Effect of Telmisartan and Amlodipine on Home Blood Pressure by Monitoring Newly Developed Telemedicine System: Monitoring Test by Using Telemedicine. Telmisartan’s Effect on Home Blood Pressure (TelTelbosu)

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We have developed a new home blood pressure (BP) monitoring system by using cellular telephone and the Internet. All data of home BP and pulse rate were directly collected by I-converter date collecting system and sent online to a main server constructed in a central data center. The home doctor can monitor the exercise data of each patient by using this system. This home BP monitoring system was directly connected to the Internet by using application service provider technology (ASP). Anytime and anywhere, each patient can check the changes of these parameters by themselves by using cellular telephone and/or the Internet. The average of the data was calculated and demonstrated online. In real time, all data were monitored and sent to the home doctor’s office. In the present study, we tried to use this monitoring system to compare the effect of some antihypertensive drugs on home BP.

To compare the effects of telmisartan (TEL) and amlodipine (AM) on home BP, home BP was monitored for eight weeks using this telemedicine system. The target point of office BP was 140/90 mmHg or less. After two weeks control period, telmisartan (TEL group: 20–80 mg/day, n = 21) or amlodipine (AM group: 2.5–10 mg/day, n = 19) was orally administrated once a day in the morning. There was no significant difference of office BP between these two groups. Systolic home BP was significantly decreased from 144 ± 4 to 134 ± 3 mmHg (TEL group) and from 143 ± 4 to 135 ± 3 mmHg (AM group), respectively. There was no significant difference in the changes of

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home BP in the morning between groups (eight weeks home systolic BP reduction, TEL: 15 ± 2 mmHg, AM: 13 ± 2 mmHg). However the reduction of home BP in the evening in TEL group was significantly bigger than AM group (eight weeks home systolic BP reduction, TEL: 13 ± 3 vs. AM: 6 ± 3 mmHg). From these data, we concluded that there is a big difference on the effects of antihypertensive agents on diurnal variation and 24hr overall BP variability in home BP. TEL has a good effect on home BP for 24 hours compared to AM. This telemedicine system has a great advantage in monitoring home BP correctly in hypertensive patients.

Keywords  home blood pressure, telemedicine, cellular telephone

Introduction

In recent decades, the rapid development of information and telecommunication technology has found application in the medical field. Computer-assisted medical activity is increasing in several fields, with wide perspectives in nephrology and dialysis accounting for the peculiar characteristics of this population, such as number, complexity, follow-up length, and economic cost (1).

Previously, we reported the telemedicine system to collect the home BP data of patients with end stage renal disease (ESRD) via a cellular phone (2,3). This telemedicine system was constructed by two different systems, the data collection and monitoring system via cellular phone, and the electric medical record sharing system via the Internet using an application service provider (ASP). When these hypertensive patients have some troubles, the urgent information communication system can send abnormal data to the physician in charge and make contact. This telemedicine system has a big advantage in hypertensive patients to monitor the home blood pressure (BP).

We expected that this telemedicine system would have great advantages in hypertensive patients on medication to monitor the effect of antihypertensive agents (2,3). It is well known that the home BP measurement can give more reliable BP information than conventional BP measurement. However, some patients could not input the data by themselves, especially elderly patients. To collect the data from automatic devices directly, we tried to develop a new telemedicine system that can directly collect the data from a fully automatic device, including BP monitor, weight scale, glucose meter, and automated peritoneal dialysis (APD) system.

In the present study, to compare the effect of long-acting antihypertensive drugs, angiotensin type 1 receptor blocker (telmisartan) and calcium channel blocker (amlodipine), we compared the changes of home BP in the morning and in the evening by using this telemedicine system.

I-Converter Data Collecting System via Cellular Telephone

To collect the data from a fully automatic device via a cellular telephone, we developed a fully automatic data collecting system, named the I-converter. This newly developed telemedicine system is shown in Figure 1. After measurement of BP by the fully automatic HEM-705IT (Omron Life Science Co., Ltd., Tokyo, Japan; 4) the I-converter was directly connected between a fully automatic BP measuring device and a cellular telephone. After a connection was established, a green signal was turned on. Then, we flipped the switch of the I-converter, and the data of BP, pulse rate (PR), and time were directly downloaded from a fully automatic device (HEM-705IT; Omron Life Science Co., Ltd., Tokyo, Japan) to the memory of cellular telephone (see Figure 1). These data were directly sent to a main
Telemedicine System to Monitor Home BP

All data, including BP, PR, and time measured in each patient, were accumulated in a main server in an offsite central data center. This main server was directly connected to a Web site system using application service provider technology (ASP). Anytime and anywhere, each patient can access this Web site. All patients using this system can monitor the changes of their data in graph by using a cellular phone or Web site system (see Figure 2). The averages of data were calculated and demonstrated in the Web site.

Outpatient Clinic: Measurement and Self-Measurement of BP at Home

Outpatient clinic BP was measured after resting for at least five minutes in the sitting position. Methods of home BP measurements were well documented in Japan Society of Hypertension (JSH) guidelines for self-monitoring of blood pressure at home (5). All patients were asked to measure home BP once in the morning within one hour of waking after micturition and once in the evening before sleep (total at least twice per day). BP must be measured in a sitting position after 3 min rest. Morning BP must be measured before breakfast and before drug ingestion. Evening BP must be measured before go to bed. In principle, home BP measurements were performed every day throughout the observation and treatment period, using a fully automatic device (HEM-705IT; Omron Life Science Co., Ltd., Tokyo, Japan), which met the criteria of the Association for the Advancement of Medical Instrumentation (4). This device based on cuff-osillometric method. All data of BP and PR

Figure 1. New telemedicine system monitoring home blood pressure using a cellular telephone. After the measurement of blood pressure using a fully automatic device (HEM-705IT; Omron Life Science Co., Ltd., Tokyo, Japan), an I-converter was directly connected to the HEM-705IT and a cellular telephone. After the connection was established, a green signal turned on. Then, we flipped the switch of the I-converter, and the data of blood pressure, pulse rate, and time were directly downloaded from a fully automatic device to the memory of the cellular phone.
measured by HEM-705IT was directly collected to the cellular telephone by using the I-converter data collecting system. These data were directly sent to the main server constructed in the central data center of the JMS Company (Japan Medical Supply Co. Ltd., Tokyo, Japan) using a cellular telephone.

**Web Site for Hypertensive Patients**

When the patients want to check the data in computer, they can access the Web site and monitor the data, including all real data, average, and graph. All data from hypertensive patients were collected to the ASP system and calculated by computer. Patients could access the I-mode site by using a cellular telephone or Internet and get the data whenever they want. If medical staff wants to get the data of these hypertensive patients, they can access the Web site. If some trouble happens with these hypertensive patients, we can get an emergency signal through on the Web site. Then we can call the patient and make a consultation using a cellular telephone.

**Patients and Methods**

**Patients**

This study was performed in a non-randomized, open, parallel manner. Forty-five hypertensive patients who were selected from a population of hypertensive outpatients at Tokorozawa Kidney Clinic (Saitama, Japan), Kawasaki Ida Hospital (Kanagawa, Japan), Sone Clinic (Tokyo, Japan), and Saiseikai-Yahata Hospital (Fukuoka, Japan) were recruited in this study. Patients with hypertension were defined as office systolic BP over 140 mmHg and/or diastolic BP over 90 mmHg, according to the criteria in the report of

![Figure 2. Changes in home blood pressure, pulse rate, and body weight shown on in Web site. Patients and doctors can monitor the changes of home blood pressure in the original record of each patient named I Systems online.](image)

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Japanese Society of Hypertension (JSH) 2000. Exclusion criteria were as follows: severe hypertension (diastolic BP over 120 mmHg), secondary hypertension, accelerated or malignant hypertension within six months prior to the study, serious liver or renal disease, or contraindication to a study drug or study procedure. Most subjects were being treated with antihypertensive drugs other than angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), and calcium channel blocker at the beginning of the observation period, and those drugs were given continuously during the observation and treatment period. All patients included in this study gave their informed consent to participation. The study was performed in accordance with the Second Helsinki Declaration and was approved by the local ethical committee.

**Study Design**

This study was performed in non-randomized, open, parallel manner. The study design consisted of a two-week observation period followed by an eight-week treatment period. After a two-week control period, telmisartan (TEL group: 20–80 mg/day, n = 21) or amlodipine (AM group: 2.5–10 mg/day, n = 19) was orally administrated once a day in the morning. After a run-in period, patients started to receive each drug once daily. Patients were assessed at 2, 4, and 8 weeks at the outpatient clinic in each hospital.

During the study, all subjects were asked to undergo the same dietary and dialysis regimen. Mean daily dietary intake was calculated from individual 24-hour food records during a three-day period and a dietician-informed daily diet program. The dietary protein intake was at least 1 g/kg daily or more, and the energy intake was at least 25 kcal/kg daily or more. Salt intake was restricted to about 7 g daily or less. We interviewed the drug compliance and the dietary regimen at the outpatient clinic every two weeks. When patients failed to come to the clinic, we interviewed them by telephone.

**Statistical Analysis**

In the present study, in each patient, the first measurements of home BP in the morning and evening were used to calculate the average of home BP. All data are demonstrated as mean ± standard error of mean (mean ± SEM). Multiple comparisons were analyzed by analysis of variance (ANOVA) with the Kruskal-Wallis test and subsequent Dunn test. A simple regression analysis was performed for corrections among the variables. A value of $p < 0.05$ was required for statistical significance.

**Results**

**Characteristics of Patients and Adverse Effects of Drugs**

For the forty-five patients recruited at baseline, a complete follow-up was performed. Five patients were omitted from this study because of poor complication of drugs (two cases) and poor measurements of BP at home (three cases). The average age of telmisartan (n = 21) and amlodipine (n = 19) groups were 51.4 ± 2.7 (male, 15; female, 6) and 54.2 ± 2.4 (male, 13; female, 6) years old, respectively. There were no significant differences of age and sex between groups. At the end of study, the average dosages of telmisartan and amlodipine were 44.76 ± 2.35 mg per day and 4.87 ± 0.30 mg per day, respectively. During this experiment, no side effect, complications, or abnormal data of blood chemistry due to telmisartan and amlodipine treatments were reported.
Changes in Systolic and Diastolic Blood Pressure in Outpatient Clinic

At the beginning of this study, there were no significant differences of BP in outpatient clinic. At eight weeks, systolic BP in outpatient clinic was significantly decreased from 167 ± 6 to 148 ± 5 mmHg (TEL group) and 164 ± 5 to 150 ± 5 mmHg (AM group), respectively (see Figure 3). Diastolic BP in outpatient clinic was significantly decreased from 97 ± 4 to 88 ± 4 mmHg (TEL group) and 95 ± 4 to 85 ± 5 mmHg (AM group), respectively. During the experiment, there were no significant differences in systolic and diastolic BP in outpatient clinic between the groups.

Changes in Systemic and Diastolic Blood Pressure in Home

At the beginning of this study, there were no significant differences of BP in systolic and diastolic home BP by using this telemedicine system. Like BP in the outpatient clinic, systolic home BP was significantly decreased, from 144 ± 4 to 134 ± 3 mmHg (TEL group) and 143 ± 4 to 135 ± 3 mmHg (AM group), respectively. Diastolic BP in home showed the same changes as systolic BP. Diastolic BP in home were significantly decreased, from 93 ± 3 to 83 ± 3 mmHg (TEL group) and 91 ± 3 to 85 ± 3 mmHg (AM group), respectively. During the experiment, there were no significant differences in systolic and diastolic BP in home between the groups.

Changes in Pulse Rate in Home

At the beginning of this study, there were no significant differences of pulse rate between two groups in the morning (TEL 68 ± 1 vs. AM 69 ± 1 beats/min) and evening (TEL 72 ± 2 vs. AM 72 ± 2 beats/min) in home. In both groups, basal pulse rates in the evening were significantly faster than that in the morning. In the TEL group, there were no significant changes in pulse rate during the experiment. On the contrary, in the AM group, the pulse

Figure 3. Changes in outpatient clinic systolic and diastolic blood pressure before and after treatment of telmisartan (TEL) and amlodipine (AM). Closed circle (●) indicates systolic blood pressure of the TEL group, open circle (○) indicates systolic blood pressure of the AM group, closed triangle (▲) indicates diastolic blood pressure of the TEL group, and open triangle (△) indicates diastolic blood pressure of the AM group. Data are expressed as mean ± SEM. NS indicates no significance compared to the AM group throughout the experiment.
rate in the morning showed a gradual increase and reached a peak level from 69 ± 1 to 73 ± 2 \( (p = 0.03247) \) at three weeks after amlodipine treatment. From three to eight weeks, pulse rate showed the same levels during amlodipine treatment.

**Changes in Home Blood Pressure in the Morning**

Figure 4 shows the changes in systolic and diastolic home BP in the morning. At eight weeks, systolic home BP in the morning was significantly decreased, from 145 ± 4 to 132 ± 4 mmHg (TEL group) and 144 ± 3 to 133 ± 4 mmHg (AM group), respectively. Like systolic BP, diastolic home BP in the morning was significantly decreased, from 93 ± 4 to 82 ± 3 mmHg (TEL group) and 92 ± 3 to 84 ± 3 mmHg (AM group), respectively. During the experiment, there was no significant difference in systolic and diastolic home BP in the morning between the groups. There was no significant difference of the reduction of home BP (delta change of BP from baseline) in the morning between groups during the experiment (at eight weeks, home systolic BP reduction, TEL: 15 ± 2 mmHg; AM: 13 ± 2 mmHg).

**Changes in Home Blood Pressure in the Evening**

Figure 5 shows the changes in systolic and diastolic home BP in the evening. At eight weeks, systolic home BP in the evening was significantly decreased, from 144 ± 4 to 130 ± 4 mmHg (TEL group) and 140 ± 4 to 134 ± 4 mmHg (AM group), respectively. Like
systolic home BP, diastolic home BP in the morning was significantly decreased, from 93 ± 3 to 84 ± 4 mmHg (TEL group) and 90 ± 4 to 86 ± 4 mmHg (AM group), respectively. During the experiment, there were no significant differences in systolic and diastolic home BP in the evening between the groups. However, the reduction of systolic home BP in the evening in the TEL group was significantly greater than in the AM group (at eight weeks, home systolic BP reduction, TEL: 13 ± 3 vs. AM: 6 ± 3 mmHg).

**Blood Pressure Reduction in Home Blood Pressure in the TEL Group**

Telmisartan treatment induced gradual reduction in home BP in the morning and evening. At six weeks, BP reduction in the morning and evening were 17 ± 4 and 11 ± 4 mmHg, respectively. During the experiment, there was no significant difference in BP reduction between the morning and evening.

**Blood Pressure Reduction in Home Blood Pressure in the AM Group**

Amlodipine treatment induced gradual reduction in home BP in the morning but not the evening. At six weeks, BP reduction in the morning was significantly greater than that in the evening (morning: 11 ± 4, evening: 4 ± 2 mmHg, \( p = 0.04268 \)). At seven weeks, BP reduction in the morning was significantly greater than that in the evening (morning: 13 ± 4, evening: 4 ± 3 mmHg, \( p = 0.02267 \)). In the AM group, during the experiment, the reduction of home BP in the morning was greater than that in the evening.
Discussion

This is the first report comparing the changes of home BP with long-acting antihypertensive drugs by using home BP monitoring system. To compare these effects, we monitored the changes of morning and evening BP in home. TEL and AM have a good effect on morning BP regulation, though TEL has a better effect on evening home BP than AM.

Recently, we have developed a telemedicine system to monitor BP and pulse rate at home (2,3). We are currently using this telemedicine system for the purpose of BP monitoring at home with hypertensive patients. We expect that this kind of telemedicine system has great advantages on hypertensive patients, especially handicapped and elderly patients who have difficulties coming to the hospital. When these patients have some troubles at home, we can monitor the changes of BP over the Internet and contact them via a cellular telephone. In addition, we can use this telemedicine system as a network system between hypertensive patients and medical staff in hospitals. Patients living remotely from the central hospital can attend the affiliated hospital periodically for routine follow-up (e.g., examination of physical condition, blood chemistry, chest x-ray, electrocardiogram). If the patient gives permission, the inspection person at each hospital can monitor the medical record of patient on the Web site. Doctors in the central hospital can confirm their data, including BP, medication, and blood chemistry, on the Web site whenever he wishes. In the future, patients will be able to receive drugs prescribed by the nephrologists in central hospital using this telemedicine system as required. Furthermore, we can use this system as an emergency alarm system. In a case of emergency, all data are available in the central hospital, and the doctors can order the necessary medication immediately.

Previously, it has been believed that the most useful BP information related to hypertension in clinical practice is the office BP. BP information for epidemiological purpose is generally also obtained in medical environments similar to those used for mass screening. Recently, there are some questions posed regarding the true representativeness of office BP, so research has focused on other ways of measuring BP, such as ambulatory BP monitoring (ABPM) and home BP measurements. From the Ohasama study, Imai et al. (6) reported that the level and the billability of hypertension as assessed by ABPM and home BP are independent predictors of cardiovascular mortality. Recently, according to a cohort study of 4939 treated hypertensive patients, Bobrie et al. (7) found that home BP measurement had a better prognostic accuracy than office BP measurement. Almost all of BP control recommendations, including JNC7 (8), 2003 WHO/ISH (9), 2003 ESH (10), and JSH 2004 (11), recognize the importance of home BP measurement. Advantages of home BP measurement have been well documented in several reports (5–7). Indeed, BP self-measurement not only provides valuable information of the home BP of the treated patient, but also improves patient’s compliance with antihypertensive therapy (12). It has been recognized for more than 50 years that self-BP measurement reading in home are different from those recorded in office (13,14). Self BP measurements is popular among patients, as indicated by the huge sales of self-monitoring devices, but self BP measurement has not been accepted as readily in medical practice as home blood glucose monitoring in diabetes has been. There are a numbers of reasons for this. The recent report of the European Society of Hypertension recommendations for conventional, ambulatory, and home blood pressure measurement described some of them:

1. To use self BP monitoring using the auscultatory technique was troublesome and time-consuming, and not suitable.
2. Self BP monitoring is subject to bias, whereby patients can record pressure of their own making.
3. Self BP monitoring may induce anxiety in some patients, who may take an obsessional interest in BP.
4. Most automated devices available for self-BP monitoring have not been validated adequately.
5. Data have been lacking to provide the evidence needed to ensure the place of self-BP monitoring.

Recently, several doctors recognized the importance of home BP measurements to predict mortality and morbidity. Previously, to monitor home BP, patients must check their home BP by themselves and write the data on their data record book. The data book record was widely used to monitor home BP because the data book record is convenient and easy to use (15–18). We have developed a different home BP monitoring system using a cellular telephone. For both patients and doctors, monitoring home BP using this telemedicine system is easy and reliable, and this system has a great advantage for hypertensive patients. This is the first report of comparing the changes of home BP with long-acting antihypertensive drugs using home BP monitoring system. To clarify the advantages of this kind of telemedicine systems, further examination must be needed.

In the present study, we monitored the effects of long-acting antihypertensive agents on home BP. TEL and AM have the same effects on home BP in the morning, and TEL has a greater effect on home BP reduction in the evening. There is a possibility that renin-angiotensin-aldosterone (R-A) system and sympathetic nerve activity may play important roles in the elevation of home BP in the evening. However, this is a preliminary small study. To clarify the effects of antihypertensive drugs on home BP, further experiments, such as a large-scale prospective randomized study using the telemedicine system, are needed.

In conclusion, we have developed a new telemedicine system to monitor home BP by using cellular telephone. There is a great difference on the effects of antihypertensive agents on diurnal variation and 24 hr overall BP variability in home BP. TEL has a good effect on home BP for 24 hours compared to AM. This telemedicine system has a great advantage to monitor home BP correctly in hypertensive patients.

References


