Short Communication

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Skin conductance algesimeter is unreliable during sudden perioperative temperature increases

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Abstract

Objectives – Pain assessment in anesthetized and non-communicative patients remains a challenge. Clinical signs such as tachycardia, hypertension, sweat and tears, have a low specificity for pain and should therefore ideally be replaced by more specific monitoring techniques. Skin conductance variability has been demonstrated to establish a patients' sensitivity to pain, but may be influenced by temperature changes that leads to profuse sweating. The aim of this pilot study was to test skin conductance changes during sudden temperature changes due to hyperthermic intraperitoneal chemotherapy (HIPEC) perfusation.

Methods – We investigated skin conductance algesimeter (SCA) in ten consecutive patients undergoing cytoreductive surgery and HIPEC. Results from the SCA was compared to other standard physiological variables at seven time points during the surgical procedure, in particular during the period with hyperthermic intraabdominal perfusion leading to an increase in the patients core temperature.

Results – Nine out of ten patients had an increase in the SCA measurements during the HIPEC phase correlating the increase in temperature.

Conclusion – SCA is unreliable to detect increased pain sensation during sudden perioperative temperature changes in adult patients.

Keywords: pain, anaesthesia, intraoperative monitoring, skin conductance, body temperature changes

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1 Introduction

General anesthesia consists of hypnosis, analgesia, and areflexia. The administration of hypnotic agents is used to prevent awareness, the analgesics to prevent autonomic and somatic responses, and muscle relaxants to prevent reflex movements [1]. Different commercial devices have been developed to monitor depth of anesthesia, like bispectral index spectroscopy (BIS) [2], auditory evoked potential [3], and state entropy [4]. These are based on analyses of the electroencephalography signal [5] and seem to be more related to the hypnotic state of the patient than to anti-nociception perceived as pain or physiological stress induced by noxious stimuli. Nevertheless, pain assessment in anesthetized and non-communicative patients remains a problem. Use of clinical signs such as tachycardia, hypertension, sweat, and tears, has a low specificity for pain and should therefore ideally be replaced by a more specific monitoring technique [6]. At least four methods are commercially available [7]: pupillometry [8], analgesia/nociception index [9,10], surgical pleth index [11], and the skin conductance algesimeter (SCA) [12–15]. These techniques assess nociception and anti-nociception through the balance between activity of the sympathetic and parasympathetic nervous system.

The SCA is a non-invasive electronic conductance meter for detecting skin conductance changes on palmar and plantar skin sites to determine a patients sensitivity to pain [16,17]. The SCA device is a class II A medical device. It is IP-protected and CE-certified. The SCA reflects the sympathetic nervous system, influenced by changes in emotions. Release of acetylcholine acts on muscarinic receptors, causing a subsequent burst of sweat and increased skin conductance. The SCA reacts immediately and is not influenced by hemodynamic variability or neuromuscular blockade. Skin conductance measured in the palmar region reflect the emotional part of the autonomous nervous system [12,13,15]. SCA registration ≥0.20 peaks per second have been shown to indicate moderate or severe pain in the postoperative setting. Skin

conductance variability to assess pain has, however, shown varying results. Furthermore, skin conductance variability may be influenced by temperature changes that leads to profuse sweating [18].

Cytoreductive surgery-hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) [19] is a national service for Norway located at the Norwegian Radium Hospital for treatment of peritoneal metastasis in certain intraabdominal cancers. Macroscopic cancerous tumours are surgically removed, and then heated chemotherapy drugs are applied intraperitonally in the abdomen to eliminate the remaining cancerous cells lining the peritoneum and remaining free tumour clusters. During the hyperthermic intraperitoneal chemotherapy (HIPEC) phase, the patients usually develop raised core body temperature up to 40.5°C due to the hyperthermic perfusate (with a temperature of 43–44.0°C) resulting in a median temperature of 42.0°C inside the abdominal cavity. Although different procedures to control patient temperature are used, raised patient temperatures are expected. Raised temperature can lead to excessive sweating. Excessive sweating can influence SCA [18,20].

The aim of this pilot study was to test SCA during the hyperthermic perfusate period, and whether this method is influenced by the patient temperature changes and not variations in noxious stimuli during general anesthesia.

2 Methods

We investigated SCA in ten consecutive HIPEC patients in this pilot study. A SCA from MedStorm Innovation AS was used as described by the manufacturer. Electrodes were attached on the palm of hand and the pain sensor attached to the wrist of the patient. The algesimeter collected, measured, and calculated data from the sensor and transferred the results by Bluetooth Low Energy connectivity to a tablet for display. The measured conductive peaks per second are reflected in the SCA index. The index is expressed numerically from 1 to 10, 1 being low probability of pain and 10 gives high probability of pain. SCA measurements were performed at seven different time points (Figure 1). To compare the results from the SCA with other physiological variables, measurements of oesophageal temperature, arterial blood pressure, pulse, minimal alveolar concentration (MAC) of inhalation agents, BIS, epidural infusions, remifentanil infusion (if used), and accumulated fentanyl at seven time points during the surgical procedure were recorded. These physiological variables and medication dosing are routinely used and registered during CRS-HIPEC at the Norwegian Radium Hospital.

General anaesthesia was induced with fentanyl and propofol. Muscle relaxation was obtained with rocuronium bromide with incremental doses guided by neuromuscular monitoring. Anaesthesia was maintained with fentanyl, remifentanil, and desflurane. All patients had a thoracic epidural catheter inserted before the start of anaesthesia, and all patients had a continuous epidural infusion with a standard solution (bupivacaine 1 mg/mL, fentanyl 2 µg/mL, and adrenaline 2 µg/mL) activated before the start of surgery and maintained throughout the procedure. All patients received a bolus before the start of epidural infusion. Rate of epidural infusion was not standardized, but was adjusted according to vital parameters at the discretion of the attending anaesthesiologist.

The study was approved by the local representative for the Norwegian Data Protection Authority (case number 23/05469).

3 Results

Six female and four male patients were included. Medium weight was 68 kg (quartiles: 58, 81) and median age was 65

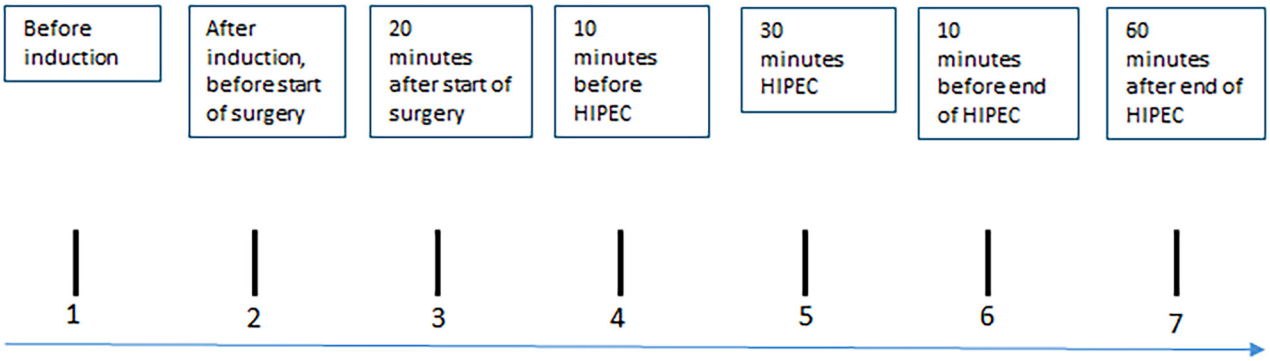

Figure 1: Flow diagram with time points for SCA measurements, oesophageal temperature, and other physiological variables.

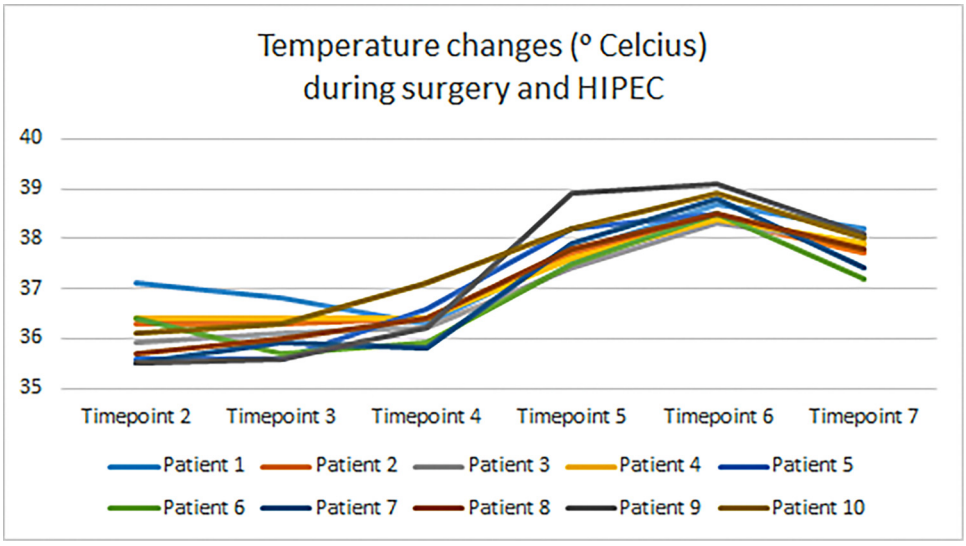

Figure 2: Oesophageal temperature changes (°C) at different time points during surgery and HIPEC.

years (quartiles: 63, 67). All patients had an increase in temperature during the HIPEC procedure (median increase from 36.2 to 38.4°C (Figure 2 and Table 1). Nine out of ten patients had an increase in SCA measurements during the HIPEC procedure (Figure 3 and Table 1) with a median SCA signal of 8 during maximum temperature increase. There were no clinical signs indicating that the patients had an increased pain sensation during the HIPEC procedure (Table 1). None of the patients received additional bolus or change in the rate of epidural infusions, nor did they receive additional opioids during the HIPEC procedure. At time point 6 (10 min before end of HIPEC) we registered a median accumulated fentanyl dose of 375 mcg (quartiles: 350, 440), a median accumulated remifentanil dose of 0.6 mcg (quartiles: 0.0, 25.9), a median accumulated epidural infusion volume of 70 mL (quartiles: 56, 81), and a MAC of 0.9 (quartiles: 0.8, 1.0).

4 Discussion

Nine out of ten patients had an increase in the SCA measurements during the HIPEC phase correlating the increase in temperature.

During the HIPEC procedure, catheters and suction drains are placed into the abdominal cavity and connected to a perfusion machine in a closed circuit system. To increase the effect of chemotherapy drugs, the solution is heated up to 43–44°C attempting to have median 42°C in the outflow abdominal catheter. The perfusion is maintained for 90 min and as a consequence, the patient core temperature increases. During this phase, the patients are not exposed to surgical stimuli.

Since the patients were not exposed to surgical pain stimuli during the HIPEC phase (besides the abdominal perfusion of heated chemotherapy drugs), while maintaining a stable

Table 1: SCA measruements and physiological variables

	Time point 1	Time point 2	Time point 3	Time point 4	Time point 5	Time point 6	Time point 7
SCA	2 (1, 6)	0 (0, 0)	0 (0, 5)	0 (0, 7)	0 (0, 0)	8 (3, 10)	0 (0, 3)
Oesophageal temperature		36.2 (35.9, 36.4)	36.1 (35.7, 36.4)	36.4 (36.2, 36.6)	37.6 (37.3, 37.7)	38.4 (38.0, 38.5)	37.9 (37.7, 37.9)
MAP		71 (64, 76)	72 (65, 101)	75 (71, 85)	66 (63, 69)	66 (63, 73)	70 (65, 73)
Pulse		77 (59, 75)	75 (65, 84)	77 (65, 83)	77 (66, 80)	84 (70, 88)	84 (73, 90)
BIS		37 (31, 48)	35 (31, 41)	40 (30, 50)	44 (30, 54)	40 (33, 47)	38 (34, 53)
MAC		0.9 (0.8, 1.0)	1.0 (0.9, 1.0)	1.0 (0.9, 1.0)	1.0 (0.9, 1.0)	1.0 (0.9, 1.0)	0.9 (0.3, 1.0)

SCA measurements and different physiological variables at specific time points according to protocol. Median values with 25 and 75 percentiles in parenthesis. SCA = skin conductance algesimeter; MAP = mean arterial pressure; BIS = bispectral index; MAC = minimum alveolar concentration.

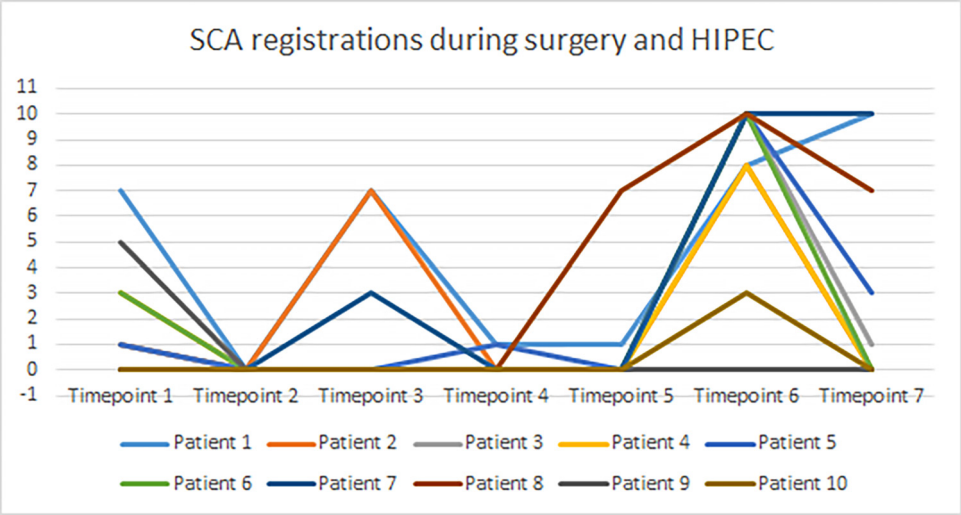

Figure 3: SCA measurements at different time points during surger and HIPEC.

anaesthesia level, we suspect that the increase in the SCA measurements were caused by the increase in core and skin temperature. It can be argued that the abdominal perfusion of chemotherapy can cause peritoneal inflammation and thus pain [21]. However, peritoneal inflammatory pain and neuropathic pain components will probably take some time to develop [21]. Furthermore, all patients received continuous thoracic epidural analgesia to reduce nociception from the abdomen which has been demonstrated to give adequate analgesic effect in patients with CRS-HIPEC [22]. In addition, there was no increase in blood pressure and only a minor increase in heart rate (probably due to increase in temperature [23]) during the HIPEC phase (Table 1).

Thermoregulation is a homeostatic process that maintains a steady internal body temperature despite changes in external conditions. The body responds by dissipating heat by activating sympathetic cholinergic fibers innervating sweat glands, leading to increased sweat and heat loss [24].

Abnormal temperature regulation and defects in sweat production in the body can indicate a dysfunction in the autonomic nervous system in a number of clinical conditions including hyperhidrosis, small fiber and autonomic neuropathies, multiple system atrophy, Parkinson disease with autonomic dysfunction, and pure autonomic failure [24].

Excessive sweating has also been observed following intrathecal morphine administration [25].

Whether increased sweating in the clinical situations mentioned above also effects SCA measurements remains to be seen.

Since the use of clinical signs such as tachycardia, hypertension, sweat, tears, and pupillary reactions, has a low specificity for pain, different monitoring techniques have been developed [1,7]. Accurate real-time acquisition and analysis of patients' response to surgically induced nociception would provide an efficient way to continuously assess the response of analgesics in order to suppress nociception and avoid under or over-dose of anesthetics. If 100% reliable, such a monitoring device would represent a "holy grail" in personalized drug administration [26]. Today, these monitoring devices all have some limitations. According to Banerjee and MacDougall [1], there appeared to be no statistically significant difference between nociception monitoring and standard monitoring with respect to intraoperative adverse events, postoperative opioid or analgesic consumption, postoperative pain, and postoperative adverse events. Thus, it is important to be aware of flaws and imperfections in each apparatus, as pointed out in this report regarding SCA in HIPEC patients during temperature increase.

5 Conclusion

With this pilot study we have demonstrated that SCA is unreliable during sudden perioperative temperature changes in adult patients. From our data, we cannot conclude that skin conductance changes are influenced by changes in temperature in other clinical conditions or in other age groups.

Research ethics: The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Research data were part of a quality assurance project and thus exempted from REC (Regional Ethics Committee) approval in agreement with national and local research guidelines. The study was approved by the local representative of the Norwegian Data Protection Authority (case number 23/050469).

Informed consent: Not applicable.

Author contributions: All authors have contributed in writing and have approved the final manuscript.

Competing interests: Ulf E. Kongsgaard is section editor for Scandinavian Journal of Pain (Clinical sciences: cancer-related pain). The authors declare no conflict of interest.

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Data availability: The raw data can be obtained on request from the corresponding author.

Artificial intelligence/Machine learning tools: Not applicable.

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