. 1).

Definition of noncompliance

From the results of the serum TC levels by compliance with an interview, compliance was defined as noncompliant when 1) poor or very poor compliance with an interview was observed twice or more than twice during the follow-up periods, 2) poor or very poor compliance with an interview was observed at the last follow-up, and 3) the follow-up became impossible because of no-response or refusing a doctor's prescription. Based on this definition, 240 (35.2%) workers had a noncompliant attitude, and 400 (64.8%) did not. The 240 noncompliant subjects included 159, 53 and 28 that met with 1), 2) and 3), respectively, of the noncompliant definition as mentioned above. Of 159 noncompliant subjects who met with 1), 23 were restored to compliance at the last follow-up (re-compliant). There was no significant difference in the noncompliant rate among subjects with different follow-up periods (<1yr, 1yr≤ and <2yr, and ≥2yr), 36.0% (31/86), 32.2% (66/205) and 36.8% (120/326), respectively.

Fig. 1. Effects of drug compliance on lipid profiles. Results are presented as the mean $\pm$ SE.

Fig. 2. Cumulative compliance rate curve. Occurrence of noncompliance was set to the endpoint, and the cumulative compliance rate was calculated using Cox proportional hazard model.

Side Effects

Symptoms that were considered to be side effects occurred in 10 cases. Adverse clinical events were detected in 24 cases. Of them, noncompliant subjects were 3 (30%) and 8 (33%) (symptoms and abnormalities in blood tests, respectively). These rate did not differ from the rate (35.2%) of noncompliant subjects.

Estimation of compliance rate

The dropped-out cases without a noncompliant attitude during the follow-up period were handled as censored cases, and the time-course rate of compliant subjects was assessed using Cox proportional hazard model by setting the occurrence of a noncompliant attitude to the endpoint. Censored cases included transferees or retirees among study subjects and subjects not to be followed up for reason of the industrial physician's (investigator's) transfer and restriction of clinic functions. The period of the endpoint (occurrence of noncompliance) was defined as the point of the second observation of the poor or very poor compliance with interviews or the last follow-up. When the re-compliant cases were excluded, the estimated rates of compliant subjects were calculated using Cox proportional hazard model, and the cumulative compliance rate at 6, 12, 24, and 36 months was 0.889 (SE=0.012), 0.807 (0.016), 0.626 (0.021) and 0.508 (0.027), respectively (Fig. 2). When they were considered as compliant, the respective cumulative compliance rate was 0.893 (0.012), 0.813 (0.015), 0.641 (0.020), and 0.529 (0.026).

Factors affecting drug compliance

Table 1 shows the association between background characteristics and compliance by hazard ratio for noncompliant, excluding the re-compliant subjects. Age was significantly and inversely associated with

noncompliance, so that the other background factors were adjusted for age. There was no significant association between the lipid profile and compliance, as well as other risk factors for IHD, except for present illnesses with hypertension and diabetes mellitus. Risk factors for IHD included a serum TC level ≥ 260 mg/dl, the presence of hypertension, presence of diabetes mellitus, family history of IHD, obesity and current smoking habit. In addition, there was no significant association between the number of risk factors for IHD and compliance.

Table 2 shows the association between compliance with drug treatment and job profile by hazard ratio adjusted for age and present medical illness of hypertension and diabetes mellitus, excluding the re-compliant subjects. The job profile included the type of job, job style, work shift, overtime work, sleep length and commuting time. In addition, we examined the effect of the stress level on compliance. Of 640 subjects, 410 answered questionnaires regarding job profiles and private-lifestyle. The questionnaire reply rate was less than 50% in 16 institutions out of a total of 27, but there were no significant differences in the reply rate among sectors and locations of industries. The adjusted hazard ratio of sales job was 1.74, but there was no significant association. The unclassified job type was significantly and inversely associated with noncompliance (hazard ratio=0.48, 95% confidence interval (CI) =0.25–0.93). The work shift, mean work overtime, sleep length, commuting time and stress level were not associated with compliance.

Association between drug compliance and private lifestyle

Marital status and living style (living with his family or alone) was not associated with drug compliance (Table 3). The habit of not taking breakfast daily was significantly associated with noncompliance (hazard ratio=1.63, 95% CI=1.09–2.44). Low frequency (1–2 d per week) of daily exercising was associated with noncompliance, showing a borderline significance (hazard ratio=1.44, 95% CI=0.998–2.07), but the very low frequency (<1 d per week) was not. Other private-lifestyle factors, including the frequency of eating dinner out or drinking alcohol, or ethanol consumption did not affect drug compliance.

Multivariate analysis

To determine factors affecting drug compliance, a multivariate analysis was performed, and the results are summarized in Table 4. Age, present illness with hypertension and the habit of not taking breakfast daily were significantly associated with a noncompliant attitude. Low frequency of daily exercising was significantly associated with a noncompliant attitude, but the very low frequency was not.

Table 1. Association between background characteristics and compliance

		n	Hazard ratio	95% CI
Age	40–44 yr	164	reference	
	45–49 yr	188	0.64	0.46–0.89
	50–54 yr	182	0.66	0.47–0.93
	55 yr–	80	0.58	0.36–0.94
			trend $p < 0.01$	
BMI (kg/m ²)		529	1.00 ^{a)}	0.96–1.03
Lipid profile				
	TC (mg/dl)	621	1.00 ^{a)}	0.999–1.01
	TG (mg/dl)	612	1.00 ^{a)}	1.00–1.01
	HDL-c (mg/dl)	585	1.00 ^{a)}	0.99–1.01
Present Medical History				
Hypertension				
	no	508	reference	
	presence	106	0.45 ^{a)}	0.29–0.71
Diabetes Mellitus				
	no	551	reference	
	presence	63	0.45 ^{a)}	0.26–0.79
Hyper-uremic acidemia				
	no	552	reference	
	presence	62	1.22 ^{a)}	0.78–1.92
Smoking habit	never- or ex-smoker	281	reference	
	current smoker	288	1.08 ^{a)}	0.82–1.43
Family History of IHD	no	445	reference	
	yes	46	1.31 ^{a)}	0.81–2.14
Number of risk factors for IHD ^{b)}		425	1.00 ^{a)}	0.86–1.15

a) Age adjusted, b) Number of risk factors is the total number satisfying the following criteria; serum TC level >260 mg/dl, presence of hypertension, presence of diabetes mellitus, family history of IHD, obesity (BMI>24.0) and current smoking habit. TC=total cholesterol, TG=triglyceride, HDL=high density lipoprotein. CI=confidence interval

Table 2. Association between treatment compliance and job associated factors

	Total informative cases (%)	adjusted ^{a)} Hazard ratio	95%CI
Type of job			
Office	64	reference	
Manufacturing	149	0.96	0.61–1.51
Sales	13	1.98	0.81–4.87
Research and development	17	0.76	0.29–1.98
Management	75	0.84	0.48–1.47
Other	61	0.48	0.25–0.93
Shift work			
Shift work	108	reference	
Non-shift work	289	1.01	0.71–1.45
Work overtime (h/month)	379	1.01	0.998–1.01
Sleeping time (h/d)	382	0.87	0.75–1.02
Commuter time (min/d)	387	1.00	0.99–1.003
Stress level (0–10, low-high)	380	1.00	0.92–1.08

a) Adjusted for age and present medical histories of hypertension and diabetes mellitus.
CI=confidence interval

Table 3. Association between treatment compliance and private lifestyle factors

		Total informative cases (%)	Adjusted ^{a)}	
			Hazard ratio	95% CI
Marital status				
	married	359	reference	
	single	34	1.30	0.79–2.14
Living style				
	living with family	351	reference	
	alone	36	1.36	0.78–2.36
Eat breakfas				
	every day	340	reference	
	occasionally or never	56	1.63	1.09–2.44
Frequency of eating dinner out (/wk)				
	<1 d	179	reference	
	1–2 d	131	0.89	0.62–1.29
	>2 d	86	0.94	0.60–1.47
Exercise (/wk)				
	>2 d	56	reference	
	1–2 d	115	1.44	0.998–2.07
	<1 d	222	1.15	0.70–1.89
Frequency of drinking alcohol (d/wk)		297	1.00	0.99–1.02
Ethanol consumption (g/wk)		297	1.00	0.999–1.002

a) Adjusted for age and present medical histories of hypertension and diabetes mellitus.

CI=confidence interval

Table 4. Multivariate analysis

	n	Hazard ratio	95% CI
Age	617	0.95	0.91–0.98
Present Medical History			
Hypertension			
no	328	reference	
presence	62	0.54	0.31–0.93
Diabetes Mellitus			
no	353	reference	
presence	37	0.63	0.34–1.18
Eat breakfast			
every day	335	reference	
occasionally or never	55	1.64	1.08–2.49
Exercise (/wk)			
>2 d	55	reference	
1–2 d	113	1.49	1.03–2.15
<1 d	222	1.25	0.76–2.07

CI=confidence interval

Discussion

To our knowledge, this is the first prospective analysis of treatment compliance in Japanese male workers. Generally, patient compliance with drug treatment is critical in the success of a treatment for chronic disease, on which a large number of papers have been published^{4,5)}. Methods used in assessing drug compliance with cholesterol-lowering drugs, included measuring the drug content in blood or urine, pill count and use of a questionnaire^{4,5)}. Each method has both advantages and disadvantages. Bruckert E. *et al.*⁶⁾ have reported that compliance assessed

by both pill count and patient interviews gave similar results in the Coronary Drug Project in a secondary prevention trial. In the present study, the patient compliance obtained from interviews was graded in 4 degrees. Because the subjects were clearly divided into two groups according to serum cholesterol levels, we defined patients who took 75% or more of the prescription as compliant, and patients who took less as noncompliant. In addition, the cases were defined as noncompliant when they were dropped out due to no-response and refused their doctor's recommendation. We considered the

occurrence of a noncompliant attitude as an endpoint and applied Cox proportional hazard model to assess the time-course rate of compliant subjects and to identify factors affecting compliance, since there was no significant difference in the noncompliance rate among subjects with different follow-up periods. The estimated rate of compliant subjects decreased time-dependently to around 50% in 3 yr. Although considering the presence of the re-compliant subjects, our results suggest that noncompliance rates are higher than that found in other populations (20%–30%)^{4–6}. In addition, considering that noncompliance was defined with stricter criteria as taking < 80–90% of the prescription in those studies, the rate of noncompliant subjects in this study seems to be considerably higher than it at first appears to be.

Traditional solutions to the problem of noncompliance include appropriate education, improved physician-patient communication and behavioral strategy⁷. In fact, this study population received much more education and support from professionals in treating hypercholesterolemia than the general population. Industrial physicians generally have better communication with patients and can explain the purpose of the medication better and the regimen in detail. With repeated health guidance sessions, the subjects of this study presumably well understood the risk of IHD in relation to hypercholesterolemia. Behavioral strategies could include simplifying the treatment regimen, the use of social support, continued follow-up, and others. In this study, most patients received a once-a-day regimen of simvastatin along with the support of industrial physicians and nurses, in addition to periodical follow-up. The subjects also had healthcare service delivery, which represents a new strategy for intervention⁷. In spite of these advantages, the results of this study still showed a high rate of noncompliance in this population.

Side effects of the drug, particularly in gastrointestinal symptoms generally affect patient compliance with drug treatment¹. In this study, however, there were no differences between compliant and noncompliant workers in the occurrence rates of side effects, and we considered three factors, educational factors, work-related issues, and private lifestyle to be related to this high noncompliance rate. We believe that if patients have adequate awareness of the importance of treatment, they generally demonstrate higher levels of compliance. There were no differences between compliant and noncompliant groups in baseline lipid profiles and baseline risk factors for IHD, suggesting that workers in this study were predicted to have little awareness of the risk factors of IHD. As mentioned in part I, the average serum TC level of subjects in this study was above 270 mg/dl¹⁰. These results indicate that there is a need for effective educational programs to promote treatment acceptance and compliance. Regarding work-related factors, no

significant association was observed with patient compliance, except for job type. The job type was likely to be associated with compliance. An unclassified job type was significantly and inversely associated with noncompliance, indicating that further detailed information regarding job types was needed. In contrast to part I of this study, the factors which affected the acceptability of drug treatment such as sleep time and stress level¹⁰, were not associated with drug compliance in part II. In general, sales persons have a higher frequency of drinking alcohol and eating dinner out than other workers in Japan. This irregular lifestyle might have lowered compliance, but in this study, these lifestyle factors did not significantly affected drug compliance. Although alcohol drinkers generally tend to discontinue the medication, because of the effect of alcohol abuse or of being in fear of increased side effects by combining drink and medication¹², there was no significant difference in compliance rates based on frequency of drinking or ethanol consumption. In regard to private lifestyle, taking breakfast daily was significantly associated with compliance. This result suggest that workers having a regularly lifestyle were more compliant with drug treatment.

As mentioned in part I of this study¹⁰, participants in this study may possibly be more health conscious, to some degree, than the general population of workers with hypercholesterolemia for the following reasons. 1) Subjects with very low health consciousness were not included, since, according to this study protocol, we could not make contact with those who did not answer even the approach for explanation of the results of periodically medical check ups. 2) Participants whom we followed up for a longer period in this study were more health conscious than participants whom we could not. For these reasons, there could be partial bias in the selection of study subjects, and the true noncompliance rate in workers might be higher. In addition, there are several problems in interpreting the results from work places in a multi-center study. The results may depend on differences in the characteristics of workers among different companies. In addition to job styles and the characteristics of each company, achievements in education on the prevention of IHD performed before this study may be important in determining drug compliance. Therefore, we consider the necessity of further comparison in compliance between types of jobs, sectors of industries, locations of industries, and educational achievements using larger populations in the future.

Based on the results of part I of this study, about half of the hypercholesterolemic workers diagnosed in periodical check-ups accepted drug treatment after when it was recommended¹⁰. This study showed that about 50% of workers who accepted treatment were compliant. Thus, only a quarter of hypercholesterolemic workers who

were detected in periodical check-up received the full benefit of drug treatment. This result indicates that developing acceptability- and compliance-enhancing programs for hypercholesterolemia is an important issue for workers' health care.

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References

- 1) JS Berg, J Dischler, DJ Wagner, JJ Raia and N Palmer-Shevin: Medication compliance: a health care problem. *Ann Pharmacother* 27, S1-S24 (1993)
- 2) Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). *JAMA* 269, 3015-3023 (1993)
- 3) W.H.O: cooperative trial on primary prevention of ischemic heart disease using clofibrate to lower serum cholesterol: mortality follow-up. Report of the Committee of Principal Investigators. *Lancet* 2, 379-385 (1980)
- 4) MH Frick, O Elo, K Haapa, OP Heinonen, P Heinsalmi, P Helo, JK Huttunen, P Kaitaniemi, P Koskinen, V Manninen, H Mäenpää, M Mäkönen, M Mänttari, S Norola, A Pasternack, J Pikkarainen, M Romo, T Sjöblom and EA Nikkilä: Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. *N Engl J Med* 317, 1237-1245 (1987)
- 5) H Maenpaa, V Manninen and OP Heinonen: Compliance with medication in the Helsinki Heart Study. *Eur J Clin Pharmacol* 42, 15-19 (1992)
- 6) E Bruckert, C Simonetta and P Giral: Compliance with fluvastatin treatment characterization of the noncompliant population within a population of 3845 patients with hyperlipidemia. CREOLE Study Team. *J Clin Epidemiol* 52, 589-594 (1999)
- 7) NH Miller: Compliance with treatment regimens in chronic asymptomatic diseases. *Am J Med* 102, 43-49 (1997)
- 8) Industrial Health Division, Industrial Safety & Health Department, Labor Standards Bureau. Results of legal medical check-up in 1999. *Roudou Eisei Kannri* 11, 6-11 (2000)
- 9) Investigating committee of guideline for diagnosis and treatment of hyperlipidemia, Japan Atherosclerosis Society: Guideline for diagnosis and treatment of hyperlipidemia in adults. *Jpn Atherosclerosis* 25, 1-34 (1997)
- 10) M Tatemichi, T Hamaguchi, M Hashira, T Hayashi, M Ito, A Nakatani, H Hiro, K Mori, Y Okubo, T Ezaki, H Sugimori and K Yoshida: Acceptability and Long-Term Compliance of Drug Treatment for Hypercholesterolemia In Japanese Male Workers. I. Acceptability of Drug Treatment. *J Occup Health* 44, 166-175 (2002)
- 11) Y Ozono, S Fukushima. Hyperlipidemia and diet for hyperlipidemia. *Iyaku Koukoku-sha*, Tokyo, 1994 1-4
- 12) JT Sullivan, CA Naranjo and EM Sellers: Compliance among heavy alcohol users in clinical drug trials. *J Subst Abuse* 1, 183-194 (1988)