Evaluation of Effects of Antiarrhythmics on Ventricular Premature Contraction

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Although subjective symptoms and brief recording of ECG have been used for an efficacy evaluation of new antiarrhythmics on ventricular premature contraction (VPC), incidence of subjective complaints in VPC was under 25% and number of VPC for 3 min did not correlate enough to those for 24 hours, indicating these parameters are not appropriate for such a trial. Number of VPC automatically counted by DECG (continous ECG recording for 24 hours) showed high accuracy, while day to day variation of VPC arose as the next problem. While cases of more than about 7,000/day showed very little day to day variation, cases of less than about 1,000/day had poor reproducibility, indicating that the former group can be used for the trials of new antiarrhythmics, but not the latter group. For cases with medium magnitude of VPC variation, DECG should be recorded twice during the period without drug administration and application of the paired t-test for number of VPC in each corresponding hour may bring a good evaluation.

SYMPTOMS thought to be relevant to arrhythmias and electrocardiogram recorded for 1 through 3 min alone have been applied to evaluate the effects of newly developed antiarrhythmics on ventricular premature contraction (VPC). However, the reliability of these parameters has not been fully examined. On the other hand, continuous ECG recording for 24 hours (DECG) has recently come to be used for this purpose!–4 but this method has also some problems. The following study was undertaken for clarifying these points.

METHODS
Patients with VPC, the DECG of which was recorded from 1978 to 1981, were studied in reference to the following items:
1) Relationship between VPC and subjective symptoms.
2) Relationship between the number of VPC for 3 min and for 24 hours.
3) Accuracy of automatic counting of VPC by DECG.
4) Daily change of VPC.
5) Evaluation of effects of antiarrhythmics with due consideration of daily change of VPC.

DECG was recorded by Avionics Model 447 and the number of VPC was automatically counted by Dynamic Electrocardioscanner (Avionics 660B).

RESULTS

Relationship between VPC and Patient's Symptoms
One hundred and eighty-nine patients (parox-
ysmal supraventricular tachycardia: PSVT 15; transient atrial fibrillation: T af 27; sick sinus syndrome: SSS 38; VPC 109) were asked to note their own complaints relevant to arrhythmias while recording DECG.

As shown in Fig. 1, the frequency of complaints was 100% in PSVT, 70.3% in T af and 42.1% in SSS. On the contrary, only 20.4% of patients with VPC felt symptoms. The relationship between the frequency of VPC for 24 hours, divided into 3 groups, and the frequency of patient's complaints was examined, but as shown in Fig. 2 the frequency of the complaints was almost the same in all 3 groups regardless of the number of VPC.

Relationship between Number of VPC for 3 min and for 24 Hours

Figure 3 shows relationship between the number of VPC for 3 min and for 24 hours in 79
patients. This relationship was rather weak, especially in cases of small number of VPC. Even in cases of large number of VPC, its number per day could not be estimated accurately from 3 min recordings.

**Accuracy of Automatic Counting of VPC by DECG**

In 48 patients the number of VPC for one hour automatically counted by Avionics 660B was compared to those in visualized ECG calculated by doctors using reproducing tapes. As shown in Fig. 4, the correlation coefficient was very high, $r = 0.99$, indicating that the accuracy of this kind of autoanalyzer was fully satisfactory. The occasional miscount by the autoanalyzer was chiefly due to noises mixed by bad contact of electrode or drift of baseline.

Daily Change of VPC

On 51 patients with VPC DECGs were recorded twice at an interval of a few days in order to examine daily change of VPC (Fig. 5). As a result, in the cases in which the number of VPC per day were more than 7,000, high correlation was obtained between the first and the second times, but in the cases below this level, especially below 1,000, it showed a wide dispersion tendency.

Evaluation of Effects of Antiarrhythmics with Due Consideration of Daily Change of VPC

From the above-mentioned results, we cannot evaluate the effect of antiarrhythmics by simply comparing the number of VPC before and after

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its administration, in view of the daily change in the cases of small number of VPC. Accordingly, for evaluating the effects of verapamil on VPC, DECGs were recorded 3 times, that is, before (B), 2 weeks after using the drug (A) and 2 weeks after using placebo (P). Then, the significance of the difference of the number of VPC in each corresponding hour was examined between B and A, and, A and P by the paired t-test.

Examples are shown in Figs. 6, 7 and 8. A case in Fig. 6 clearly showed a large number of VPC per day. After administration of verapamil, the number of VPC per day remarkably decreased and after the replacement by a placebo, it increased again. In this case, the number of VPC in each corresponding hour showed definitely significant differences between B and A, and, A and P by the paired t-test. Therefore, this drug
was evaluated as effective in this case.

In Fig. 7, the number of VPC per day after administration of verapamil was smaller than that in B and P. However, no significant difference was obtained between A and P by the paired t-test, although a significant difference was observed between B and A. Consequently, the efficacy of the drug on this case should be evaluated as "undecided".

Figure 8 shows a case which had small number of VPC, that is, 1,722, before drug administration. After administration of verapamil, the number of VPC per day decreased by about 50% as compared to that during the placebo period, but no significant difference was obtained either between B and A or A and P by the paired t-test. We concluded that it was ineffective in this case.

The effects of verapamil were evaluated by this method in 11 cases (Table I). Seven cases (66.7%) are effective, 2 undecided and 2 ineffective.

DISCUSSION

The above-mentioned results indicate that the ratio of the number of arrhythmia to the patients' own complaints is considerably smaller in VPC than in other tachyarrhythmic groups. Accordingly, it is not appropriate to use the patients' complaints as an index for the evaluation of the antiarrhythmic effect against VPC.

The number of VPC from a brief ECG recording, such as for 1–3 min has been frequently utilized in the traditional analysis of antiarrhythmics. However, the number of VPC during a brief period had little significant correlation to those in 24 hours, as seen in the present study. Therefore, it is risky to evaluate the effects of antiarrhythmics by this method.

On the other hand, the automatic counting of VPC by newly developed DECG has a high accuracy. It is consequently proposed to use DECG for the evaluation of the effects of antiarrhythmics. However, the daily variation of the
number of VPC has become a problem in investigating VPC using DECG. In our results, the cases with more than 7,000 VPC per day have almost little daily variation, indicating a high reproducibility. Therefore, in evaluating effects of new antiarrhythmics in almost all cases, it is satisfactory to compare DECGs between before and after drug administration. However, the cases with a small number of VPC per day have problems. Especially those having less than 1,000 VPC have a poor reproducibility, and thus, it is not appropriate for use. In the cases in which the number of VPC is within the range mentioned above, namely about 1,000–7,000 per day, we can obtain the reliable results by recording DECG 3 times and applying a statistical method to examine the significance of the difference between the periods with and without drug administration in each corresponding hour.

In the cases with couplet, triplet or ventricular tachycardia as the background of VPC, we proposed to evaluate the arrhythmia according to Lown's criteria. However, the accuracy of automatic interpretation of such risky VPC should be improved further and their daily changes should also be fully investigated in the future.

REFERENCES

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