

Ambulatory Blood Pressure in Normotensive and Hypertensive Subjects

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Introduction

The variability of clinic blood pressure measurements (1, 9) casts doubt on its use as a method of classifying patients as hypertensive. In addition, blood pressure recordings by patients or their relatives have shown that clinic blood pressure tends to overestimate blood pressure (12, 14). This has been confirmed using both invasive and non-invasive ambulatory blood pressure recorders (7, 19, 20). Since the majority of hypertensive patients fall into the category of borderline or mild hypertensives (4) these studies suggest that many patients so classified in the clinic may be normotensive and therefore do not require any treatment. However, few studies on ambulatory blood pressure outside hospital have included truly normotensive subjects (3, 11, 16) and in only one has the relationship between clinic and ambulatory blood pressure been analysed for normotensives (18). It is therefore unclear whether hypertensive patients exhibit normal blood pressures outside the clinic since previous studies define normal blood pressure on the basis of clinic blood pressure measurements only. In this study we compare ambulatory and clinic blood pressure behaviour in normotensive and hypertensive subjects.

Methods

The study population consisted of 68 drug-free subjects. Normotensive subjects (N = 15) consisted of healthy volunteers recruited for an unrelated study who had no history of hypertension and whose blood pressure was normal (< 150/90 mm Hg) on at least three separate occasions. Thus, none of these subjects were under review as possible

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and this was confirmed by the high pressures recorded in the hospital at the beginning of ambulatory recording in these patients.

More important than a mean discrepancy between clinic and ambulatory blood pressure recordings was the finding of a poor relationship between these two parameters. Clinic recordings poorly predicted ambulatory blood pressure. Thus, although the mean hourly recordings for the three groups appeared distinctly separated, there was a marked degree of variation between patients in the percent time spent above normal limits, nearly all subjects displaying normal blood pressure at some point in the day. Similarly, although there was only a small mean difference between clinic and ambulatory recordings in borderline hypertensives, in 43% of cases mean daily blood pressure fell within the normal range for both systolic and diastolic blood pressure as defined by the normotensive group. In contrast, in normotensive subjects mean hourly blood pressure rarely exceeded accepted normal limits and no patient exhibited a mean ambulatory blood pressure above 150/90 mm Hg. If the degree of variation in ambulatory blood pressure was due solely to the method used then one would expect misclassification of normotensive subjects by this method. Thus, the variation seen in mean ambulatory blood pressure in hypertensive subjects reflects a real difference between subjects.

Although there was no significant difference in systolic blood pressure variability between groups, systolic variability increased with increasing blood pressure. This is consistent with previous studies using twenty-four hour intra-arterial (8, 17) and non-invasive ambulatory blood pressure recorders (16) and lends support to the use of this system in the assessment of blood pressure variability. Relative variability as measured by the coefficient of variation was similar at all levels of blood pressure.

In conclusion, when compared with normotensive subjects, ambulatory blood pressure falls within the normal range in many hypertensive patients, particularly borderline hypertensives. However, in the individual patient this cannot be predicted from clinic blood pressure measurements.

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Discussion II: Clinical Significance of Blood Pressure Variability

Question to Mr. Fitzgerald:

How many blood pressures did you take before saying this is the clinical blood pressure? And a second question would be: the Remler machine requires the patient to inflate the cuff. Could this be an explanation that you miss the proper blood pressure at midday time, say, at about 12 to 2 p.m.?

Mr. Fitzgerald:

To your first question: We took three recordings at the clinic. I think most people — if a patient would come to them with a high blood pressure — would try to define the blood pressure with three recordings. In that sense we were looking at how people would normally classify patients in the clinic and compare them with ambulatory blood pressure. The inflation of the cuff does not appear to lead to an increase in blood pressure. We have done this in 50 patients comparing recordings taken by them and recordings taken by an observer in a randomised fashion. And there was no mean difference between the two methods.

Question to Mr. Fitzgerald:

Do you have an explanation why you missed the drop at midday?

Mr. Fitzgerald:

Well, I don't think the drop at midday is a well defined entity, neither in intra-arterial monitoring nor in non-invasive monitoring.

To Mr. Fitzgerald:

In intra-arterial monitoring it is defined.

Mr. Fitzgerald:

Now, I don't know why it did not occur in our ambulatory monitoring. But it is not related to a pressure effect of inflating the cuff.

Mr. Millar-Craig:

Perhaps we could kick off by returning to the point that somebody made to Dr. Mann with regard to the effects of nightwork on blood pressure variability.

Mr. Mann:

We have not gone out to study shiftwork specifically. It is a considerable undertaking to try and do that. In fact, there is one thing I did not tell you. One of the subjects was excluded from the analysis of the group of 145, because he was a nightworker. Now we have looked at his trace. And clearly the curve is different from those which we have conventionally seen with people on daytime shifts. The curve is different in that the high points are not during the conventional daytime phase, the highest points are at 5 o'clock in the evening. Interestingly, the lowest point of the whole curve is at 3 a.m. in the morning, which is during the time when he is actually resting between patrols of the factory, but not asleep. Also of interest is the fact that his blood pressure very clearly started to rise at the end of his sleep period before he had awoken. We can't take too many conclusions, especially only one subject being studied here. The curve has been altered, but it certainly has not been directly reversed in accordance with his physical activity pattern.

Mr. Dienstl:

In the score of the night you had a score 5 without any sleep. Do you have such a profile of anybody who had not slept during the whole night?

Mr. Mann:

No, I don't think we had anybody with a 5. It is just there for completeness. I don't think anybody went through without sleep. We have done one or two other experiments on ourselves with staying up and working through the whole night, throughout the whole 24 hours, and there did seem to be very little fall in blood pressure during the night and in fact, my own rose very steeply toward the end of the night period.

Mr. Dienstl:

Do you have experience with blind people?

Mr. Mann:

No, we haven't done any recordings on that particular group. It would certainly be interesting to know.

We have got some recordings on patients with autonomic failure and they are very interesting because the circadian variation is completely inverted. Partially, as one might expect, their blood pressure is higher when they lie flat than when they are upright during the day.

Let me show you a slide: Six patients with autonomic failure contrasted with a group of six control subjects with hypertension and with normal blood pressure. As you can see, the curve is completely inverted from the normal. There is a gradual rise during the day which does seem to be very consistent a feature of these subjects. And there is a gradual fall during the night. So they are clearly very different from others.

Question to Mr. Mann:

If I understand your slides correctly the overall difference between day and night blood pressure would be in the order of magnitude between 14 to 16 mm Hg. This seems to me very low. We have done a lot of experiments in direct intra-arterial measurement and we found differences in hypertensive subjects of about 40 mm Hg between day and night time. Could it be an explanation that some of your patients did not sleep as well as they would have slept without the machine?

Mr. Mann:

Our nighttime falls are in fact quite a bit larger than that. There was a very wide spread as you might have seen from the slide. I can't remember exactly what it was but it was anything from a rise of about 15 mm Hg to a fall of up to 100 mm Hg. So it was in fact a much bigger spread than that.

Question to Mr. Fitzgerald:

What you have shown is very similar to the experience one gets by self-control of patients with mild or borderline hypertension. A lot of these patients are normotensive under home conditions. Do you think it is an advantage — I ask this from a practical point of view — to use such a device with a lot of estimations or only to advise the patient to take his pressure two times or four times a day?

Mr. Fitzgerald:

I think it is useful to use this device to define those patients. Sokolow in 1966 showed that the risk of hypertension was better correlated to ambulatory blood pressure measurement than to clinical pressure measurement. So it seems that the ambulatory measurement does identify patients who are at a lower risk. In other words, they are normotensive outside the hospital.

In home recording we have some experience too. One reason for using home recording might be that the feed-back mechanism would make the patient take his tablets. Or, if he was not on any medication it might at least help him to get his weight down or try some other methods of getting his blood pressure controlled. Certainly, home-recording is used to identify patients who have normal blood pressure outside the clinic. But one must always be a bit worried about fictitious results.

Mr. Millar-Craig:

I wonder if Dr. Gould would like to comment on Dr. Fitzgerald's findings. I know he has looked at this subject in great detail.

Mr. Gould:

We made a comparison with home blood pressure recordings against intra-arterial recordings, the Remler method against intra-arterial and the Avionics techniques against intra-arterial recordings. In terms of simple accuracy we found really no difference between the self-recorded and the Remler against intra-arterial recordings, whereas the Avionics was quite inaccurate.

More recently, we have undertaken a study involving placebo and Moduretic over quite a long period of time. We asked patients to record their home blood pressure twice each day for a period of several weeks. And it was interesting that during the placebo and untreated periods the blood pressure continued to fall for about the first four weeks until Moduretic was added. We feel that home blood pressure recording is the cheapest method and that it is as accurate as any other non-invasive recording. It could be perfectly adequately used for recording the ambulatory blood pressure.

Question to Mr. Mann:

To make it clear, may I ask you once more about blood pressure variability. Is it a variability of the basal blood pressure or is it a combination of the variability of basal blood pressure with blood pressure during physical exercise and mental stress?

Mr. Raftery:

When I am not a believer in the concept of basal blood pressure this is due to other work we have done when we have tried to compare the reproducibility of nighttime blood pressure with daytime blood pressure. Nighttime blood pressure in the same individual is as variable from night

to night as daytime blood pressure. And I think the nice sort of cosy feeling we get in terms of basal blood pressure and supplements which has been around for a while is founded on straw. We should measure blood pressure variability as a whole and forget any reference point of basal blood pressure. I feel mean 24-hour blood pressure is a better reference point than basal.

Mr. Mann:

I think we all of us labour under the delusion that we spend most of our time being very vigorous and very active, either mentally or physically. And I would challenge that very strongly. Because when you think how closely you can reproduce these hourly mean pressures that seems to me to be wrong. Because in all these studies we had made no effort to standardise the patients' mental or physical activity. We were looking at a mean pressure over a one-hour period picked at random. At this moment in time and at another moment in time we were coming up with the same pressure. But when we examined the diary cards to see what people were actually doing or what they said they were doing it was surprising how dull and how similar the cards were. People are not very active for long periods of time. You may, for example, think that if you play squash or do some very vigorous, active game of tennis that this is going to influence your mean pressure over the hour of which you do it. But in fact, the amount of time you spend elevating your blood pressure during that hour is really quite small. And it will certainly alter the mean, but only to a very small degree. And by and large, what one is looking at here in these curves is pressure. If the patients are doing nothing and if they are as active as they normally are you come up with much the same answer every time. So I would not call it "basal blood pressure", because basal blood pressure is something which has been defined by Smirk in a different sense, but certainly I would call it blood pressure, because that is the thing we are talking about. It is very repeatable.

Mr. Skrabal:

I was surprised by the fact that in all British studies reported today peak blood pressure occurred in the early morning hours, whereas in most studies from the continent peak blood pressures occur during the late afternoon. Does anybody of the panel have an explanation for that? Do you think it could be due to differences in working behaviour? I think this point is of relevance because it clearly affects the wanted duration of anti-hypertensive drugs.

Mr. Mann:

Well, I suppose it is very tempting to suggest that the continentals differ because they have a very large and a very satisfying meal in the late afternoon, whereas Englishmen eat the most disgusting food and under no circumstances could get excited about it. But I don't think it is as simple as that. I think if we measure the blood pressure in hypertensive continentals by our technique we come up with the same answer. I remember that many years ago Dr. Millar-Craig examined this point by going through the literature to find out when the peak blood pressures for the day were reported. And he came up with a fifty-fifty split. Half of the authors said that it was in the morning and the other half said that it was in the afternoon. But nobody seems to agree completely about this and I would suspect again that these reports are artifacts of the method of recording and that we just don't know until we study continentals. But I really do suspect that continentals will do much the same as Englishmen, I think. We are in the Common Market after all.

Mr. Mallion:

My question to Dr. Mann: You spoke of a cosinor analysis used by many cardiologists. Did this method give you new data on blood pressure?

Mr. Mann:

Yes, but it is not a method which we have used very much. Mr. Altman referred to it earlier today. It is a method of fitting one simple sine wave to the 24-hour data. As he showed, the convolutions of the blood pressure curve over 24 hours don't like being fitted into one simple harmonic curve. And really, to give any accurate representation at all we would need further harmonic analyses. Dr. Altman has achieved what looks like a satisfactory fit with using three harmonics. We have explored one or two patients and compared our results with the cosinor analysis. In fact, the amplitude derived from the cosinor analysis looks very similar to the day-night difference and the harmonically derived mean has corresponded quite closely with our 24-hour mean. So these two indices seem to correspond quite well, but I don't think the analysis is very useful for describing the curves because they differ so much. They don't like being fitted into a simple sine wave.

Mr. Alicandri:

Dr. Raflery, your observation that the profile of the 24-hour blood pressure is constant after the placebo period is very interesting, but it is

very provocative. Do you have any data on borderline hypertensive patients or on very mild hypertensive patients?

Mr. Rattery:

The quick answer is no. And I would not attempt to be dogmatic about any other sort of hypertensives other than the ones we have studied. All our patients were hypertensives as defined and the definition was a systolic greater than 160 and a diastolic greater than 95. And these were clinic measurements that were taken and it was a purely clinical diagnosis. Now when you come to study patients of that kind with intra-arterial blood pressure you often come up with the most surprising results.

By definition these people are clinically hypertensive, so we classify them as hypertensives and we describe them as hypertensives. But in fact, if you examine the blood pressures as has already been pointed out for a large proportion they are not hypertensives at all. Even though you would accept, on a clinical basis, that they were.

Now, you have raised the question of borderline hypertension. I think that this kind of observation, as Sir George Pickering pointed out many years ago, makes the whole concept of borderline hypertension and labour hypertension a nonsense. Those things don't exist, except in our minds. Because the definition entities do not hold up under scientific analysis. They just don't! The quick answer to your question is no, we have not studied borderline hypertension, but if you care to take the data you find a lot of people in our studies who will satisfy your criteria of borderline hypertension. But we don't find any differences between them.

Question to the panel:

How in 1983 should we as doctors decide between patients to treat and patients not to treat. We have got this problem of borderline hypertensives, true hypertensives and normotensives. I would like to ask the panel to give its opinion on how we should decide.

Mr. Rattery:

This is the most difficult and the most tortuous question to answer. There is no defined rule by which you could make up your mind which patient you are going to treat and which patient you are not. To begin with that: you have no authority to go to who will tell you definitively that these are

patients who must be treated, and this is the borderline, and patients who are below these levels may not be treated. Because such an authority just does not exist. So one way of going about it is to look what people actually do. Now we know that the statistics tell us that cardiovascular disease arises in certain patients with certain levels of blood pressure. But we know that all these statistics are based on measurements of blood pressure taken with patients usually in a sitting position, not in a lying position, but in a sitting position, and taken under extremely varying conditions. Sometimes the patients rest for five minutes, sometimes they don't. It just depends on what the physician felt like at the time. You will also find that in none of the publications on insurance statistics anyway is there any definition of whether Korotkoff 5 or Korotkoff 4 was used for diastolic pressure. There is simply a statement of what diastolic pressure is. So if you are going to be precise about things you should say that you should measure the blood pressure exactly the same way. The patient walks in, he sits down in a chair, you put a cuff round his arm and you measure the blood pressure by whatever method comes into your head at the moment and that is the figure on which you are going to decide whether to treat him or not.

If you are going to be logical about it, but of course we are not logical and we tend to do things in a different way and you will find that the literature is full of statements such as "you must measure the blood pressure three times". Now, why three? Why not seven? Well, in Chinese culture seven is a magic number, in our culture three is a magic number so we measure it three times and we say well, we measure it three times and when we are still unhappy about it, well, we go back and measure it four times. And having measured it four times and we are still not entirely certain, we measure it five times. And even as recently as six months ago no lesser an authority than Bill Mile published an article in which he said that if you are not happy about the blood pressure — whatever "happy" may mean — he did not define what he meant by "happiness" — but if you are not happy about it you go back and measure it again. And then, if you are not happy, you go back and measure it again. Well, that is pretty unsatisfactory, but that is what we do.

Whether it is right or wrong is another matter. We just don't know. But that is what people do. There are no statistics to prove whether it is good, whether it is bad, whether it is indifferent or whether you are being very clever picking out people who are going to get cardiovascular disease. That is just the way we do it.

Mr. Mann:

I agree with Dr. Raftery.

Mr. Ruilope:

I think with mild hypertension we advise the patients to take a restricted sodium diet and low calory intake if they are overweight. And we have found that about 9 to 10% of the patients, of hypertensive patients, can be controlled with these measures. If this is not enough we treat them with a diuretic.

Mr. Millar-Craig:

Dr. Fitzgerald, how would you decide? You presented some very interesting data suggesting that 9% of your borderlines were in fact normotensives.

Mr. Fitzgerald:

It was 43%. I agree with Dr. Raftery, there are millions of hypertensives and the more the definition of the level of blood pressure comes down we are moving into a curve in which we are accumulating millions of hypertensives that would require treatment. I think it is extremely important that we define the blood pressure well in terms of measurement. And if you can't do the type of things that have been suggested by the symposium, the one thing you can do is to be more careful about blood pressure measurements.

Mr. Millar-Craig:

I would like to go on record by saying how profoundly unhappy I am about this discussion. Because it must be a sign of my increasing senility. I don't think I have ever been agreed with ever before on a panel and I have three other speakers agree entirely with what I say. That has got to have some meaning. And I don't like it very much.