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Intra-Operative TENS with Regard to Intra-Operative Opioid Demand and Analgesic Consumption within One Week after Major Spinal Surgery

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Abstract

Background: Preincisional and postoperative Transcutaneous Electrical Nerve Stimulation (TENS) has shown an opioid sparing effect in the treatment of postoperative pain after major spine surgery. The aim of this study was to test the effect of TENS applied intraoperatively on intraoperative demand for fentanyl.

Methods: Forty-eight patients scheduled for dorsal lumbar fusion were enrolled and divided into two groups by random numbers. Group A received TENS preoperatively, intra-operatively and postoperatively. Group B received this treatment pre- and postoperatively only. Fentanyl was given during surgery if systolic blood pressure and or heart rate increased 15% over baseline level. Bispectral index (BIS) was maintained between 40 and 50. The total amount of fentanyl administered intra-operatively was recorded. Physician-determined analgesics were given postoperatively to achieve a visual analogue pain score below 3. The total amount of analgesics given, postoperative nausea and vomiting, and stomachache up to the seventh day after surgery were recorded.

Results: The two groups were comparable on demographic variables. The intra-operative demand for fentanyl differed significantly between A versus B. (P>0.0000001). No significant differences were detected in total amount of administered analgesics, postoperative nausea and vomiting, nor stomachache up to the seventh postoperative day.

Conclusion: Intra-operative TENS reduces intra-operative demand for fentanyl during major spinal surgery. This may be considered especially important in patients who suffer from obstructive sleep apnea syndrome.

Keywords: Transcutaneous electrical nerve stimulation; Intra-operative; Fentanyl; Major spinal surgery; Postoperative analgesia

Introduction

Preincisional and postoperative transcutaneous electrical nerve stimulation (TENS) has been proven to be effective in opioid sparing in postoperative analgesic [1-5]. Preoperative and intra-operative electric acupuncture reduces intra-operative alfentanil demand [6]. The effect of TENS administered intra-operatively on acute pain was investigated in an animal model only [7]. Furthermore the influence of intra-operative TENS on postoperative analgesic requirement within seven days has not yet been studied. This study was performed to elucidate a probable impact of intra-operative TENS on intra-operative fentanyl demand and on postoperative analgesic consumption in major spinal surgery. The threshold of sufficient postoperative pain therapy was set on a visual analogue scale (VAS) less than 3.

Patients, Material and Methods

The study was approved by the local Ethic Committee and registered on European Clinical Trials Database (EudraCT number 2013-003609-25). A prospective, double blinded, randomized, sham controlled, monocentric study was conducted at the neuroanesthesiological department of Paracelsus Medical Univerisity, Salzburg, Austria from September 2013 to March 2014. After written informed consent 48 opioid naive patients of both sex American Society of Anesthesiologists (ASA) grade I to III planned for lumbar interbody fusion of two (PLIF1) or three (PLIF2) lumbar vertebrae were enrolled. Patients suffering from a known allergy against drugs mentioned afterwards were excluded. We hypothesized that intra-operative TENS influences the intra-operative demand on fentanyl and the consumption of analgesics up to the seventh postoperative day. Patients were randomized and divided into 2 groups. The zero hypothesis of this study is that no difference exists between the groups in total intra-operative amount of fentanyl, in total postoperative use of piritramid, tramadol, paracetamol, diclofenac, naproxen, clonidine and metamizol, in total amount of PONV attacks and in total amount of stomach ache episodes up to the seventh postoperative day. According to a previous study on TENS [1] 4 cutaneous self-adhesive electrode pads sized 16 cm^2 were attached on either side in a distance of 5 cm to the planned skin incision before induction of anesthesia. To avoid dampening by surgical washing the pads were covered with a plastic film. The TENS electrodes were connected to the TENS device (tens 1000 s, D-82490, Farchant, Germany) and stimulated in a synchronized fashion with a bidirectional electrical current, a frequency of 100 Hz, and wave a pulse width of 0.25 ms without bursts. The intensity was set on 10 to 25 mA (the highest intensity tolerated). After injection of fentanyl 1.5 μgkg^{-1} anaesthesia was induced by propofol and rocuronium was given to alleviate intubation. A canula was inserted into left radial artery to measure blood pressure continuously. Anesthesia was maintained by sevoflurane to achieve a Bispectral Index (BIS) between 40 and 50 throughout the whole operation. After induction the treating anesthesiologist was kept unaware to which group the patient was randomized. In patients of group A TENS therapy was continued intra-operatively and for 24 hours postoperatively. In patients of group B TENS therapy was stopped before positioning

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prone and restarted immediately after skin closure. In both groups the non-transparently covered TENS device was placed between patient´s thighs (Figure 1). The average Systolic Blood Pressure (SBP) and Heart Rate (HR) recorded after positioning prone and before skin incision recorded at five minutes interval was taken as the baseline reading. The anesthesiologist, unaware of patient´s group was told to administer fentanyl 1 $\mu g.kg^{-1}$ in case of increasing systolic blood pressure (SBP) and/or heart rate (HR) of more than 15% from baseline reading. A forced air warming blanket was used to keep body temperature over 36°C. Depending on the cause decline of systolic blood pressure below 80 mmHg was treated either with fluids or phenylephrine. A cell saver machine for intra-operative blood salvage was used to prevent a hemoglobin level less than 8 $mg.dl^{-1}$. 20 minutes before the expected end of skin closure piritramid 0.08 $mg.kg^{-1}$ and diclofenac 75 mg will be administered intravenously. Time from end of operation to extubation and time from extubation to first request for analgesics were recorded. The staff of the recovery unit and of the ordinary ward administered on demand the prescribed analgesics piritramid IV, paracetamol IV, diclofenac IV, metamizol IV and dexametason IV to achieve a VAS of less than 3 additionally to oral diclofenac, naproxen and tramadol up to the seventh postoperative day. The number of different analgesics which were given to the patient to achieve VAS <3 was noted in this study. Postoperative nausea and vomiting (PONV) and stomach ache were recorded until the same day.

Statistical Methods

Sample size computation

An a priori sample size computation was done based on following assumptions. The standard deviation of intra-operative amount of fentanyl $\mu g\ kg^{-1}\ min^{-1}$ was assumed to be 0.015 in both groups. Based on this assumption and in order to detect a clinical relevant difference of 0.015 (or more), the sample size for this study was set to be 24 in each group to find the aimed clinical relevant difference with a power of 90%. No drop-outs were assumed.

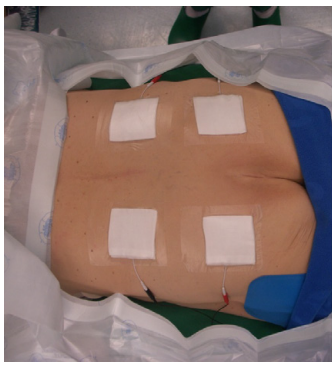

Figure 1: Four cutaneous electrode pads were positioned atthe dermatomal levels corresponding to the vertical skin.

Randomization

Randomization was done by using computer-generated random numbers based on Efron's method to achieve a balanced design.

Data analysis

Data consistency was checked and data were screened for outliers and normality by using quantile plots. Per-protocol-analyses were done. Fisher's Exact test and Pearson's Chi-Squared test and Wilcoxon-Mann-Whitney test were used to analyze cross tabulations. 95% Pearson-Clopper confidence intervals were computed for selected probabilities. Unpaired Student t-tests without the assumption of variance homogeneity were used to compare variables among both groups. The assumption of variance homogeneity was tested using Levene's test. 95% confidence intervals were computed for the true effect - the difference of means between both groups. Whisker plots with 95% confidence intervals were used to illustrate the results. No correction for multiple comparisons was done. All reported tests were two-sided and p-values less than 0.05 were considered as statistically significant. All statistical analyses in this report were performed by use of STATISTICA 10 (Hill, T. and Lewicki, P. Statistics: Methods and Applications. StatSoft, Tulsa, OK) and StatXact 10 (Cytel Software 2013, Cambridge MA, USA) and were done by one of the authors.

Results

All of the 48 enrolled patients finished the study. Concerning sex (P=0.38), height (P=0.91), weight (P=0.64), type of operation (P=1.0), and current intensity (P=0.27) the groups did not differ significantly. Variables influencing systolic blood pressure and heart rate showed no statistical significant difference: baseline heart rate (P=0.18), baseline systolic blood pressure (P=0.40), infused crystalloids (P=0.42), infused colloids (P=0.19), re-infused cell salvage (P=0.061), and urine output (P=0.018) (Table 1).

A pair-wise comparison of intra-operative fentanyl administration in the two groups showed either related to the total intra-operative amount (difference of means: 4.15 (CI 95%: 3.3-5.0), P<0.0000001, Figure 2) or related to amount per minute of operation´s duration (difference of means 0.020, (CI 95%: 0.013-0.026), P=0.0000004, Table 2, Figure 2) showed a statistical difference.

No statistical difference was found between both groups in time between end of operation and extubation (P=0.16, Table 3) and in time between extubation and the first request on analgesic.(P=0.67, Table 4

	Mean A	Mean B	Std.Dev. A	Std.Dev. B	Mean Difference	Confidence	Confidence	p
Height cm	172.0	171.7	9.6	9.1	0.29	-5.13	5.72	0.91
Weight Kg	83.4	81.4	17.0	11.6	1.96	-6.49	10.41	0.64
Base Line heart rate b/min	58.6	61.4	7.6	6.4	-2.79	-6.89	1.31	0.18
Base line systolic blood pressure mmhg	102.9	99.5	15.5	12.0	3.38	-4.66	11.41	0.40
Duration of op min	176.1	201.8	42.0	50.8	-25.67	-52.75	1.42	0.06
Infused crystalloids ml	2500.0	2645.8	531.6	699.1	-145.83	-506.68	215.01	0.42
Infused colloids ml	529.2	725.0	392.8	608.8	-195.83	-493.54	101.87	0.19
Reinfused cell savage ml	84.0	171.7	121.1	187.9	-87.8	-179.6	4.1	0.061
Urine output ml	420.8	350.4	206.4	147.3	70.4	-33.8	174.6	0.180

Table 1: Height, weight, base line heart rate, duration of operation infused colloids, reinfused cell salvage, and urine output by group.

	Mean A	Mean B	p	Valid N	Std.Dev.	Std.Dev.	Mean difference	Confidence	Confidence
Intraop.amount fentanyl µgkg^{-1}	3.34	7.49	<0.0000001	24	0.82	1.96	4.15	5.02	3.28
Intraop.amount fentanyl µgkg^{-1}min^{-1}	0.02	0.04	0.0000004	24	0.007	0.014	0.020	0.026	0.013

Table 2: Intraoperative amount of fentanyl by group.

	Mean A	Mean B	p	Std.Dev.	Std.Dev.	Mean 1	Confidence	Confidence
Time from extubation to first request on analgesic in minutes	72.1	67.1	0.67	44.6	34.4	5.00	-18.15	28.15

Table 3: Comparison of pain free time after extubation.

		Number of analgesics within 7 post-operative days	Number of analgesics within 7 post-operative days	Number of analgesics within 7 post-operative days	Number of analgesics within 7 post-operative days	Number of analgesics within 7 post-operative days	Number of analgesics within 7 post-operative days	
	Group A/B	**1**	**2**	**3**	**4**	**5**	**6**	**Row**
Count	**A**	2	2	7	8	5	0	24
Row%		8%	8%	29%	33%	21%	0%	
Count	**B**	0	2	9	8	4	1	24
Row%		0%	8%	38%	33%	17%	4%	
Count	**All groups**	2	4	16	16	9	1	48

P=0.74; Wilcoxon-Mann-Whitney test

Table 4: Quantity of different analgesics by group.

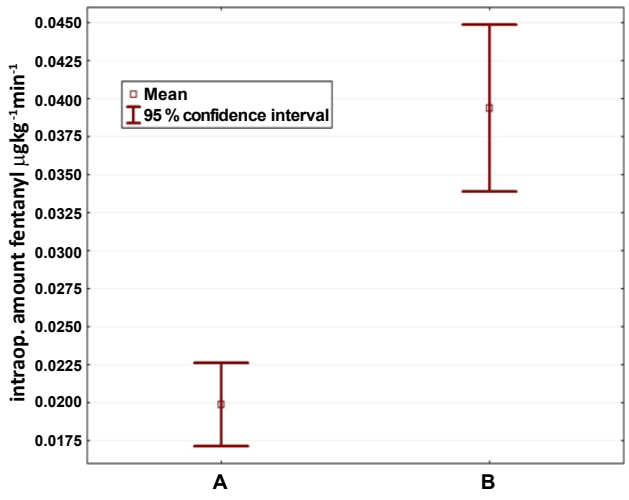

Figure 2: Total intraoperative fentanyl amount per group.

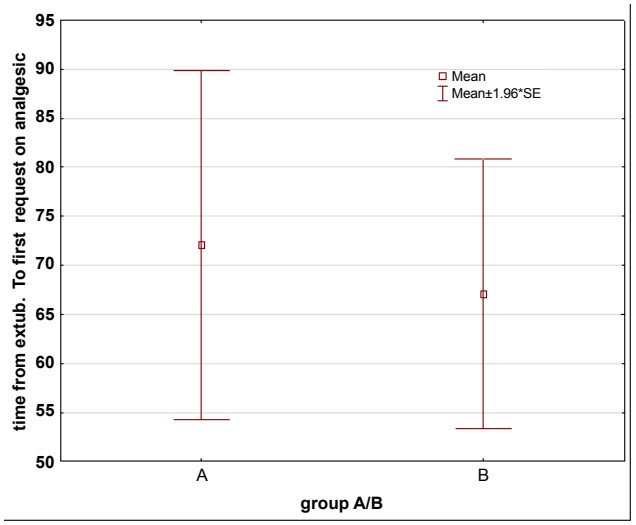

Figure 3: Time from extubation to first request on analgesic in minutes per group.

and Figure 3).

Comparison of analgesics administered up to the seventh postoperative day showed no statistical relevant difference between the groups (P=0.74, Table 4).

Postoperative stomach ache occurred in no patient. (P=1.0).

Regarding PONV no significant difference was found between the groups. (P=0.06) (Table 5).

Discussion

Our study shows that intra-operative TENS therapy reduces the intra-operative opioid demand in major spinal surgery. Furthermore the pain free time between end of anesthesia and first request on analgesics is not influenced by intra-operative TENS. These findings fit to previous studies, which evidenced the opioid sparing effect of TENS administered pre- and postoperatively [1,2,5]. We assume that all mechanisms of TENS, decrease of transmission in A-delta and C fibres, release of metenkaphaline and dynorphine, activation of the periaqueductal grey, release of ir-dynorphine, and increase of serotonin are still working under sevoflurane [7-11]. This goes with Sandin´s assumption that increase of BIS in patients treated with TENS under sevoflurane anesthesia is not caused by TENS but by epileptogenic activity due to sevoflurane [12]. Our study closes the gap of knowledge between TENS used preoperatively for relieve of chronic lower back pain and postoperatively for treatment of acute pain after major spinal surgery. The proofed opioid sparing effect of TENS may contribute to restrict intra-operative fentanyl treatment especially in patients, who suffer from obstructive sleep apnea syndrome to avoid postoperative bradypnea and desoxygenation [13]. Our finding contradicts the statement that TENS is nothing else than placebo [14,15].

Concerning the second part of our study the supposed

	Group A/B	Number of episodes of PONV	Number of episodes of PONV	Number of episodes of PONV	Row
		0	1	2	
Count	A	22	2	0	24
Row Percent		92%	8%	0%	
Count	B	16	7	1	24
Row Percent		67%	29%	4%	
Count	all groups	38	9	1	48

Wilcoxon-Mann-Whitney, P=0.06

Table 5: Quantity of postoperative nausea and vomiting by group.

postoperative analgesic sparing effect of TENS administered intra-operatively additionally to preincisional and to postoperative TENS could not be proved. This contradicts Inoue´s findings which showed a long lasting effect of intra-operative TENS regarding alleviation of thermal hyperalgesia in halothane anesthesized rats [16]. We were not able to treat patients with analgesics within seven days postoperatively per protocol. These analgesics were prescribed per intention to treat based on physician´s experience. This was the weakness of this study.

Although this study verifies the efficacy of intra-operative TENS in incisional and muscular pain further studies will be necessary to elucidate its effect on deep visceral pain caused by abdominal operations.

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