Countermeasures on the Influence of Psychiatric Drugs on the ECG

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INTRODUCTION

Previously, we reported on the ECG changes brought about by psychotropic drugs or neuroleptics[1]. Abnormalities in ST, T waves which are attributed to psychotropic drugs appear at high incidence, are generally deemed nonspecific changes, and are left untreated. Tachycardia and other changes in the ECG are also not regarded as significant changes, and at present, measures taken do not go beyond changing the method of administering the psyc hotropic drugs. For instance, reducing the frequency of administration, decreasing the dosage, or changing the kind of psychotropic drugs to be administered. However, there are many cases in which psychotropic drugs cause arrhythmia or blokage due to the Adams-Stokes syndrome, resulting in death[2].

In this report, studies were made on ECG changes upon administration of various heart medicines, as symptomatic therapy, or by changing the dosage and means of administration of psychotropic drugs. We have attempted to discover how such alterations affect changes which are considered the result of standard means of administering psychotropic drugs.

MATERIALS AND METHODS

Of the 203 cases in the Kitsunan Hospital, who showed ECG changes following administration of psychotropic drugs, as reported in previously[1], 140 cases showing ST, T changes, incomplete BBB, and tachycardia

were selected as the subjects for this study.

Patients with changes in ECG were divided into two groups; Group 1 consisted of patients in which a heart medicine was administered jointly with psychotropic drugs. The method of administering the psychotropic drugs was unchanged, and Group 2, in which no heart medicine was administered, but alterations in the way of administration of the psych;tropic drugs, e.g., reduction in dosage, and changes in the kinds of drugs, were made. The ECG examination was carried out every month, and an overall judgement on the results of ECG was made three months later.

A total of 79 patients showing T changes was divided into two groups —the heart medicine— administered group and the non-administered group. 57 patients of the administered group were subdivided into the diltiazem group, the co-enzyme Q_{10} group, the carbochromen group and the beta-blocker group. Reduction in the dosage of the psychotropic drugs, or changes in the kind of drugs used were made in 22 patients of the non-treated group. For the non-administered groups, the dosage of psychotropic drugs was reduced by one third and the frequency of administration was decreased from three, to two times a day in 11 cases, and the kinds of psychotropic drugs were changed from thioridazine to perphenazine, from levomepromazine to pericyazine, and from tricyclic antidepressant to thiothixene in the remaining 11 cases.

26 patients showing ST changes were also divided into similar groups. One of these heart disease medicines —diltiazem, co-enzyme Q_{10}, carbochromen, beta-blocker, molsidomine and oreiprenaline— was used in 18 cases. No heart medicine was administered, but the method of administering the psychotropic drugs was changed in 8 cases.

Of the cases of bundle branch block, 20 cases of incomplete BBB were divided into a heart medicine-administered group, with 10 cases, and the non-administered group, with 10 cases, for judgement on the results. One of these heart medicines —diltiazem, co-enzyme Q_{10} and carbochromen— was administered.

Of 11 cases of sinus tachycardia, with a heart rate of 110/min or more, observations were made on the clinical course by administering beta-blocker in 2 cases, and by reducing the dosage or changing the kinds of psychotropic drugs in 2 cases.

RESULTS

Improvement on T changes in the ECG was noted in 41 patients (71.9%) of the heart medicine-administered group and 14 (63.6%) of

the non-administered group. But no significant difference was observed between the two groups, nor was there any difference in efficacy between the different heart medicines administered (Table 1).

Improvement on ST changes in the ECG was observed in 13 cases (72.2%) of the administered group, while efficacy was noted in 6 cases (75.5%) of the non-administered group (Table 2). In this case also, there was no significant difference in the improvement rating between the administered group and non-administered group.

Efficacy on BBB was observed in 7 cases (70.0%) of the administered group, and 6 cases (42.8%) of the non-administered group. There was a clear difference in the improvement rating between the administered group and non-administered group (Table 3).

Efficacy on tachycardia was observed in 1 case (50.0%) of the heart medicine administered group and 7 cases (77.8%) of the nonad-

Table 1. Efficacy on T changes

	Very good	Improved	Poor	Total
Heart-medicine-administered group	12	29	16	57
Diltiazem	5	8	4	17
Co-enzyme Q_{10}	3	10	3	16
Carbochromen	3	6	4	13
Beta-blocker	1	5	5	11
Non-administered group	12	2	8	22
Total	24	31	24	79

Table 2. Efficacy on ST changes

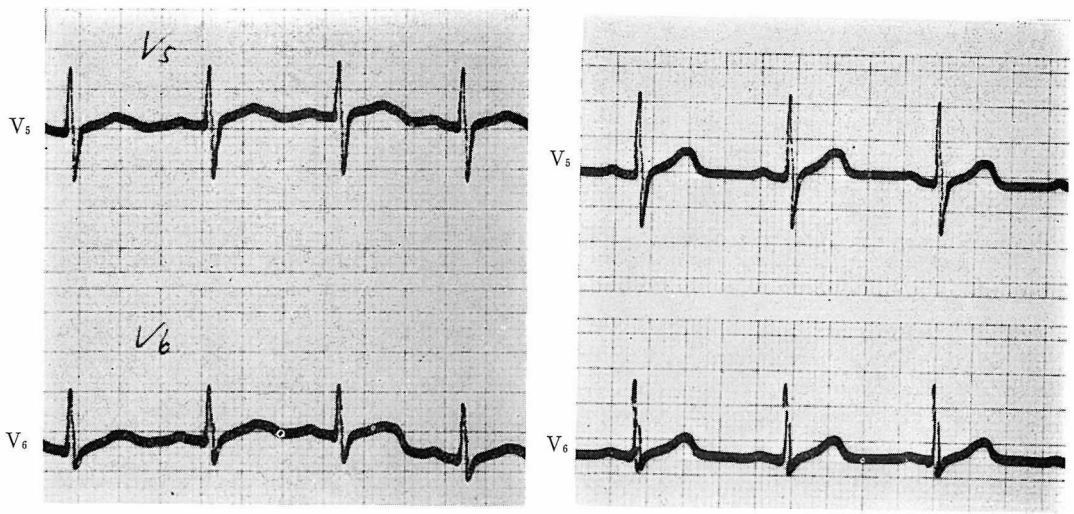
	Very good	Improved	Poor	Total
Heart-medicine-administered group	9	4	5	18
Diltiazem	3	1	1	5
Co-enzyme Q_{10}	2	1	1	4
Carbochromen	2		1	3
Beta-blocker	2	1	1	4
Molsidomine		1		1
Oreiprenaline			1	1
Non-administered group	5	1	2	8
Total	14	5	7	26

Table 3. Efficacy on bundle branch block

	Very good	Improved	Poor	Total
Heart-medicine-administered group	2	5	3	10
Diltiazem	1	3	1	5
Co-enzyme Q_{10}	1	2	1	4
Carbochromen			1	1
Non-administered group	6		8	14
Total	8	5	11	24

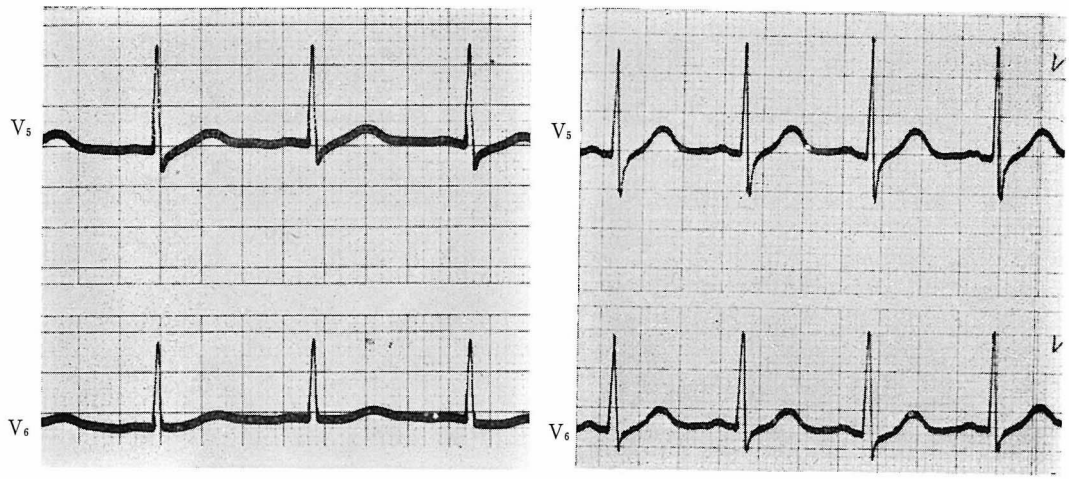
Table 4. Efficacy on tachycardia

	Very good	Improved	Poor	Total
Heart-medicine-administered group (Beta-blocker)		1	1	2
Non-administered group	4	3	2	9
Total	4	4	3	11



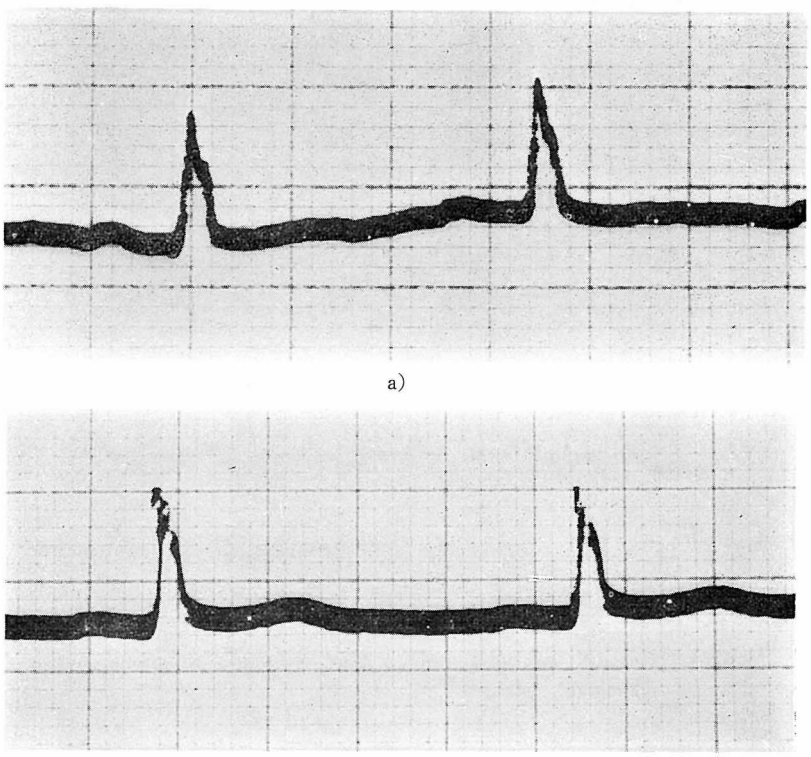
a) b)

Fig. 1. 22 year-old female. On oral administration of levomepromazine 200mg/day for a year.
a) Blunt T wave observed in Leads $V_{5,6}$
b) T change improved following a 3-month oral administration of diltiazem 90mg/day



a) b)

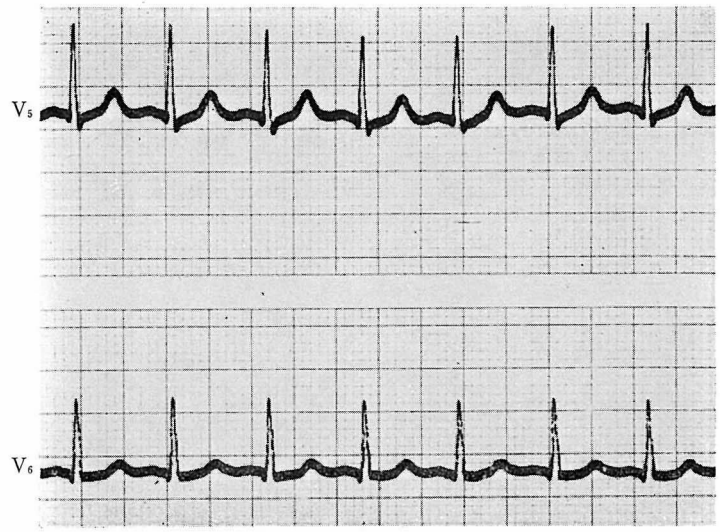
Fig. 2. 41 year-old male. On oral administration of haloperidol 9mg/day for 10 months.
a) Junctional ST seen depressed in Leads $V_{5.6}$
b) Improved following a 2-month oral administration of coenzyme Q_{10} 30mg/day



a)

b)

.Fig. 3. 43 year-old male. On the oral administration of clocapramine 150mg/day for six months.
a) Findings of incomplete BBB shown in Lead aVf.
b) Improved following a 2-month administrationof coenzyme Q_{10} 30mg/day.



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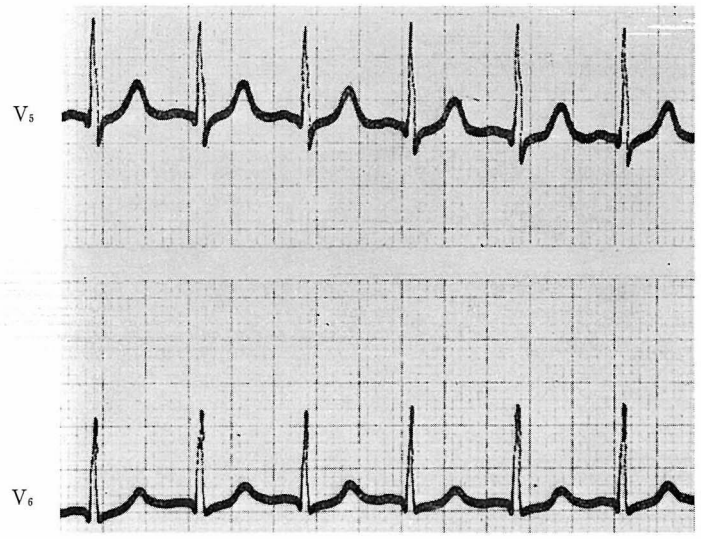

b)

Fig. 4. 25 year-old male. On the oral administration of chlorpromazine 150mg/day for two months.
a) Sinus tachycardia, heart rate 130/min.
b) Heart rate 110/min one month after administration of chlorpromazine was discontinued annd switched to propericiazine 60mg/day per os.

ministered group (Table 4).

Figs. 1-4 show cases in which T change, ST change, incomplete BBB and tachycardia were improved.

Measurements were made of serum electrolytes (Na, K, Mg and Cl) on three occasions, but no particular relationship was observed between the val es obtained and changes in the ECG.

DISCUSSION

Changes in ECG, particularly ST and T changes, are often observed during the administration of psychotropic drugs (Yamada et al.[1], Okamoto et al.[3], Suwa et al.[4], Sakai et al.[5]). The mechanism of which is believed to be due to a phenothiazine derivative exerting an inhibitory effect on Na^+, K^+ dependent ATPase which is present in the fascia and takes part in the maintenace of the membrane potential (Loestma et al.[2]). Administration of phenothiazine derivatives to animals is reported to lower the Na concentration in the myocardium (Huston et al.[6]). Therefore, the influence of the phenothiazine derivative on the metabolism of electrolytes, or the enzyme system, is considered to bring on a change in the ECG.

Furhtermore, phenothiazine derivatives are believed to have a quinidine-like effect on the heart, and that consequently, phenothiazine acts directly on the heart to bring on ST, T changes (Sakai et al.[5]). Phenothiazine derivatives increase the coronary flow transiently, and subsequently, when the concentration of the drug in the blood is low, the coronary flow decreases, but in high concentrations, the drug cuts off the coronary flow completely. Of the other drugs which bring on a marked decrease in the coronary flow, thioridazine is said to be the most potent, followed by perphenazine, prochlorperazine, chlorpromazine, levomepromazine and prometha zine in that order (Landmark et al.[7], Langslet[8]).

When the level of these drugs in the blood becomes high, atrioventricular heart blockage appears. Coronary angiograms and myocardial biopsies were taken in cases in which phenothiazine and its related compounds brought abnormalities in the heart. Such abnormalities, as were seen in electron microscopic observations on the myocardium, revealed degeneration of mitochondria, degeneration of the muscular fiber and increased accumulation of glycogen. These findings resemble myocardosis caused by alcoholism, which is believed to impair the individuals energy potential (Alexander et al.[9]).

Meanwhile, drugs of the imipramine group and amitriptyline group

or tricyclic antidepressants are liable to cause QT prolongation and ST, T changes in the ECG, even in standard doses, compared with phenothiazine derivatives (Hollister[10], Kelly et al.[11]). Tricyclic antidepressants are believed to directly effect the myocardium (Cassano et al.[12]), while psychotropic drugs primarily act on the central nervous system, and they naturally act on the autonomic nervous system also. There is also a possibility that this central change exerts an influence on the ECG.

For ST, T changes on the ECG, isosorbide dinitrate, a combined preparation of potassium oxalate and sodium acetate and ergostamine tartrate are effective (Wendokos[13]). A combined preparation of aspartic acid Mg salt and Na salt is also reported to be effective (Wada et al.[14], Taguchi[15]).

Changes in the ECG, such as ST, T changes, BBB, and tachycardia were improved upon administration of various heart medicines, but it should be noted that equal efficacy can be obtained through a reduction in the dosage of, or change in the kind of psychotropic drug being administered. This observation suggests that careful administration of the psychotropic drugs is the most important countermeasure against such changes.

In administering psychotropic drugs, ECG examinations should be performed periodically, while the minimum dosage capable of controlling psychotic symptoms is used. Combined use of thioridazine, chlorpromazine, levomepromazine and tricyclic antidepressants are liable to cause a change in ECG and should be avoided.

In cases where changes in ECG have been observed, despite the utmost care having been exercised, combined administration of heart medicine could possibly be effective.

SUMMARY

An attempt to improve ECG changes was made for 140 patients showing ST, T changes, incomplete BBB and tachycardia. These patients were selected from 203 in-patients of Kitsunan Hospital who showed ECG changes following administration of psychotropic drugs.

The patients were divided into two groups: in one which psychotropic drugs were administered as usual, but a heart medicine was also employed, and one group in which the way of administration of psychotropic drugs was changed, and no heart medicine was administered.

Among 79 cases that showed T changes, improvement in one form or another was observed in 41 out of 57 cases of the heart medicine-

administered group and 14 out of 22 cases in which no heart medicine was administered.

Among 26 cases that showed ST changes, improvement was noted in 13 out of 18 cases of the heart medicine-administered group and 6 out of 8 cases in which no heart medicine was administered.

Among 24 cases that showed incomplete BBB findings, improvement was found in 7 out of 10 cases of the heart medicine-administered group and 6 out of 14 cases in which no heart drug was administered.

Regarding tachycardia changes, 1 out of 2 cases of the betablocker-administered group and 7 out of 9 cases of the non-administered group showed improvement.

So far as these ECG changes are concerned, these was no distinctive difference in improvement between the heart medicine-administered group and the non-administered group. Thus, it may be stressed that studying the way of administration of psychotropic drugs is important in dealing with ECG changes arising from the administration of psychotropic drugs.

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