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AUTONOMIC NERVOUS SYSTEM MONITORING TO EVALUATE SURGICAL STRESS: EFFECTS OF LIDOCAINE INFILTRATION DURING TONSILLECTOMY

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ABSTRACT
This research compared autonomic nervous system (ANS) responses to surgical stress in tonsillectomy and determined the influence of pre-incisional infiltration of lidocaine. Intraoperative monitoring of 23 adult patients (ASA I2) undergoing elective bilateral tonsillectomy assessed plethysmography based indices, heart rate (HR), pulse to pulse interval (PPI), plethysmographic pulse amplitude (PPGA), autonomic nervous system state (ANSS), autonomic nervous system state index (ANSSI), Surgical Pleth Index (SPI) and entropy measures. Laryngoscopy stimulated and tracheal intubation elicited noticeable sympathetic response indicated by augmented HR, diminished PPI and PPGA, as well as increased SPI. Tonsils loaded with lidocaine showed lower sympathetic responses as demonstrated by lower HR, extended PPI, increased PPGA, reduced ANSS/ANSSI, and reduced SPI than saline-treated sites, showing better nociceptive suppression. The value of entropy was similar across groups indicating the same hypnotic depth. These results indicate the value of ANS-based, non-invasive monitoring in quantifying nociceptionantinociception balance and that local lidocaine infiltration reduces autonomic responses of stress during tonsillectomy, which may lead to enhanced intraoperative physiological stability.

KEYWORDS: Autonomic nervous system (ANS), Plethysmography, Anaesthesia monitoring, Surgical nociception, Peripheral perfusion.

INTRODUCTION:

The stress of surgery is physiological due to the greater release of pituitary hormones and the sympathetic nervous system (SNS). The activation of the hypothalamus leads to the stimulation of the sympathetic arm of the ANS which causes an increased release of catecholamines by the adrenal medulla along with a greater release of norepinephrine by the presynaptic nerve terminals(1). This reaction helps modify cardiovascular parameters such as increased heart rate (HR) and an augmented vascular smooth muscle tone that are in the majority governed by sympathetic cholinergic pathways. Magnitude of this stress response is minimized during general anesthesia by the action of hypnotic medications and analgesic medications, although not completely(2,3). Ambiguities during the autonomic change by pain or stress include reduction in the amplitude of the peripheral finger plethysmographic signal(4). The changes give the understanding of the relationship between nociception and antinociception (NAN) in the process of surgery. The SNS

stimulation is facilitated along neural pathways; the result of which is an almost immediate physiological response, slow, longer-lasting responses are mediated by the circulation of epinephrine and norepinephrine released by nerve endings. It is thus essential to find dependable and objective indicators of poor analgesia, which can be used by clinicians to track the autonomic activity in order to change the anesthetic control(5,6). ANS influences the cardiac functions, both sympathetic and parasympathetic, whereby the sympathetic arm increases the cardiac speed and the parasympathetic decelerates(7). Therefore, in diverse clinical practices, HR based on electrocardiography (ECG) is widely employed as an indicator of autonomic balance.

Complementary information is offered by pulse rate (PR) of pulse oximetry(8). Notably, analysis of the plethysmographic pulse wave amplitude (PPGA) which is displayed in most pulse oximeter displays provides useful information on circulatory status as compared to monitoring with the ECG alone. The waveform indicates various hemodynamic variables, such as ventricular contractility, stroke volume, venous pressure and sympathetic vasomotor tone of digital arterioles(9,10). Slow, rhythmic changes in the baseline signal of the plethysmographic signal occur during respiratory activity, whether spontaneous or caused by positive pressure ventilation and may appear as a waveform of arterial pressure(11,12). Autonomic tone variations due to pain and stress as well as hypovolemia are linked to the reduction in peripheral pulse amplitude. Furthermore, perfusion of the fingertips and pulse amplitude are also sensitive to the local skin temperature because vasoconstriction decreases the blood flow and signal amplitude. Having fingertip temperature elevated over 30C of C has been indicated to enhance the accuracy of the peripheral plethysmographic recordings, pointing out the interaction between local perfusion and autonomic activity(13,14,15). Considering these physiological principles, the autonomic responses observed in surgical operations will serve as a non-invasive procedure of measuring the nociceptive stimulation and the success of analgesic treatment. Pulse amplitude and other plethysmographic measurements can be sensitive markers of increases in sympathetic activity and can be used to compliment standard cardiovascular measures, e.g. HR measured by ECG and non-invasive blood pressure measurements(16). Using both fast and slow autonomic responses measures, clinicians are able to identify instances of inadequate analgesia and optimize the anesthetic depth. The aim of the current research was to research the autonomic effects during laryngoscopy and tracheal intubation and to test whether one tonsil pre-incisional lidocaine infiltration affects the surgical stress response during tonsillectomy(17). Our goal was to understand how the local anesthesia affects the sympathetic activation and other indicators of autonomic activity by comparing the anesthetic response and autonomic response of the tonsil which had been treated with lidocaine to the contraelastic of saline-infiltrated tonsil at the same state of anesthesia(18). The knowledge of such responses would help to improve perioperative observation, analgesic control, and make new conclusions about the dynamic nature of the relationship between local anesthesia, sympathetic nervous system activity and systemic stress reactions during surgery.

METHODS

In this study, twenty three adult patients were recruited. The patients were all aged 18 to 65 and their body weights were 54-90kg. All the patients were to be subjected to an elective bilateral tonsillectomy in the diagnosis of chronic tonsillitis. Stringent inclusion and exclusion criteria were used to reduce confounding variables that might affect the autonomic nervous system (ANS) activity, and hence, affect the study results. These exclusion criteria were the age of the patients (below 18 years and above 65 years), cardiovascular or central nervous system disease, and known medical conditions that can influence ANS activity (such as diabetes mellitus). Patients who are taking drugs that modify the ANS, central nervous system, or cardiovascular system as well as those with a history of alcohol or drug abuse/psychiatric diseases were excluded to prevent confounding autonomic and hemodynamic values. Every patient was fasted overnight and no premedication was administered to them in order to reduce the effect of pharmacologic values on the autonomic

parameters. Preoxygenation was administered through 100 percent oxygen administered by a face mask and the normal physiological parameters at the baseline before anesthesia were recorded (19). The induction of anesthesia was done intravenously using fentanyl and propofol. Anesthesia was also sustained using sevoflurane 8% in oxygen over a rebreathing circuit and a carbon dioxide absorber with a fresh gas flow rate of 5 L/min. Tracheal intubation was not applied until a state entropy (SE) value of less than 30 was met. Some adjustments in anesthesia were minor, such as the supplementation of fentanyl (1 1g/kg) or propofol in case there was movement during laryngoscopy before successful intubation (20).

The pressure of the tracheal tube cuff was kept at 22 cm H 2 O which would provide a sufficient degree of seal without causing a lot of pressure. Anesthesia of surgery was supported by sevoflurane in a gas mixture of 40 percent oxygen in air with SE maintained at 30-40. The end-tidal CO 2 was maintained at normocapnia, and end-tidal CO_2 was over 5.3 kPa. After intubation and placing of the mouth gag, random infiltration with 7.5 mL of 1% lidocaine and 0.9% saline of one tonsil and a separate tonsil respectively. The depth of anesthesia was kept at the level of surgery. When surgery was complete, sevoflurane was discontinued and patients were slowly disconnected and ventilator weaned (21). monitored until the recovery of consciousness and opening of eyes. Intraoperative monitoring and data collection were provided with the help of both the standard and advanced methods. The monitoring of the entropy and electrocardiography (ECG) were introduced before the induction in accordance with the manufacturer instructions (22). The tip of the left middle finger and a pulse oximeter probe were fitted with a surface temperature sensor and a pulse oximeter probe respectively. To avoid interference with pulse oximetry, a non-invasive blood pressure cuff was applied to the right arm, upper part. A left-hand intravenous line was put in, to administer room-temperature Ringer acetate (23). The entire monitoring information were recorded in real time using a software system based on a laptop that allows real-time visualization and offline analysis. Quantitative indices of ANS activity were also employed to complement the intraoperative physiological responses evaluation in addition to routine monitoring. The autonomic nervous system state (ANSS) was determined by the product of pulse-to-pulse intervals (PPI) and pulse plethysmographic amplitude (PPGA). ANSS values were measurements of changes in autonomic modulation in real-time and variation in either of these components signified sympathetic or parasympathetic variations. An index of offline autonomic nervous system state (ANSSI) was used to normalize such parameters and the autonomic variations were expressed as a percentage of the maximum ANSS of every patient. These settings enabled beat-to-beat monitoring with the induction, intubation, surgical stimulation and emergence to assess ANS responses in detail and determine the impact of local anesthetic infiltration on surgical stress physiology.

RESULTS:

Table 1 presents the results of the autonomic and hemodynamic variables on laryngoscopy and tracheal intubation. The increase in heart rate (HR) was statistically significant and small with median heart rate decreasing below 60 beats/min to about 65 beats/min ($P = 0.031$). In line with this the pulse-to-pulse (P-P) interval was marginally diminished which again is in line with sympathetic activation through airway manipulation. Significant reduction of pulse plethysmographic amplitude (PPGA) was found right after tracheal intubation, and it partially recovered in two minutes. The trend implied transient peripheral vasoconstriction and decreased digital perfusion in reaction to sympathetic stimulation. Autonomic status indicators, such as state of the autonomic nervous system (ANSS) and the index of autonomic nervous system state, (ANSSI) did not show statistically significant deviations ($P > 0.001$) but trends indicated that sympathetic modulation was increasing during airway instrumentation. In the same way, Surgical Pleth Index (SPI) increased significantly, ($P = 0.022$) following intubation, which is a temporary response to a nociceptive stimulus. These results support the idea that laryngoscopy and intubation produce sympathetic reactions that were mild tachycardia, low pulse amplitude, temporary autonomic imbalance, despite a sufficient level of anesthetic depth.

The side treated with a lidocaine showed a slight decrease in HR than the saline side [63 (41-84) vs. 67 (38-91) beats/min, P = 0.015], and the P-P interval, which was a sign of reduced sympathetic activity. PPGA also rose considerably over lidocaine infiltration compared to saline (P < 0.001), which supports the idea of better peripheral perfusion and less sympathetically mediated vasoconstriction. Reduced ANSS and ANSSI scores were found on the side of lidocaine treatment, which is in line with the inhibition of the autonomic stress response. Parallel to it, the values of SPI became much lower (P < 0.001), which indicated a decrease in the nociceptive activation. No significant differences were found in non-invasive arterial systolic pressure (NIAPsyst), state entropy (SE) or response entropy (RE) suggesting an equal level of cortical suppression and level of anesthetic depth between conditions. The RE-SE gradient was slightly lower following infiltration of lidocaine (P = 0.003), which is indicative of a lower activation of muscle of the face and better analgesia. The temperature of fingers (Tf) was similar in both conditions. These findings, combined, suggest that laryngoscopy and tracheal intubation cause quantifiable sympathetic and hemodynamic responses. Preoperative local lidocaine infiltration at the surgical site suppressing autonomic responses during tonsillectomy suggests that this method could be useful as a way of dampening nociception and promoting intraoperative autonomic stability and stability in anticipation of general anesthesia use.

TABLE 1: Autonomic and haemodynamic variants in the course of laryngoscopy and intubation of the trachea

Parameter	1 min before	1 min after	2 min after	P-value
HR (beats min^{-1})	60 (34–78)	62 (36–82)	65 (38–83)	0.031
P–P interval (s)	1.020 (0.790–1.850)	1.000 (0.760–1.810)	0.960 (0.740–1.790)	0.031
PPGA (%)	7.85 (3.00–12.10)	5.90 (2.00–12.30)	6.45 (3.70–14.00)	<0.001
ANSS (%·s)	7.40 (2.60–17.00)	5.70 (1.80–17.80)	6.40 (3.40–19.00)	<0.001
ANSSI	42.00 (12.00–65.50)	49.20 (17.50–78.00)	40.10 (11.00–63.00)	<0.001
SPI	21.0 (8.0–53.0)	22.5 (8.0–54.0)	20.0 (8.0–38.0)	0.022

TABLE 2: Comparison of autonomic and haemodynamic variables between lidocaine- and saline-infiltrated tonsils

Parameter	Lidocaine-infiltrated	Saline-infiltrated	P-value
HR (beats min^{-1})	63 (41–84)	67 (38–91)	0.015
P–Pint (s)	0.915 (0.710–1.520)	0.905 (0.670–1.640)	0.015
PPGA (%)	7.30 (2.50–10.90)	5.95 (2.60–12.00)	<0.001
ANSS (%·s)	6.60 (1.90–12.90)	5.40 (1.85–16.50)	<0.001
ANSSI	42.80 (13.50–72.40)	50.60 (12.00–77.10)	<0.001
SPI	29 (12–48)	33 (11–52)	<0.001
NIAPsyst (mm Hg)	79 (63–110)	82 (67–113)	NS
SE	26 (18–40)	25 (10–41)	NS
RE	28 (10–52)	27 (9–54)	NS
RE–SE	1 (0–13)	2 (0–28)	0.003
Tf (°C)	32.9 (31.8–34.8)	32.7 (31.7–34.7)	NS

DISCUSSION:

This experiment with 23 adult patients showed that when anesthesia was induced, a gradual rise in fingertip temperature occurred in the first 10 minutes, which agrees with the concept of peripheral vasodilation with sympathetic relaxation(24). An increase in plethysmographic pulse amplitude (PPGA) was concomitant with an increase in sympathetic vasoconstrictor tone in the digital arterioles. The above results are consistent with the anticipated hemodynamic changes after administering propofol, fentanyl, and sevoflurane as each of them leads to vasodilation and

sympathetic depression. Nonetheless, the laryngoscopy and tracheal intubation induced a temporary and acute decrease of PPGA, which represented temporary peripheral vasoconstriction as a result of nociceptive input and sympathetic excitation(25). The parameters of the autonomic nervous system (ANS) evidenced the statistically significant changes at one and two minutes after intubation compared with the parameters measured one minute prior to intubation (Table 1). The observations confirm the sensitivity of parameters derived using plethysmography in the identification of acute sympathetic responses to airway manipulation.

When the anesthetic depth decreased, peripheral vascular tone progressively recovered to baseline with surgical stimulation and significant decreases in PPGA and fingertip temperature were found after the removal of sevoflurane. In tonsillectomy, all descriptors of ANS, with the exclusion of non-invasive arterial pressure (NIAP) indicated statistically significant differences between saline infiltrated and lidocaine treated tonsils (Table 2). Response entropy (RE) and state entropy (SE) changes showed more facial muscle activity of the saline group in case of surgery manipulation ($P = 0.002$), which confirms the analgesic effect of local anesthetic infiltration. Recording of non-invasive arterial pressure measurements at intervals of five minutes failed to reliably identify sudden nociceptive changes, which highlights weaknesses of intermittent observations of NIAP. Fasting-related hypovolemia and peripheral vasoconstriction was prevented by Ringer acetate until the fingertip temperatures reached above 30^{o}C during induction; two of the patients exhibited slow replacement of peripheral temperature. Due to low responsiveness of skin temperature sensor to changes in temperature, the changes in transient PPGA with particular relation to ones that occur during laryngoscopy did not appear as instant changes in the temperature of fingertips.

Future research can be done on the directly opposite effects of fluid treatment and external warming techniques (e.g., forced-air warming) on peripheral temperature and autonomic conditioning in anesthesia. The monitoring system used a Take Snapshot marker to indicate the stimulation events. Though the averaging of the signals was done with a time interval of 10 seconds, a small temporal shift of the markers, the delay did not have any significant impact on the ANS responses trends. The values of SPI which are based on the raw pulse waveform were not affected by averaging delay. An increased accuracy of beat-to-beat can be introduced in future studies by adding continuous recording forms like invasive monitoring of the arterial pressure. Similarly, larger averaging windows can be used to filter sharp changes in entropy due to brief bursts of electromyographic activity in response to nociceptive inputs. Pulse amplitudes can also be artificially minimized by mechanical compression by spring-loaded pulse oximetry sensors that might mimic sympathetic activation.

Autonomic nervous system has been a challenge to assessment in intraoperative. Conventional sympathetic observations may involve a form of invasive neural activity, but non-invasive devices like pulse plethysmography provide viable, continuous options. Perioperative nociception has also been suggested to be monitored using skin conductance. The Surgical Pleth Index (SPI) can give normalized plethysmographic measurement whereas the autonomic nervous system status (ANSS = PPGA × PPI) can give beat-to-beat analysis of sympathovagal balance. The state index of the autonomic nervous system (ANSSI = 100 -(ANSS/ANSSmax)x90) is similar to SPI, except that it is normalized using a nonproprietary standard. Sympathetic activation and nociceptive imbalance is indicated by increases in SPI and ANSSI. Along with peripheral pulse amplitude, cardiac filling time is also a significant predictor of autonomic behavior during anesthesia. ANSS and entropy monitoring can help to optimize the timing of airways interventions, such as laryngoscopy and intubation. Small and intermittent vagal events were noted, which consisted of temporary bradycardia with the enhancement of pulse amplitude and the restoration of sympathetic activity. The question on whether preoperative anticholinergic agents can prevent such responses is a subject of further research. Pulse oximetry, motion-sensitive and probe movement-sensitive, needs firm

probe contact and maintains a temperature of perfusion and autonomic evaluation of the fingertips above 30 °C. Comprehensively, the present study shows that non-invasive ANS monitoring is a practical measure to conduct dynamic physiological responses to anesthetic induction, airway manipulation, and perioperative stimulus in a sample of 23 patients. This approach provides a viable way of real-time measurement without invasive lines as well as can be useful in the customization of intraoperative control to reduce stress responses.

CONCLUSION:

This study utilized 23 adult patients revealed that autonomic nervous system (ANS) descriptors including HR, PPI, PPGA, ANSS, ANSSI, SPI, and RESE are delicate and reliable markers of nociceptive stimulation in general anesthesia. These parameters constantly identified sympathetic excitation in the course of laryngoscopy and tracheal intubation and could clearly distinguish autonomic responses between toniglial infiltrated with lidocaine and saline-treated tonsils and thus was capable of measuring the analgesic effects of local infiltration. The ANS-based indices reflected real-time, non-invasive, and more specific information on the nociceptive and antinociceptive balance in comparison to the traditional hemodynamic markers. Individual anesthetic and analgesic titration can be facilitated by their incorporation into perioperative surveillance to prevent either insufficient analgesia or overdose administration. The results indicate that ANS monitoring is capable of helping to increase intraoperative stability, individualized care, and patient safety. Clinical benefits such as postoperative recovery and long-term outcomes need to be validated in further studies using larger and more diverse populations of surgical patients.

REFERENCES:

1. Paloheimo M, Uutela K, Sahanne S. *Lidocaine infiltration before tonsillectomy reduces operative stress.* Acta Anaesth Scand. 2007;54:48.
2. Desborough JP. *The stress response to trauma and surgery.* Br J Anaesth. 2000;85:109–117. doi:10.1093/bja/85.1.109
3. Hamill RW, Shapiro RE. *Peripheral autonomic nervous system.* In: Robertson D, ed. *Primer on the Autonomic Nervous System.* Elsevier Academic Press; 2004:20–28.
4. Warner DS, Warner MA. *Sympathetic nervous system: evaluation and importance for clinical general anesthesia.* Anesthesiology. 2008;109:1113–1131.
5. Calhoun DA, Oparil S. *Hypertension and sympathetic nervous system activity.* In: Robertson D, ed. *Primer on the Autonomic Nervous System.* Elsevier Academic Press; 2004:241–244.
6. Dorlas JC, Nijboer JA. *Photo-electric plethysmography as a monitoring device in anaesthesia.* Br J Anaesth. 1985;57:524–530. doi:10.1093/bja/57.5.524
7. Guignard B. *Monitoring analgesia.* Best Pract Res Clin Anaesth. 2006;20:161–180. doi:10.1016/j.bpa.2005.09.002
8. Høymore SC. *Antinociceptive monitors: tools or fools?* Acta Anaesthesiol Scand. 2008;52:1035–1037.
9. Korhonen I, Yli-Hankala A. *Photoplethysmography and nociception.* Acta Anaesthesiol Scand. 2009;53:975–985. doi:10.1111/j.1399-6576.2009.02026.x
10. Murray WB, Foster PA. *The peripheral pulse wave: information overlooked.* J Clin Monit. 1996;12:365–377. doi:10.1007/BF02077634
11. Awad AA, Ghobashy AM, Ouda W, et al. *Different responses of ear and finger pulse oximeter waveforms to cold pressor test.* Anesth Analg. 2001;92:1483–1486. doi:10.1097/00000539-200106000-00026
12. Natalini G, Rosano A, Franceshetti ME, et al. *Variations in arterial blood pressure and photoplethysmography during mechanical ventilation.* Anesth Analg. 2006;103:1182–1188. doi:10.1213/01.ane.0000202380.22997.24

13. Allen J, Frame JR, Murray A. *Microvascular blood flow and skin temperature changes in the fingers following a deep inspiratory gasp.* Physiol Meas. 2002;23:365–373. doi:10.1088/0967-3334/23/2/312
14. Shamir M, Eidelman LA, Floman Y, et al. *Pulse oximetry plethysmographic waveform during changes in blood volume.* Br J Anaesth. 1999;82:178–181.
15. Sessler DI. *Skin temperature gradients are a validated measure of fingertip perfusion.* Eur J Appl Physiol. 2003;89:401–402. doi:10.1007/s00421-003-0812-8
16. Kallio H, Lindberg LI, Majander AS, et al. *Measurement of surgical stress in anaesthetized children.* Br J Anaesth. 2008;101:383–389. doi:10.1093/bja/aen204
17. Huiku M, Uutela K, van Gils M, et al. *Assessment of surgical stress during general anaesthesia.* Br J Anaesth. 2007;98:447–455. doi:10.1093/bja/aem004
18. Struys MMRF, Vanpetegheim C, Huiku M, et al. *Changes in surgical stress index in response to standardized pain stimuli during propofol-remifentanil infusion.* Br J Anaesth. 2007;99:359–367. doi:10.1093/bja/aem173
19. Wennervirta J, Hynynen M, Koivusalo AM, et al. *Surgical stress index as a measure of nociception/antinociception balance during general anesthesia.* Acta Anaesth Scand. 2008;52:1038–1045.
20. Storm H, Myre K, Rostrup M, et al. *Skin conductance correlates with perioperative stress.* Acta Anaesthesiol Scand. 2002;46:887–895. doi:10.1034/j.1399-6576.2002.460721.x
21. Paloheimo MPJ, Penttinen M. *ANS-spot and autonomic nervous system stability during general anaesthesia—a new pain indicator.* Br J Anaesth. 2004;93:489.
22. Paloheimo M, Kallio H. *Continual monitoring of autonomic responses and hypnosis is essential in timing of endotracheal intubation.* Br J Anaesth. 2008;100:878.
23. Teng XF, Zhang YT. *The effect of contacting force on photoplethysmographic signals.* Physiol Meas. 2004;25:1323–1335. doi:10.1088/0967-3334/25/5/020
24. Neukirchen M, Kienbaum P. *Sympathetic nervous system.* Anesthesiology. 2008;109:1113–1131. doi:10.1097/ALN.0b013e31818e435c
25. Ledowski T, Ang B, Schmarbeck T, et al. *Monitoring of sympathetic tone to assess postoperative pain: skin conductance vs. surgical stress index.* Anaesthesia. 2009;64:727–731. doi:10.1111/j.1365-2044.2008.05834.x.