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Nitric oxide metabolites before and after spinal anesthesia with lidocaine

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Abstract

Background and objectives: The molecular mechanism of hypotension post spinal anesthesia is unknown. This study hypothesized that the sympathectomy from spinal anesthesia would cause an increase in nitric oxide (NO) levels.
Methods: 36 ASA 1 or 2 patients undergoing extracorporeal shock wave lithotripsy were prospectively enrolled. Plasma levels of NO reaction products were measured pre and post spinal anesthesia.
Results: The mean NO metabolite level significantly decreased (15.9 +/- 10 vs. 13.9 +/- 8.7 μM, $P < 0.0001$) after spinal anesthesia. There was no correlation between NO and MAP.
Conclusions: Contrary to our hypothesis, plasma NO levels significantly decreased after the administration of intrathecal lidocaine. Vasodilatation produced by intrathecal lidocaine does not appear to be mediated by NO.

Key words: hypotension, nitric oxide, spinal anesthesia, sympathectomy

Abbreviations: NO – nitric oxide.

Introduction

Nitric oxide (NO) is the major physiological regulator of basal blood vessel tone [1]. Endogenously produced NO in endothelial cells causes hyperpolarization of vascular smooth muscle cell membranes resulting in vasodilatation. Intravenous and volatile anesthetics directly act on the endothelium of vascular smooth muscle cells and facilitate the release of NO; however, the effect of spinal anesthesia on NO release has not been studied [2]. Although intrathecal administration of local anesthetics for spinal anesthesia produces vasodilation and a decrease in blood pressure, the cellular mechanism is not well described and the contribution of NO to this vasodilation is unknown. We hypothesized that plasma levels of NO would increase after spinal anesthesia with lidocaine; this would implicate NO as the etiology for the decrease in blood pressure from spinal anesthesia.

Methods

After University of Rochester IRB approval and written informed consent, 36 ASA 1 or 2 patients undergoing extracorporeal shock wave lithotripsy were enrolled in this prospective study. Exclusion criteria included systemic steroids in the past two weeks and current use of nitrates. An intravenous catheter was placed in all patients prior to intrathecal

injection and a baseline blood sample was obtained. Blood pressure and pulse rate were recorded at baseline and every two minutes for the first ten minutes. Patients were given 250 ml of Ringer's lactate and spinal anesthesia was then administered with 80 mg of hyperbaric lidocaine (1.6 ml of 5% lidocaine hydrochloride plus dextrose 7.5%). The patients were placed supine and their positions were adjusted to obtain at least a T-8 sensory level. A second blood sample was obtained 10 minutes after administration of the spinal block or earlier if the patient had a drop in mean arterial pressure greater than 20% of the baseline. Hypotension was treated with a fluid bolus and intravenous ephedrine as indicated. Blood samples were collected in non-heparinized tubes and placed in ice. Plasma was separated by centrifuging samples at 3000 G for 20 minutes and then stored at -80 degree Celsius. After deproteinization of the plasma we determined plasma levels of reaction products of nitric oxide using chemiluminescence method (Sievers 280 NOA, Sievers Instruments, Inc., Boulder, CO).

Statistical analysis

Sample size was determined to be approximately 34 patients with a power of 0.8 and alpha of 0.05 to demonstrate a difference in NO metabolite levels of 2 μM with a standard deviation of 4 μM. Paired t test was used to compare the paired data and t test was performed on non-paired data. If the normality test failed, the Wilcoxon Signed Rank Test was performed. The Pearson product moment correlation was performed on MAP vs. NO metabolites. P value < 0.05 was considered significant.

Results

There were 36 patients entered into the study and all completed the study. There were 17 males and 19 females. The mean age was 51.5 yrs ± 16 years (range 22 – 84 years) and the mean weight was 78.9 ± 19.9 kg (range 45.3 – 120.8 kg). Four patients received intravenous ephedrine and five received a fluid bolus prior to drawing the post-spinal NO metabolite level.

After administration of the spinal anesthetic, the MAP decreased in each patient and the mean NO metabolite level significantly decreased (P<0.0001) (Table 1). Figure 1 shows that 26 patients had a decrease in NO metabolite level, nine patients had an increase, and there was no change in one patient. There was no difference in the magnitude of the decrease in MAP (-23.8 mmHg vs. -22.2 mmHg, P = 0.79) between the 26 patients with a decrease in NO metabolites and the nine patients with an increase in NO metabolites. Figure 2 demonstrates no correlation between NO metabolite levels and MAP (P > 0.05, R^2 = 0.02).

Discussion

Spinal-anesthesia-induced hypotension is due to sympathetic denervation, resulting in a decrease in preload and afterload [3]. This study demonstrated that contrary to our hypothesis, this decrease in systemic blood

Table 1: Nitric Oxide (NO) metabolites and mean arterial pressure (MAP) pre and post spinal anesthesia. Mean ± SD. Median (25% - 75%).

	Pre spinal	Post spinal	Difference	P value
NO metabolite (μM)	15.9 ± 10	13.9 ± 8.7	-2.02 ± 2.85	<0.0001
MAP (mmHg)	106 (95 - 117)	76.5 (64 - 94.5)	- 29.5	<0.0001

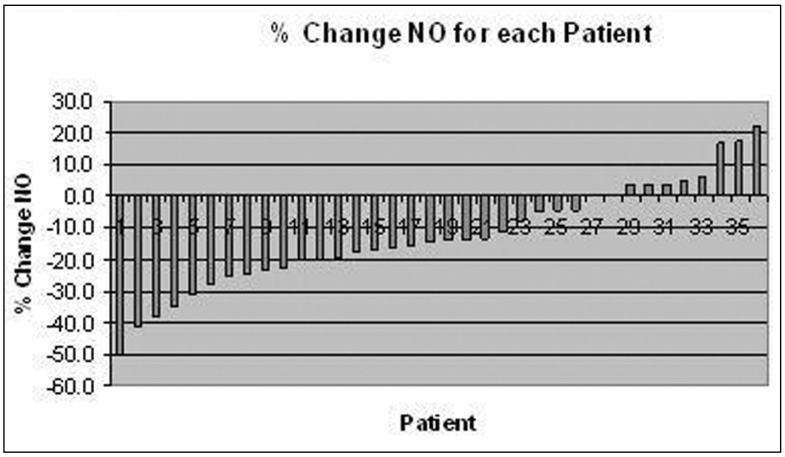

Figure 1: Percent change in nitric oxide (NO) metabolites in ascending order for each patient, pre and post spinal anesthesia.

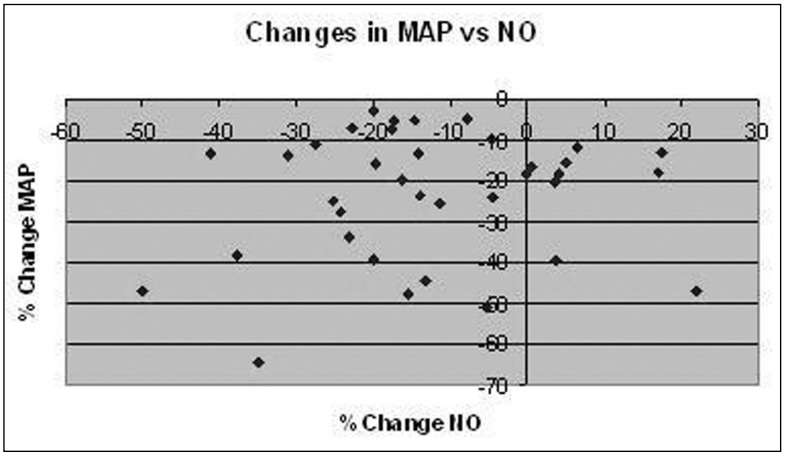

Figure 2: Percent change in nitric oxide (NO) metabolites versus percent change in mean arterial pressure (MAP), pre and post spinal anesthesia.

pressure is not due to an increase in nitric oxide levels. The observed decrease in the level of NO metabolites after spinal anesthesia is probably due to a reduction in oxygen demand relative to supply in the muscles below the spinal block. The block of somatic motor fibers reduced muscle activity and oxygen consumption, thus reducing the secretion of NO by vascular endothelium. Blocking of the nitric oxide induced skeletal muscle dilator response by sympathectomy has been described [4]. Alternatively, compensatory vasoconstriction of the area above the block level mediated by endogenous NO could have resulted in a decrease in NO release.

There are no other studies specifically looking at the effect of spinal anesthesia on NO metabolite levels, although there are several studies with conflicting findings. In a study looking at subjects with sympathetic denervation from autonomic failure, NO did not play a significant role in exercise induced hypotension [5]. A study in rats also found that the autonomic nervous system did not modulate NO release [6]. Our results were consistent with these findings. In contrast, one study detected an increase in dura mater NO in rats that were sympathectomized [7], and another study in patients after thoracic sympathectomy for anhidrosis noted an increase in vasoconstrictor response to NO synthase inhibition [8].

Our study predicts that NO inhibitors would not be an appropriate treatment for

spinal induced hypotension but needs further investigation, and the best treatment remains volume and ephedrine [3].

Conclusions

Plasma NO metabolite level significantly decreased after the administration of intrathecal lidocaine. Vasodilatation produced by intrathecal lidocaine does not appear to be mediated by NO. For future study, the mechanism of NO decrease after spinal anesthesia may be elucidated by obtaining simultaneous venous blood samples from above and below the sympathectomy to detect differences in nitric oxide levels.

References

1. Kuo PC, Schroeder RA. The emerging multifaceted roles of nitric oxide. Ann Surg 1995; 221: 220-235
2. Toda N, Toda H, Hatano Y. Nitric Oxide Involvement in the effects of anesthetic agents. Anesthesiology 2007; 107: 822-842
3. Salinas FV, Sueda LA, Liu SS. Physiology of spinal anaesthesia and practical suggestions for successful spinal anaesthesia. Best Practices & Research Clinical Anaesthesiology 2003; 17: 289-303
4. Joyner M J, Dietz N M. Sympathetic vasodilation in human muscle. Acta Physiol Scand 2003; 177: 329-36
5. Akinola AB, Smith G, Land J. et al. Nitric oxide and exercise-induced hypotension in human sympathetic denervation. J Physiol 1997; 505: 18P-19P
6. Ferrari AU, Radaelli A, Mori Ileana et al. Nitric oxide-dependent vasodilation and the regulation of arterial blood pressure. J Cardiovasc Pharmacol 2001; 38 (Suppl 2): S19-S22
7. Tore F, Korkmaz OT, Dogrukol-Ak D, and Tunçel N. The Effects of Vasoactive Intestinal Peptide on Dura Mater Nitric Oxide Levels and Vessel-Contraction Responses in Sympathectomized Rats. J Mol Neurosci 2010; 41: 288-293
8. Lepori M, Sartori C, Duplain H, Nicod P, Scherrer, U. Sympathectomy potentiates the vasoconstrictor response to nitric oxide synthase inhibition in humans. Cardiovasc Res 1999; 43: 739-43

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