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ORIGINAL ARTICLE

Defining intra-operative hypotension – a pilot comparison of blood pressure during sleep and general anaesthesia*

J. C. L. Soo,[1] S. Lacey,[2] R. Kluger[3] and B. S. Silbert[3]

1 Anaesthetic Registrar, 2 Staff Anaesthetist, 3 Senior Staff Anaesthetist, St Vincent's Hospital, Melbourne, Victoria, Australia

Summary

The scientific justification for particular values of intra-operative hypotension is poorly substantiated. To provide a rationale for appropriate values we recorded blood pressure measurements at home for 24 h using an automated non-invasive ambulatory blood pressure measurement device. These blood pressures were compared with blood pressure measured before and during general anaesthesia in 18 subjects undergoing elective day surgery. We confirmed that a pre-operative reading taken upon admission to hospital is significantly elevated compared to a usual daytime blood pressure in the same patient. The median (IQR [range]) increases in systolic and mean arterial pressures were 10 (2–15 [−5 to 59]) mmHg, p = 0.003 and 10 (5–14 [−5 to 35]) mmHg, p = 0.002, respectively. When using this admission blood pressure measurement as a 'baseline', systolic and mean arterial pressures decreased during sleep by 41 (30–46 [6–83]) mmHg and 34 (26–36 [6–58]) mmHg, respectively (p = 0.001). This decreased even further intra-operatively: systolic blood pressure by 49 (36–64 [15–96]) mmHg and mean arterial pressure by 36 (26–46 [8–66]) mmHg (p = 0.001).

Correspondence to: B. Silbert
Email: brendan.silbert@svhm.org.au
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Haemodynamic aberrations during anaesthesia have clinical implications. Hypotension is one of the commonest intra-operative incidents, and many investigators have reported the independent association of intra-operative hypotension with adverse peri-operative outcomes such as stroke and myocardial ischaemia [1–3]. However, despite its potential importance, no universally acceptable definition of intra-operative hypotension exists [4]. Some practitioners use a percentage change from baseline blood pressure, whilst others use an absolute fall in blood pressure (systolic or mean). Both methods rely on an accurate assessment of baseline blood pressure which may vary according to the time and circumstance of the measurement.

Circadian variation of blood pressure is well recognised, and studies have established that blood pressure whilst asleep falls below that of awake blood pressure [5, 6]. Blood pressures recorded during sleep may therefore provide a relevant baseline blood pressure from which intra-operative hypotension may be calculated. However, only one published study has examined the relationship between blood pressure during sleep and during general anaesthesia [7]. In that study, patients were admitted to the ward the evening before surgery and blood pressure was monitored with an intra-arterial line. The hospital environment and the presence of an intra-arterial line may potentially affect blood pressure by raising anxiety levels (hospital) and causing discomfort (arterial line). This may result in blood pressure values higher than those experienced in the patient's normal sleeping environment.

Automated non-invasive ambulatory blood pressure monitoring enables the recording of the circadian

rhythm of blood pressure under everyday circumstances [8]. When used during sleep, ambulatory blood pressure monitoring does not cause an increase in blood pressure [9]. Although sleep is not the same as pharmacologically induced general anaesthesia, both the states represent a situation of decreased sympathetic drive. It is possible that the blood pressure values recorded during sleep may indicate what is acceptable as a low blood pressure during general anaesthesia.

The aim of this prospective observational study was therefore to measure blood pressure values during wakefulness and sleep in patients scheduled for elective surgery, and to compare them with the blood pressures observed during general anaesthesia.

Methods

Following local institutional ethics committee approval, all ASA-1 or -2 patients scheduled for elective day surgery (hernia repair or knee arthroscopy) attending a pre-admission clinic between June and December 2008 were invited to participate. Written informed consent was obtained from all participants. Exclusion criteria included inability to give informed consent or comprehend instructions regarding the use of the automated non-invasive ambulatory blood pressure device for language or cognitive reasons, inability to wear blood pressure cuffs on both arms (e.g. arterio-venous fistula, previous axillary dissection, limb amputation) or contra-indication for general anaesthesia. Subjects taking anti-hypertensive medication were not excluded, and were instructed to take their usual medication on the morning of surgery.

Each subject was fitted with a SpaceLabs 90207 automated non-invasive blood pressure (NIBP) device (SpaceLabs Healthcare, Issaquah, WA, USA) for a continuous period of 24 h within 6 weeks of their scheduled surgery. During this time, blood pressure was measured on an hourly basis whilst at home. Standard and large adult cuffs were fitted as appropriate, such that the bladder of the cuff was at least 40% of the circumference of the limb being measured. On the day of surgery, a baseline pre-operative blood pressure was taken upon admission using a NIBP device. The same automated non-invasive ambulatory device that had been worn for measurements at home was reprogrammed to measure blood pressure every 6 min during anaesthesia. The anaesthetist was blinded to readings taken by the automated non-invasive ambulatory blood pressure device but was able to measure NIBP every 3 min on the contra-lateral arm using a Datex-Ohmeda S5 series monitoring machine (Datex HQ, Los Angeles, CA, USA).

The anaesthetic technique was standardised and consisted of induction with propofol (2–3 $mg.kg^{-1}$) and alfentanil (10–15 $\mu g.kg^{-1}$) or fentanyl (1–2 $\mu g.kg^{-1}$), followed by maintenance with sevoflurane or desflurane in oxygenated air with additional opioids as required. No premedication was given. Either laryngeal mask airway insertion, or tracheal intubation preceded by a non-depolarising neuromuscular blocking drug, was performed at the anaesthetists' discretion. There was no restriction on fluid or vasopressor administration because we wanted to follow normal clinical practice to obtain generalisable results. Blood loss and fluid therapy were recorded.

The following five systolic (SBP) and mean arterial (MAP) pressure measurements were defined for analysis;

1 Pre-operative: baseline pre-operative blood pressure taken upon admission. Only a single pre-operative blood pressure was measured since typically, in clinical practice, only one pre-operative blood pressure is used as a baseline.
2 Median daytime: median of the hourly blood pressures taken during the waking hours (09:00-21:00).
3 Median sleep: median of the hourly blood pressures taken during the sleeping hours (midnight to 06:00).
4 Sleep nadir: lowest of the hourly blood pressures taken during the sleeping hours (midnight to 06:00).
5 Intra-operative nadir: lowest intra-operative blood pressure recorded by the automated non-invasive ambulatory blood pressure device.

Differences in SBP and MAP between the different periods were analysed using Wilcoxon signed-rank test with the Holm-Bonferroni step-down procedure [10] to correct for multiple comparisons. Spearman non-parametric correlation coefficient and Wilcoxon signed-rank test were used to examine associations between SBP and MAP changes and age, body mass index, pre-existing hypertension, fluid balance, airway management (LMA or ETT) and use of vasopressors. Stata 11™ (StataCorp LP, College Station, TX, USA) was used for data analysis.

Results

Of the 23 subjects recruited, five were not studied: four subjects received spinal anaesthesia and one patient was non-compliant with the automated non-invasive ambulatory blood pressure device at home.

Table 1 Details of patients (n = 18) undergoing anaesthesia. Values are median (IQR [range], number or number (proportion).

Age; years	65 (59–71 [43–78])
Male/female	12/6
Body mass index; kg.m^{-2}	28.7 (27.7–33.4 [23.4–39.6])
Known hypertension	13 (72%)
Tracheal tube/laryngeal mask airway	7/11
Operating time; min	60 (43–75 [30–125])
Vasopressor use: metaraminol/ephedrine	6/7
Volume of intra-operative fluid administered; ml	1000 (1000–1425 [1000–2000])

Patients' details are summarised in Table 1. Figure 1 summarises data from all subjects during the 24-h ambulatory period and intra-operatively. Typically, blood pressures fell during sleep, rose in the early morning and pre-operatively, and tended to decrease in the early intra-operative period. The intra-operative blood pressure nadir occurred at a mean (SD) of 15 (13) min after induction.

Table 2 shows the SBP and MAP measured at the different times: pre-operative, median daytime, median sleep, sleep nadir and intra-operative nadir.

Figure 2 shows each subject's SBP measured at the different times. The intra-operative SBP nadir was lower than the sleep SBP nadir in 12 of 18 subjects. Figure 3 shows each subject's MAP at the different times. The intra-operative MAP nadir was lower than the sleep MAP nadir in 11 subjects.

Tables 3 and 4 show differences in SBP and MAP, respectively, when comparing SBP and MAP measured at each time. There were significant differences in SBP in all comparisons and MAP in all comparisons except for the difference between sleep nadir and intra-operative nadir.

No correlation was found between the falls in SBP or MAP during sleep or during anaesthesia with age, pre-existing anti-hypertensive medication use, body mass index, intra-operative fluid balance, mode of airway or vasopressor use.

Discussion

We have shown that measurements of both SBP and MAP change according to the time and circumstance of the measurement. In particular, the pre-operative blood pressure measurement is significantly higher than median daytime blood pressure. This is important because pre-operative blood pressure is typically taken as the baseline value from which it is common practice to calculate the presence of intra-operative hypotension. Median pre-operative SBP was 10 mmHg (6.8%) higher and pre-operative MAP was 10 mmHg (9.5%) higher than the median of the daytime readings.

However, normal daytime blood pressure may not be the best guide to the lowest blood pressure that can be tolerated during general anaesthesia. Median sleep blood pressure was significantly below the blood pressures recorded during daytime. Median sleep SBPs were 12 mmHg (8.9%) lower than median daytime SBP and median sleep MAPs were 6 mmHg (6.3%) lower than median daytime MAPs. This is consistent with non-anaesthesia related studies investigating

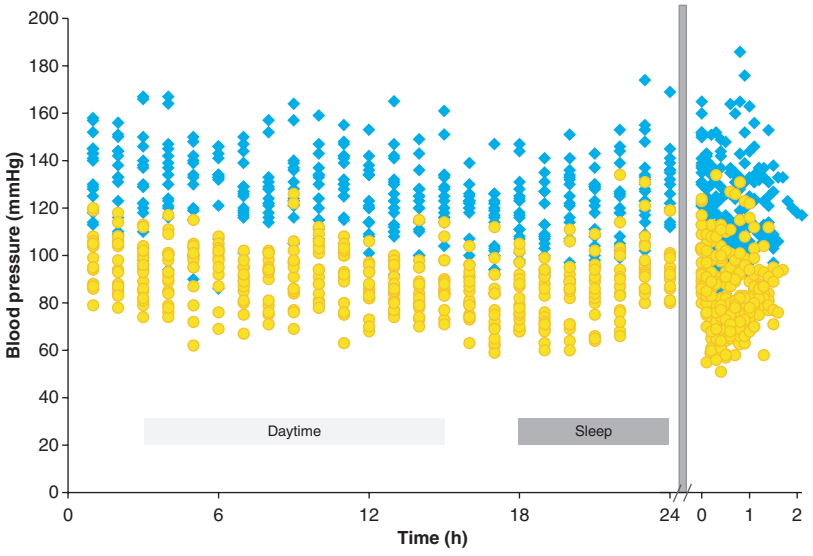

Figure 1 Summary of systolic blood pressure (◆) and mean arterial blood pressure (●) measured pre-operatively (Pre-op; hourly for 24h) and intra-operatively (Intra-op; every 6 min) for each of the eighteen subjects.

Table 2 Systolic and mean arterial pressures at different time points (n = 18). Values are median (IQR [range]).

	Systolic blood pressure	Mean arterial blood pressure
Pre-operative BP; mmHg	135 (128–151 [119–169])	99 (95–110 [89–121])
Median daytime; mmHg	128 (119–138 [110–147])	94 (86–98 [78–105])
Median sleep; mmHg	122 (111–125 [94–144])	86 (76–92 [64–105])
Sleep nadir; mmHg	101 (91–106 [80–122])	70 (63–75 [55–85])
Intra-operative nadir; mmHg	87 (81–97 [71–126])	64 (59–70 [50–105])

Pre-operative BP: pre-operative baseline blood pressure measured on day of admission. Median daytime: median blood pressure measured between 09:00 and 21:00. Median sleep: median blood pressure measured between midnight and 06:00. Sleep nadir: lowest blood pressure measured between midnight and 06:00. Intra-operative nadir: lowest blood pressure measured intra-operatively.

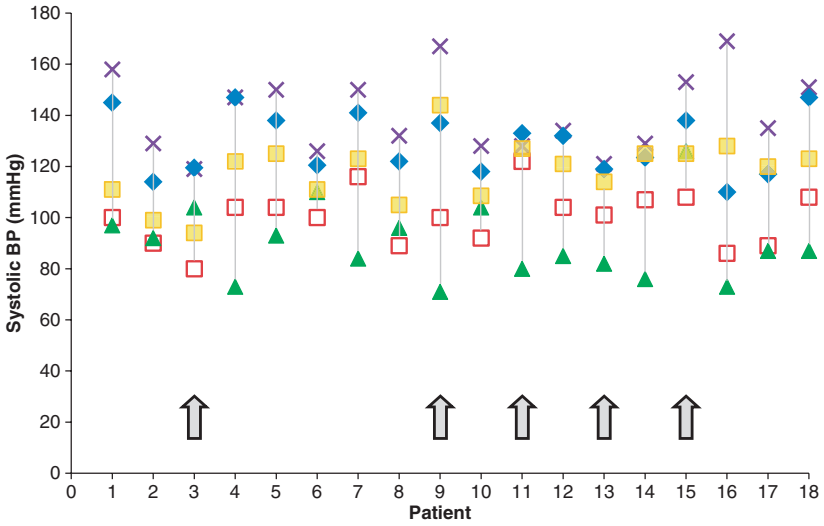

Figure 2 Systolic blood pressure measured at each time point for each subject. Pre-operative baseline blood pressure (×), median daytime blood pressure (◆), median sleep blood pressure (■), lowest blood pressure during sleep (sleep nadir) (□) and lowest blood pressure intra-operatively (intra-operative nadir) (▲). ⇧ denotes patients not on anti-hypertensive medications.

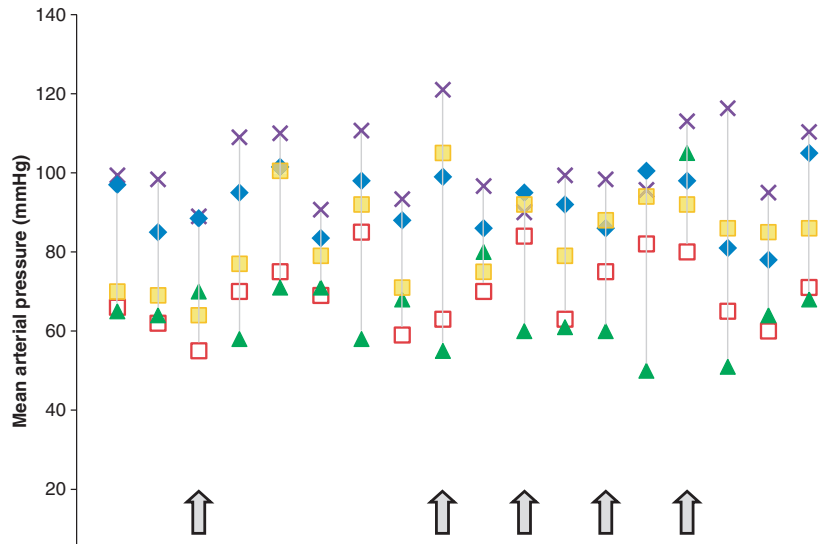

Figure 3 Mean arterial blood pressure measured at each time point for each subject. Pre-operative baseline blood pressure (×), median daytime blood pressure (◆), median sleep blood pressure (■), lowest blood pressure during sleep (sleep nadir) (□) and lowest blood pressure intra-operatively (intra-operative nadir) (▲). ⇧ denotes patients not on anti-hypertensive medications.

nocturnal variation in blood pressure, which describe a systolic night-to-day ratio of 0.9 to 0.8 as 'normal' [11, 12] (i.e. systolic blood pressure falls by 10–20% during sleep). In this present study sleep nadir blood pressures were 41 mmHg (29.3%) (SBP) and 34 mmHg (33.4%) (MAP) lower than the pre-operative blood pressures.

Table 3 Differences in systolic blood pressures at different time points (n = 18). Values are median (IQR [range]).

	Difference in systolic BP	% change	p value
Median daytime – median sleep; mmHg	12 (5–18 [–18 to 34])	8.9	0.01
Pre-operative BP – median daytime; mmHg	10 (2–15 [–5 to 59])	6.8	0.003
Pre-operative BP – median sleep; mmHg	25 (15–28 [1–47])	16.8	0.001
Pre-operative BP – sleep nadir; mmHg	41 (30–46 [6–83])	29.3	0.001
Pre-operative BP – intra-operative nadir; mmHg	49 (36–64 [15–96])	37.0	0.001
Median sleep – intra-operative nadir; mmHg	33 (7–47 [–10 to 73])	27.8	0.003
Sleep nadir – intra-operative nadir; mmHg	12 (–7 to 29 [–24 to 42])	12.9	0.045

Pre-operative BP: pre-operative baseline blood pressure measured on day of admission. Median daytime: median blood pressure measured between 09:00 and 21:00. Median sleep: median blood pressure measured between midnight and 06:00. Sleep nadir: lowest blood pressure measured between midnight and 06:00. Intra-operative nadir: lowest blood pressure measured intra-operatively.

Table 4 Differences in mean arterial blood pressures at different time points (n = 18). Values are median (IQR [range]).

	Difference in mean BP	% change	p value
Median daytime – median sleep; mmHg	6 (1–17 [–7 to 27])	6.3	0.01
Pre-operative BP – median daytime; mmHg	10 (5–14 [–5 to 35])	9.5	0.002
Pre-operative BP – median sleep; mmHg	21 (10–25 [–2 to 32])	19.5	0.001
Pre-operative BP – sleep nadir; mmHg	34 (26–36 [6–58])	33.4	0.001
Pre-operative BP – intra-operative nadir; mmHg	36 (25–46 [8–66])	35.2	0.001
Median sleep – intra-operative nadir; mmHg	19 (5–32 [–13 to 50])	23.7	0.006
Sleep nadir – intra-operative nadir; mmHg	3 (–4–14 [–25 to 32])	4.0	0.29

Pre-operative BP: pre-operative baseline blood pressure measured on day of admission. Median daytime: median blood pressure measured between 09:00 and 21:00. Median sleep: median blood pressure measured between midnight and 06:00. Sleep nadir: lowest blood pressure measured between midnight and 06:00. Intra-operative nadir: lowest blood pressure measured intra-operatively.

In practical terms, this suggests that decreases in SBP or MAP of approximately 30% would likely be well tolerated by patients, assuming that blood flow distribution does not change during anaesthesia. Interestingly, these estimates of acceptable pressure changes are consistent with current clinical practice. Many anaesthetists define intra-operative hypotension as a decrease in blood pressure of 30% from pre-operative blood pressure [13], although we are unaware of any previous study that has established this value.

The present study also measured the lowest blood pressure observed during anaesthesia during normal clinical management of the patient. The intra-operative SBP nadir was significantly lower by 12 mmHg (12.9%) than the sleep nadir. The intra-operative MAP nadir was only 3 mmHg (4%) lower than the sleep nadir, which was not statistically significant. These findings suggest that intra-operative hypotension may be undertreated because most subjects had an intra-operative nadir lower than that measured during sleep. The lack of a standardised definition of hypotension [13] may be contributing to this 'undertreatment'.

Our findings that intra-operative SBP frequently drifts below SBP during sleep are consistent with the previous work of Berger et al. [7]. In their study, continuous intra-arterial monitoring of blood pressure was initiated the evening before gynaecological tumour surgery and continued for 36 h. Twenty-six out of the 34 patients received night-time sedation before surgery and all patients received pentobarbitone 90 min pre-operatively. Seven patients received epidural anaesthesia. Their surrogate marker for pre-operative blood pressure was an average value of 15 consecutive readings taken at intervals of 1 min before induction. They concluded that, in normotensive patients under 65 years of age, a fall in MAP of 15% was similar to the lowest values that occurred during normal sleep. This is a smaller decrease than in our study; however, the use of epidural anaesthesia and premedication may have attenuated the readings taken as a pre-operative baseline.

Berger et al. also showed a correlation between age and the fall in blood pressure during sleep, with younger patients showing a more abrupt decrease in blood pressure than older patients [7]. They also

showed that known hypertensives had a smaller fall in blood pressure during sleep than non-hypertensive patients. Our pilot study included both hypertensive and non-hypertensive patients; however, we were unable to observe any significant differences between the two groups, probably due to our small and heterogenous sample. In addition, in contrast to the study by Berger et al., all our patients continued antihypertensive medications peri-operatively.

Physiological sleep is a different state to the pharmacological state of general anaesthesia. However, both involve a decrease in sympathetic nervous activity and in this respect, the normal decrease in blood pressure during sleep may provide some guidance as to what is an acceptable low blood pressure during anaesthesia.

Although the accuracy of automated non-invasive blood pressure monitoring has been questioned [14], the accuracy of the SpaceLabs 90207 automated non-invasive blood pressure device has been validated by comparison with intra-arterial blood pressure monitoring as well as mercury sphygmomanometers in various studies [15, 16]. We did not consider the measurement or comparison of diastolic blood pressure in our study as the accurate measurement of diastolic pressure is problematical [17]. Furthermore the accuracy of the SpaceLabs 90207 device for diastolic blood pressure measurement has not been validated [18].

Apart from a small sample size, another major limitation of our study was the use of intermittent rather than continuous blood pressure readings, thereby potentially missing true nadir blood pressures. Ideally, a reliable, continuous non-invasive device for blood pressure measurement in both the home and operating theatre should be used in future studies.

The present study provides perspective on the question of what constitutes potentially clinically significant hypotension in the peri-operative period. Using a single baseline blood pressure measured upon admission, a decrease in SBP or MAP of approximately 30% resulted in blood pressures similar to the nadir values that occurred during normal sleep. Intra-operative nadir blood pressures were usually lower than this, and often lower than nadir sleep blood pressures, suggesting that the intra-operative period is associated with falls in blood pressure greater than those seen during physiological sleep. The question of whether this is placing subjects at undue risk would require outcome studies. Conceivably, older and hypertensive subjects may be at greater risk from such hypotension than younger subjects.

Large prospective outcome studies are clearly required to guide our intra-operative blood pressure management. These should include patients with vascular risk factors, involve randomisation to different blood pressure targets and utilise better blood pressure measurement technology.

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Competing interests

No external funding and no competing interests declared.

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