Original Aritcle

Efficacy of a new blood pressure monitor (inflationary non-invasive blood pressure, iNIBP™): a randomised controlled study

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Summary

Automated non-invasive blood pressure monitors are useful in patients undergoing surgery, but it may take some time to measure blood pressure, particularly when there are marked changes in the pressure. The inflationary non-invasive blood pressure monitor (**iNIBP™**) uses a new measurement method, whereby the cuff is slowly inflated whilst simultaneously sensing oscillations, to determine the diastolic blood pressure first and then the systolic pressure. Once the systolic pressure is determined the cuff deflates rapidly. We hypothesized that the inflationary non-invasive blood pressure monitor would measure the pressure more quickly than the conventional non-invasive blood pressure monitor. We studied 66 patients undergoing general anaesthesia, comparing the time taken to measure the blood pressure between the two monitors at times when there were marked changes (defined as increases or decreases by 30 mmHg or greater) in the systolic blood pressure. We then studied 30 volunteers to evaluate firstly the accuracy of the inflationary non-invasive blood pressure monitor, comparing it to the mercury sphygmomanometer. We then compared the degree of pain during cuff inflation between the automated non-invasive blood pressure and inflationary non-invasive blood pressure monitors. The median (IQR)[range]) time to measure the blood pressure, at the timings when there was a marked change in the systolic blood pressure was significantly longer for the non-invasive blood pressure monitor (38.8 (31.5-44.7) [18-130] sec) than for the inflationary non-invasive blood pressure (14.6 (13.7-16.4) [11.5-35.5] sec) ($p = 0.001$, 95%CI for median difference 22 - 25 sec). In the volunteer study, Bland-Altman plots showed good agreements between the two monitors, with the mean difference of 0 [95% limits of agreement -12 to 11] mmHg for the systolic blood pressure; 2 [-6 to 10] mmHg for the mean blood pressure; and -3 [-16 to 9] mmHg for the diastolic blood pressure). Pain during measurement was significantly more for the non-invasive blood pressure monitor (22 of 30 volunteers had less pain with the inflationary non-invasive blood pressure , and 3 for the non-invasive blood pressure). We have shown that the inflationary non-invasive blood pressure measured the blood pressure significantly more quickly

than the conventional non-invasive blood pressure monitor and the speed of measurement was not significantly affected by marked changes in the blood pressure.

Introduction

Blood pressure is a vital sign and is repeatedly measured during anaesthesia. Non-invasive blood pressure (NIBP) is measured using an automated non-invasive sphygmomanometer, with oscillometric method. The automated monitoring device uses the mechanism of deflationary blood pressure measurement: the cuff is inflated to a target inflation pressure and then deflated step-wise while sensing oscillations, to determine the systolic blood pressure, followed by the diastolic blood pressure.

One major problem with this system is that it may take a considerable time to measure blood pressure, particularly when the blood pressure is high. If the systolic blood pressure is higher than the target inflation pressure, the cuff is re-inflated to the pressure 30 mmHg higher than the initial target inflation pressure. If the systolic pressure is still higher than the inflation pressure, the target inflation pressure is adjusted to 40 mmHg or 60 mmHg higher than the initial target inflation pressure, depending on the degree of the amplitude sensed by the cuff. In addition, even if subsequently the blood pressure has acutely decreased, the blood pressure cuff inflates to the pressure where the original reading was made (which maybe 20 mmHg or 40 mmHg higher than the initial target inflation pressure.) These adjustments may result in an unduly long time to produce a measurement. Additionally, because of high inflation pressures, several complications such as pain, petechiae, radical nerve injury or compartment syndrome may occur [1, 2].

Recently the inflationary non-invasive blood pressure (**iNIBP™**) monitor (Nihon Kohden, Tokyo, Japan), a novel blood pressure monitoring device, has been developed. This device uses a new oscillometric method whereby the cuff is slowly inflated, whilst simultaneously sensing oscillations, to determine the diastolic blood pressure first and then the systolic pressure. Once the systolic pressure is determined, the cuff deflates rapidly. The mean blood pressure is calculated and is indicated simultaneously with the systolic and diastolic blood pressures. With this new measurement mechanism it is not necessary to adjust the target inflation pressure or to increase the cuff pressure greater than the systolic blood pressure.

We hypothesized that, compared with the conventional NIBP monitoring device, the iNIBP would measure the blood pressure faster, particularly when the blood pressure has suddenly increased or decreased. There have been two observational studies on the use of the iNIBP [3, 4], but no studies on the accuracy of the iNIBP.

The main aim of the study was to compare the time required to measure the blood pressure, between the conventional NIBP and the iNIBP at the times when there was a marked change (defined as an increase or a decrease by 30 mmHg or greater) in the systolic blood pressure. The secondary aims of the study were to confirm the accuracy of the iNIBP measurement and to evaluate the degree of pain during measurement.

Methods

The study was approved by the research ethics committee of the Dokkyo Medical University Saitama medical centre. Written informed consent was obtained from all the participants. We studied 66 patients (ASA physical status 1-3) undergoing elective surgery, in whom a neuromuscular blocking agent was used as part of the anaesthetic procedure. Exclusion criteria included: age < 20 y (the age of majority in Japanese Civil law); those had undergone, or scheduled for, mastectomy; or those with pathological changes to the arms.

Patients were randomly allocated to two groups pre operatively. In one group (the NIBP group), blood pressure was measured using a conventional automated sphygmomanometer, with oscillometric method (Nihon Kohden, Tokyo, Japan), in the second group, iNIBP was used. Random allocation was by tossing a coin.

In the operating room an ECG and a pulse oximeter were attached and the appropriate blood pressure cuff was applied to the patient's arm. The blood pressure was set to measure automatically

every 2.5 min and all the results were recorded. An intravenous cannula was then inserted either at the back of the hand or the wrist of the other arm.

After pre-oxygenation, anaesthesia was induced with intravenous thiopentone or propofol, and neuromuscular blockade was produced with rocuronium. Anaesthesia was maintained either with sevoflurane in oxygen or with intravnenous Propofol, analgesia was provided by fentanyl and continuous infusion of remifentanil.

The primary outcome measure was the time taken to measure the blood pressure at the times when there was a marked change (defined as an increase or a decrease by 30 mmHg or greater) in the systolic blood pressure. The Shapiro-Francia W-test, which analyses the normality of data distribution [5], showed that time to measure the blood pressure was not normally distributed. Therefore, Mann-Whitney-U test was used to compare the time taken between the two groups. The 95% confidence interval (CI) for median difference [6] in the time was also calculated.

The iNIBP device monitoring device measures the blood pressure with the above-described new method, however if there are irregular pulses (e.g. body movement or arrhythmias), it automatically abandones this new method and switches to the conventional method to measure blood pressure. We assessed the incidence of failed measurements by the new method.

The average time taken to measure the blood pressure after a marked change in the blood pressure for the conventional blood pressure monitor is approximately 40 sec (double the time to measure the pressure), with the standard deviation of 13 sec. Therefore we considered a difference of 10 sec in the measurement time between the two monitors would be clinically meaningful. Thirty measurements for each group would be required to detect this difference, with a power of 0.8, and $P = 0.05$. We expected that a marked blood pressure change would occur on average once per each patient during anaesthesia and thus 30 patients would be required for each group. We decided to study 66 patients, with a possible drop out of 10% of patients

In the second part of the study, we studied 30 volunteers to evaluate the accuracy of the iNIBP. Volunteers were anaesthetic staff or medical residents who agreed to participate to the study and provided written informed consent.

We used a modified version of the assessment method for the efficacy of an automated non-invasive sphygmomanometers described in the second edition of the International Organization for Standardization (ISO 81060-2: 2013). Before measurements each volunteer was asked to sit comfortably in a chair in a dim room, with their back, elbow and forearm supported, with their legs uncrossed and feet flat on the floor. After at least 5 min, the blood pressure cuff was applied with the middle of the cuff at the level of the right atrium of the heart.

Using a cross-over design, the blood pressure was measured using the iNIBP and a mercury sphygmomanometer (based on the ISO statement that a mercury sphygmomanometer should be used as a reference monitor to assess the efficacy of an automated measurement device). Blood pressure was measured first with one monitor and then with the other. This was repeated four times (eight measurements in total) with a one minute interval between measurements. During measurements each volunteer was recommended to be as relaxed as possible and to avoid talking during the procedure. For mercury sphygmomanometry two observers measured the blood pressure simultaneously and independently using a double stethoscope. The diastolic blood pressure was determined at the last audible Korotkoff sound (*i.e.* the fifth phase or K5). If either observer detected significantly irregular heart rhythm (such as bigeminy, trigeminy, ventricular premature beat, or atrial fibrillation) the measurement was excluded. The mean value of these two observers' values was regarded as the reference value.

In a separate arm of the volunteer study we assessed the degree of pain of the arm during cuff inflation between the automated NIBP and iNIBP monitors. Volunteers were allocated by block randomization with blank envelopes into two groups: in one group, the blood pressure was measured using the automated NIBP first and iNIBP in the second. In the other group, the blood pressure was measured using iNIBP first and automated NIBP in the second. For the iNIBP, a newly

designed cuff (YAWARACUFF2, Nihon Kohden, Tokyo, Japan) which is a part of the iNIBP monitor was used. Each volunteer was blinded as to the allocation by placing a drape over the inflation cuff and the monitor. The degree of the pain was evaluated by Numerical Rating Scale (NRS).

For the first part of the volunteer study, the Bland and Altman method for multiple observations per individual [7, 8] was used to assess agreement with the systolic, diastolic blood pressure or calculated mean blood pressure between the two monitors. We considered a mean systolic blood pressure of 110 mmHg to be normal, with the standard deviation of approximately 10 mmHg. We considered that a difference of 20 mmHg (1.96 x standard deviation) in reading the systolic blood pressure between the two different monitors would be clinically meaningful. A total of 30 subjects for each would be required to detect this difference, with a power of 0.8, and $P = 0.05$.

Wilcoxon matched pairs signed-rank sum test was used to compare the degree of pain during measurements between the automated NIBP and iNIBP monitors.

A p value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS version 24 (Armonk, NY, US), with manual calculations for the Bland and Altman method.

Results

All 66 patients completed the main study (Figure 1). Baseline characteristics were similar between the groups, although there was apparent difference in the proportion of sex (Table 1).

There were 2,695 blood pressure measurements in total in 35 patients allocated to the NIBP group and 2,785 measurements in 31 patients allocated to the iNIBP group. There were 69 occasions of marked changes in blood pressure for the NIBP and 71 occasions for the iNIBP.

The median (IQR)[range]) time to measure the blood pressure, at the times when there was a marked change in the systolic blood pressure, was significantly longer for the NIBP (38.8 (31.5-44.7) [18-130] sec) than for the iNIBP (14.6 (13.7-16.4) [11.5-35.5] sec) (p=0.001, 95%CI for median

difference 22-25 sec) (Figure 2). In addition, the median time to measure the blood pressure in all measurements was significantly longer for the NIBP (25.3 (22.1-28.9) [14.8-130.2] sec) than the iNIBP (14.2 (13.2-15.0) [9.0-36.9] sec) (P = 0.001) (Figure 3). For the iNIBP, there was no significant difference in the time taken to measure the blood pressure when there were acute changes in the blood pressure, compared to when the blood pressure was stable.

For the iNIBP, the iNIBP mode was switched automatically to the conventional NIBP mode, to measure the blood pressure 426 times (15%).

Thirty volunteers (15 males and 15 females) were recruited to the study and all participants completed the study. The characteristics of male volunteers (mean, standard deviation [age]) were as follows: age: 27 (3) [25-32] yr; weight: 68 (8) [54-82] kg; height: 172 (5) [164-180] cm. The characteristics of female volunteers were as follows: age: 30 (6) [25-44] yr; weight: 51 (6) [43-60] kg; height: 160 (6) [156-171] cm.

Subject profile plots for the systolic blood pressure and diastolic blood pressure (Figure 4) indicate that the blood pressures measured by two monitoring devices were generally similar for each participant. The Bland-Altman plots (for multiple observations per individuals) for the systolic blood pressure or the diastolic blood pressure (Figure 5) indicate good agreements between the two monitors. The mean difference was 0 (95% limits of agreement -12 to 11) mmHg for the systolic blood pressure, 2 (-6 to 10) mmHg for the mean blood pressure, and -3 (-16 to 9) mmHg for the diastolic blood pressure).

The degrees of pain during blood pressure measurements for the automated NIBP and iNIBP are shown in Fig. 6. Twenty-two of 30 (73%) volunteers stated that pain was lower for the iNIBP monitor than the NIBP monitor, 3 (10%) volunteers stated that pain was greater for the iNIBP monitor. The remaining 5 (17%) volunteers stated no difference between the two monitors. Pain was significantly more for the NIBP monitor than for the iNIBP monitor (p=0.001) (Fig. 6).

Discussion

We have shown that the iNIBP, a blood pressure monitor with a new measurement concept, can measure the blood pressure more quickly than the conventional automated blood pressure monitoring device. This is particularly so when there was a marked change in the blood pressure. We also have shown that there is a good agreement between the iNIBP and a mercury sphygmomanometer.

With the conventional automated NIBP monitoring device, if the systolic blood pressure rises higher than the target inflation pressure, the cuff deflates and re-inflates to a pressure 30 mmHg higher than the initial target inflation pressure. It therefore takes a longer time to measure the pressure. We found that when there was a marked increase or decrease in the blood pressure, the speed of measurement by the conventional NIBP was significantly slowed and sometimes took more than 2 min. In contrast, the speed of measurement by the iNIBP was not significantly affected.

Excessively high blood pressure, in particular, a sudden increase in the blood pressure during general anaesthesia may be associated with complications such as ischaemic heart disease or rupture of an aneurysm. There has also been growing evidence that even short periods of hypotension (1–5 min) during general anaesthesia are associated with increased risks of acute kidney injury and myocardial injury [9, 10]. Therefore, frequent measurements of the blood pressure (e.g. 2-3 min) are useful to detect marked changes in the blood pressure and ensure prompt treatment. One major problem with the conventional NIBP monitor is that, when the blood pressure has changed suddenly, there is a marked delay in measuring the blood pressure, delaying prompt treatment. Our study indicates that the use of the iNIBP is theoretically advantageous over the conventional NIBP monitor in this respect. Whether or not the use of the iNIBP truly minimizes the delay in treating hypertension or hypotension (and thus truly reduces complications) may be assessed by comparing the use of the iNIBP and a direct arterial blood pressure monitor in a future study.

Excessive inflation pressure during measuring the blood pressure is more likely to cause discomfort and pain and may cause injury to the arm. In our study the volunteers felt less pain during measurement by the iNIBP monitor, compared with the conventional NIBP monitor. Possible reasons for this difference are that the peak inflation pressure and time to measure the blood pressure are less for the iNIBP monitor than for the conventional NIBP monitor. In addition, the iNIBP monitor uses a newly developed cuff, called the YAWARACUFF2 (Yawara in Japanese means “soft”), which might also have reduced pain during measurements. The manufacturer states that the YAWARACUFF2 can be purchased individually, and the price of it is, in principle, the same as the conventional cuff. In addition, this new cuff can be used not only for the iNIBP monitor, but also for the conventional NIBP monitor manufactured by the Nihon Kohden.

One major limitation of the iNIBP is that the new inflational measurement mechanism (iNIBP mode) may not function when there is body movement or arrhythmias. In our study, in 15% of measurement points, the iNIBP mode was switched automatically to the conventional NIBP mode, to measure the blood pressure. Therefore, the iNIBP mode may not be useful in the patients with an irregular heart rhythm, such as atrial fibrillation. Nevertheless in these situations the iNIBP monitor does measure the blood pressure, by automatically switching to the conventional deflational mode.

There are several limitations to our study. One limitation is that more robust comparisons between the NIBP and iNIBP devices could have been made in the main study, by performing a cross-over study. We did not carry out a cross-over study because we expected that a marked blood pressure change would occur, on average, once per each patient during anaesthesia, so that we judged that it would be difficult to obtain at least one primary outcome measure for each device if a cross-over study was used.

Another limitation of the study is that, although we used a simple method of “tossing a coin” for randomization (which is as valid as the use of a table of random numbers [11]), this method may be associated with uneven number of patients allocated to the groups. This problem could have been minimized by pair matching before randomization or stratified randomization.

For the volunteers, we evaluated the accuracy of the iNIBP, by comparing it with a mercury sphygmomanometer. Those volunteers were in good health and relatively young, so that we could not assess the accuracy of the iNIBP for measuring abnormally high or low blood pressures. Therefore, our study could not assess the accuracy of the iNIBP in measuring extremes of blood pressure. We also did not include patients or volunteers with significantly irregular heart rhythm in the accuracy part of the study.

In the part of the study comparing pain during measuring the blood pressure between the automated NIBP and iNIBP monitors, we attempted to blind the volunteers to the allocation order, but it was obviously difficult, due to a shorter time and a lower peak inflation pressure for the iNIBP monitor. In addition, the difference in the degree of pain between the two monitors, despite significant, may not be clinically meaningful, as no hypertension was detected in any volunteer. Pain during measurements may indicate when an excessively high cuff inflation pressure is required which is more likely to cause complications, such as intolerable discomfort, petechiae, or nerve injury.

The iNIBP is now available in major countries (including Europe, North America, Asia) and the cost of the monitor is similar to the conventional automated NIBP monitor. In addition, the NIBP unit of the Nihon- Kohden monitoring system can be replaced by the iNIBP.

In conclusion, we have shown that, compared with the conventional automatic blood pressure monitor, the iNIBP measures blood pressure significantly faster and the speed of measurement was not significantly affected by marked changes in the blood pressure. The iNIBP is potentially useful during anesthesia, where prompt recognition of marked blood pressure changes is necessary.

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Table 1. Characteristics of patients allocated to the conventional automated non-invasive blood pressure with oscillometric method (NIBP group) or to the inflationary non-invasive blood pressure monitoring device (Nihon Kohden, Tokyo, Japan)(iNIBP group) group. Values are number (proportion) or mean (SD).

	NIBP group n = 35	iNIBP group n = 31
Sex; men	21 (60%)	12 (39%)
Age; y	64 (13)	61 (17)
Height; cm	160 (11	161 (9)
Weight; kg	59 (16	61 (15)
ASA physical status (1/2/3)	7/26/2	9/20/2
Systolic blood pressure; mmHg	145 (23)	147 (25)
Diastolic blood pressure; mmHg	86 (15	89 (13)
Heart rate; bpm	75 (15)	73 (13)

Figure legends

Figure 1. CONSORT flowchart for the clinical study.

Figure 2. Time taken to measure the blood pressure for the non-invasive blood pressure monitor and inflationary non-invasive blood pressure monitor (median and IQR), at the times when the systolic blood pressure had acutely increased or decreased more than 30 mmHg from the last systolic blood pressure.

Figure 3. Time taken to measure the blood pressure for the non-invasive blood pressure monitor and inflationary non-invasive blood pressure monitor (median and IQR) for all the measurements.

Figure 4. Subject profile plots for the systolic blood pressure and diastolic blood pressure between the two measurement devices. Three lines of the same colour indicate the values obtained in the same volunteer.

Figure 5. Scatter plot of difference between the two measurement devices against the average of the two (Bland and Altman method for multiple observations per individual), for systolic blood pressure and diastolic pressure. The central horizontal line indicates the mean difference between the two methods, whereas the upper and lower horizontal lines indicate the upper and lower 95% limits of agreement. Three circles of the same colour indicate the values obtained in the same volunteer.

Figure 6. Degree of pain (numerical rating scale) of the arm during cuff inflation with the automated inflationary non-invasive blood pressure monitor and inflationary non-

invasive blood pressure monitor monitors in volunteers (values are slightly displaced on the y-axis for the inflationary non-invasive blood pressure monitor, when there were the same values).