

Application of pulse transit time to noninvasively beat-to beat monitor individually vascular side effects by thiopental

Yuan-Chun Lan, MD^{1,2}, Ching-Hui Shen, MD³, Hsung-Ming Kang, MD³, Fok-Ching Chong, Prof.¹

¹Graduate Institute of Biomedical Electronics and Bioinformatics, National Taiwan University, 106, Taiwan, Republic of China

²Department of Anesthesiology, Cardinal Tien Hospital, Taipei country, 231, Taiwan, Republic of China

³Department of Anesthesiology, Veteran General Hospital, Taichung, 407, Taiwan, Republic of China

Abstract. Pulse transit time (PTT) is the time of a pulse wave traveling between two arterial sites. It may offer immediately beat-to-beat vascular information. The aim of our study was to monitor pharmacologically vascular variation affected by thiopental by PTT. Methods: 10 healthy women, aged 25-56ys, undergoing gynecological surgery under general anesthesia were collected. Anaesthesia was induced by thiopental (5mg/kg). PTT measurements were obtained from R wave of electrocardiogram and pulse wave of photoplethysmograph. PTT of each subject before and after thiopental given were analyzed by student's t-test. Results: After thiopental given, PTT of each subject showed increased. Baseline and increase value of PTT of each patient were significantly different ($P < 0.001$, by student t-test). The time course of change was clearly visualized in PTT. PTT successfully revealed not only the magnitude but also the course of change about vessels by thiopental. In addition, the onset time, peak time and duration in aspect of vascular side effect seem to be revealed. This tool may be as pharmacology parameter to monitor the vascular side effects of other drugs or even to monitor the power of vasoactive drugs.

Key words: pulse transit time, thiopental, vascular change

1. Introduction

Clinically, thiopental-the anesthetic induction agent- results in unavoidable vasodilatation, especially leading to lethal problems (hypotension) in critical patients because of excess or intolerable vasodilatation(1-3). Several methods have been used to measure the changes of vessels.

The thermodilution measured by pulmonary artery catheter is the most accurate method to assess vascular variation, however, it is an invasive way (4-8). Some noninvasive way (Doppler ultrasound) or invasive way (intravascular ultrasound) could evaluate the variation of vessels, but the inconvenience limits the uses due to the needs of experts and the results only represent the regional changes of the measured site (9-14).

Pulse transit time (PTT) is the time of arterial pulse wave transmitted between two arterial sites (15-16). In the past, PTT was used to evaluate the vascular changes. Vasoconstriction shortens the PTT, while vasodilatation increases the PTT (17-20). PTT offers beat-to-beat vascular information. Each arterial pulse wave begins with each contraction of the heart, and ends by the pulse wave travels to the terminal branches of arteries (15-16). The initial time can be obtained easily by the R wave of electrocardiogram. The terminal time can be taken by the wave of pulse photoplethysmograph on the finger. The difference of these two time point is PTT. PTT measured by R wave and photoplethysmograph has been used for several studies, including obstructive sleep apnea, autonomic failure, as well as vascular reactivity (19).

PTT obtained from electrocardiogram and pulse photoplethysmograph offers the convenience because these two equipments are the mandatory during any kinds of anesthesia. The goal of this study was to assess its value for observing the variation.

2. Materials and Methods

Studies were approved by the local ethics committee. The written consent was obtained from 10 healthy women without any drug history, aged 25-56ys, and undergoing gynecological surgery under general anesthesia. All these patients were induced by thiopental (5mg/kg) which is the world widely used anesthetic induction agent. Because several drugs were given following the induction in the entire anesthesia course, we only recorded PTT before next drugs given.

The electrocardiogram was detected using a standard three-lead configuration (Lead II), with the signal sampled at 300 Hz. The pulse photoplethysmograph was placed on right index finger. PTT was detected between R-wave peak and the initial upstroke point of the pulse wave. (Figure 1)

Due to observing pharmacological characters on vessels, PTT data of each subject were divided to two parts. First part was the time before thiopental injection and it represented baseline value. Second part represented the time since thiopental injection. All values were calculated as means \pm SD and compared among subjects. The changes of PTT of each subject were analysis by student's t-test.

3. Results

All subjects were healthy. Average height and weight were 158.2 cm (SD=3.87) and 51.3 kg (SD=8.25), respectively. Preoperative electrocardiograms were normal in all subjects. PTT was recorded in each heart beat of every subject.

During the induction course of anesthesia, PTT in different period illustrated similar changes among all subjects. (Figure 2) This figure revealed that PTT gradually increased after thiopental given, and followed by the plateau. Mean baseline PTT of was 270.9 ms (SD=18.3). 36.82 sec (SD=4.05) after thiopental given to patient, PTT began to increase. The time course of increase of PTT could be revealed in all subjects. The mean interval was 41.12 sec (SD=13.14). The plateau of PTT was 344.82 ms (SD=28.32). Baseline and plateau of each patient were significantly different (P<0.0001, by student t-test). (Table I)

Table I. Mean PTT before and after thiopental given of each subject.

Subject	Mean baseline PTT (ms)	Time of PTT starting to increase after thiopental (sec) – onset time	Time of PTT from initial increased time point to plateau(sec)	Mean plateau PTT (ms)	Changes in PTT (ms)
mean	270.9	36.82	41.12	344.82	71.17
SD	18.3	4.05	13.14	28.32	34.7

4. Discussion

Moens-Korteweg's equation defines pulse wave velocity (PWV) in terms of the incremental Young's modulus of the arterial wall (21):

$$PWV = \sqrt{(Eh / \rho D)} \quad \text{equation 1.}$$

Where E is the incremental Young's modulus, h is the thickness of the arterial wall and D is the diameter of the artery.

Documented evidences suggest that PTT which is inversely correlated to PWV (15, 20-21). In certain distance, pulse wave velocity determinates pulse wave transit time. Vasodilatation correlates with the changes of wall thickness or diameter of the artery. Hence, vasodilatation could change PTT.

Among all these 10 patients, the onset time of the vascular change by thiopental could be assessed clearly and immediately. It gave us the important information about the precise time that thiopental began to affect vessels.

Another interesting finding from this study was PTT could give us the time course that thiopental changed the vessels from initial increased time point to peak. This method is noninvasive and easy. In addition, it seems to be capable of observing the onset time, peak time and duration of vascular pharmacology, however, it needs future works to establish the relationship.

The plateau of PTT of each subject was statistical significant differences (P<0.0001) to baseline of PTT. The magnitude of variation was from 35.1 ms to 148.8 ms, and mean was 75.32 (SD=33.7) ms. In previous study, it

illustrated 28.2 (SD=20.4) ms. The different results between the previous study and our study may due to that they measured the total effect of three drugs, and we used only thiopental. The magnitude of change may represent the power that thiopental affected vessel in each patient, however, the magnitude needs more study to quantify. The period of plateau might offer useful information that how long thiopental would affect the vessels. The magnitude of variation of Subject 10 was 148.8 ms. The phenomenon needs further study to research. PTT successfully revealed not only the magnitude but also the course of change by the vasoactive agent – thiopental. In addition, the onset time, peak time and duration in aspect of vascular effect seem to be evaluated.

5. Conclusion

The application of this simple physiologic measure may be able to assess the pharmacologic conditions of vasodilator drugs. The simple, non-invasive and beat-to beat measuring nature of PTT technique may then be considered as a possible surrogate of evaluating vascular change on pharmacology or pathology. In addition, electrocardiography and photoplethysmograph are mandatory equipments in any kinds of anesthesia and every intensive care unit. Both vasoconstrictor and vasodilator drugs are used commonly, especially in critical patient. Further studies are required to assess by this method.

Figures

Figure1. PTT was detected between R-wave peak and the initial upstroke point of the pulse wave.
ECG=electrocardiogram, PPG=photoplethysmograph.

Figure 1

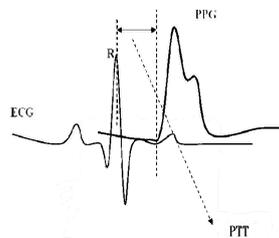
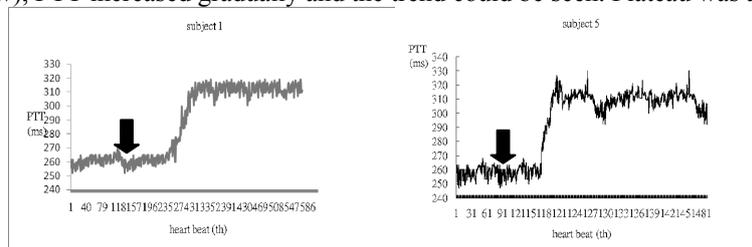


Figure2. The beat-to beat PTT of subject (1,5) showing the thiopental resulted in the similar picture. After thiopental given (arrow), PTT increased gradually and the trend could be seen. Plateau was also observed.



6. References

- [1] Eckstein JW, Hamilton WK, McCammond JM: The effect of thiopental on peripheral venous on peripheral venous tone. *Anesthesiology* 22:525-528 (1961)
- [2] Stella L, Torri G, Castiglioni CL: The relative potencies of thiopentone, ketamine, propanidid, alphaxalone and diazepam. A statistical study in man. *Br J Anaesth* 51:119-122 (1979)
- [3] Morgan DJ, Blackman GL, Paull JD, Wolf LJ: Pharmacokinetics and plasma binding of thiopental. II: Studies at cesarean section. *Anesthesiology* 54:474-480 (1981)
- [4] Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. *Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter*. *N Engl J Med* 283:447-51 (1970)
- [5] Pinsky MR. Hemodynamic monitoring in the intensive care unit. *Clin Chest Med* 24:549-560 (2003)
- [6] Fegler G: Measurement of cardiac output in anesthetized animals by a thermodilution method. *Q J Exp physiol* 7:66-72 (1954)
- [7] Kelso LA: Complications associated with pulmonary artery catheterization. *New Horizons* 5:259-263 (1997)

- [8] Harvey RM, Enson Y: Pulmonary vascular resistance. *Adv Intern Med* 15:73-93, 1969 Horimoto M, Takenaka T, Igarashi K, Inoue H, Akino M. [Invasive examination of cardiovascular disease] *Rinsho Byori*. 48(2):128-37 (2000)
- [9] Faulx MD, Wright AT, Hoit BD. Detection of endothelial dysfunction with brachial artery ultrasound scanning *Am Heart J*. 145(6):943-951 (2003)
- [10] Rubba P, Iannuzzi A, Faccenda F, De Leo F, Pauciullo P. Non-invasive vascular detection of early signs of atherosclerosis in hypercholesterolemic children: why and how. *Nutr Metab Cardiovasc Dis*. 11 Suppl 5:10-15 (2001)
- [11] Gill, R.W. Pulsed Doppler with b-mode imaging for quantitative blood flow measurement. *Ultrasound Med Biol* 5:223-235 (1979)
- [12] Gill, R.W. Measurement of blood flow by ultrasound: Accuracy and sources of error. *Ultrasound Med Biol* 11: 625-641 (1985)
- [13] [13]. Wesche, J. The time course and magnitude of blood flow changes in the human quadriceps muscles following isometric contraction. *J Physiol* 377:445-462 (1986)
- [14] [14]. Saltin B, Rådegran G, Koskolou MD, Roach RC. Skeletal muscle blood flow in humans and its regulation during exercise. *Acta Physiol Scand* 162:421-436 (1998)
- [15] R.P. Smith, J.Argod, J.L. Pepin, P.A. Levy, pulse transit time: An appraisal of potential clinical applications, *Thorax* 54: 452-458 (1999)
- [16] M. Nitzan, B. Khanokh, Y. Slovik. The difference in pulse transit time to the toe and finger measured by photoplethysmography. 23(1):85-93 (2002)
- [17] R. Asmar, A. Benetos, J. Topouchian, P. Laurent, B. Pannier, A.M. Brisac, et al. Assessment of arterial distensibility by automatic pulse wave velocity measurement. Validation and clinical application studies. *Hypertension* 26:485-490 (1995)
- [18] J. Allen, A. Murray. Prospective assessment of an artificial neural network for the detection of peripheral vascular disease from lower limb pulse waveforms. *Physiol Meas* 16:29-38 (1995)
- [19] J.E. Naschitz, S. Bezobchuk, R. Mussafia-Priselac, S. Sundick, D. Dreyfuss, I. Khorshidi, et al. Pulse transit time by R-Wave-Gated infrared photoplethysmography: review of the literature and personal experience. *J Clin Monit* 18:333-342 (2004)
- [20] D.J. Pitson, J.R. Stradling, Vaule of beat-to-beat blood pressure changes, detected by pulse transit time, in the management of the obstructive sleep apnoea/hyponocea syndrome, *Eur Respir J* 12:685-92 (1998)
- [21] Stevanov M, Baruthio J, Eclancher B. Fabrication of elastomer arterial models with specified compliance. *J Appl Physiol* 88:1291–1294 (2000)