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The effect of remifentanil used during caesarean section on maternal hemodynamics and neonatal outcome – comparison of two dosing regimens

Ефекат примене ремифентанила током царског реза на хемоднамику породиље и неонатални исход – поређење два режима дозирања

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SUMMARY

Introduction/Objective To present and compare maternal and neonatal effects of two remifentanil dosing regimens, used during induction-delivery period of elective caesarean section in attempt to attenuate maternal cardiovascular response to surgical stress.

Methods Seventy-seven ASA I-II parturients were randomly divided in three groups and received: A-1 μg/kg remifentanil immediately before the induction to anesthesia followed by 0.15 μg/kg/min infusion, interrupted after skin incision; B – 1μg/kg remifentanil bolus immediately before the induction; C- no remifentanil until delivery. Hemodynamic (blood pressure, heart rate) and BIS changes after endotracheal intubation, skin incision, peritoneal incision and delivery, intraoperative anesthetics consumption and neonatal outcome have been compared between groups.

Results Hemodynamic response to intubation was significantly attenuated ($p<0.001$) in groups A and B compared to C. Hemodynamic response to skin incision, peritoneal incision and delivery was significantly attenuated in group A compared to B and C. Thiopentone dose in groups A and B was lower than in group C ($p<0.001$); sevoflurane and remifentanil consumption was less in group A compared to B and C ($p<0.001$). Apgar scores at 1st minute were ≥8 in all neonates, with no differences in neonatal heart rate, oxygen saturation and umbilical blood gas values (all within normal range).

Conclusion 1μg/kg remifentanil bolus followed by 0.15μg/kg/min stopped after skin incision, successfully blunted maternal hemodynamic stress response throughout whole induction-delivery period, reduced anesthetic consumption, without affecting neonatal outcome, so it can be considered effective as well as safe to use during induction-delivery period of caesarean section.

Keywords: anesthesia; obstetrical; remifentanil

САЖЕТАК

Увод/Циљ Приказати ефекте на породиљу и неонатус два режима дозирања ремифентанила примењеног током царског реза у периоду од увода у анестезију до порођаја, у циљу супримирања матерналног кардиоваскуларног одговора на хируршки стрес.

Методе Седамдесет седам породиља *ASA* I-II статуса је методом случајног избора подељено на три групе: *A* – 31 породиља је примила непосредно пре увода у анестезију 1 *μg/kg* болус ремифентанила, настављен инфузијом од 0,15 *μg/kg/min* прекинутом по начињеном резу коже; *B* – 27 породиља је примило непосредно пре увода у анестезију болус ремифентанила од 1 *μg/kg*; *C* – 19 породиља, које нису примиле ремифентанил пре рађања неонатуса. Упоређиване су промене хемодинамике и *BIS*-а у периоду од увода до екстракције, интраоперативна потрошња анестетика и ремифентанила и неонатални исход.

Резултати Хемодинамски одговор на интубацију је супримиран ($p<0,001$) у групама *A* и *B* у односу на *C*. Хемодинамски одговор на инцизију коже, инцизију перитонеума и на екстракцију је значајно супримиран у групи *A* у поређењу са *B* и *C*. Потрошња тиопентона је смањена ($p<0,001$) у групама *A* и *Б* у поређењу са групом *C*.

Потрошња севофлурана и ремифентанила је била мања у групи *A* у поређењу са групама *B* и *C* ($p<0,001$). Апгар скорови у првом минуту су код свих неонатуса били ≥8; није било разлика у фреквенци рада срца, сатурацији хемоглобина кисеоником и вредностима гасних анализа умбиликалне крви (све у референтним границама).

Закључак Болус ремифентанила 1 *μg/kg* апликован на уводу у анестезију и настављен инфузијом од 0,15 *μg/kg/min* до инцизије коже, успешно је супримирао матернални хемодинамски стресни одговор на хируршки стрес током целог периода од увода до екстракције, смањио потрошњу анестетика и аналгетика, при томе без штетних ефеката по неонатусе, па се може сматрати и ефикасним и сигурним режимом за коришћење од увода у анестезију до рађања неонатуса.

Кључне речи: анестезија, акушерска; ремифентанил

INTRODUCTION

When performing general anesthesia (GA) for caesarean delivery anesthetists can experience conflicting situation called “the dilemma of obstetrics anesthesia”: while it is important to ensure an appropriate maternal level of anesthesia, it is also necessary to avoid

neonatal respiratory depression caused by the medications that parturient receives [1,2]. Resolving the problem of neonatal well-being by reducing as much as possible doses of anesthetics given to the mother and omission of opioids during induction to delivery period (I-D), result in light anesthesia with increased risk of intraoperative awareness and exaggerated neuroendocrine stress response to surgical stress, possibly leading to severe cardio- and cerebrovascular complications [1-5]. Remifentanil, ultra-short acting synthetic opioid, could be the appropriate drug to use for the attenuation of maternal stress response during the I-D interval, where a brief but intense analgesia without prolonged effect is desirable [2,4,6-9]. Remifentanil has rapid onset of action (1-1.5 min), rapid redistribution and metabolism dependent on nonspecific tissue and plasma esterases; its context sensitive half time is 3 min; it crosses the placenta, but appears to be rapidly metabolized and redistributed in the fetus, leaving the small possibility of neonatal adverse effects [2,4,7,9,10].

In studies reporting the use of remifentanil during the I-D period dosing regimens were different; hemodynamic stability was often achieved at the expense of neonatal respiratory depression [2,4,6-9,11-16]. In present study we investigated the effects of two remifentanil dosing regimens, used during the I-D period, on maternal hemodynamics and neonatal outcome in attempt to find the best compromise between the attenuation of maternal stress response and avoidance of neonatal adverse effects.

METHODS

The study was institutionally approved and has Medical faculty of Niš Research Ethics Committee approval No 12-2466-1. Seventy seven ASA physical status I-II women with singleton term pregnancy, who were scheduled for elective caesarean section and have given written informed consent, were enrolled in this prospective, randomized controlled study, performed at Clinic of Gynecology and Obstetrics Niš, from April 2015 until July 2017. Exclusion criteria were maternal morbidity and signs of fetal compromise. All patients refused or had absolute/relative medical contraindications to regional anesthesia.

In the operating room patients were placed supine with left uterine displacement, standard monitoring - NIBP, electrocardiography, pulse oxymetry, capnography (using bed side monitor, model BSM-2301k, Nihon Kohden Corporation, Tokyo, Japan) and bispectral index (BIS) electroencephalogram (BIS-Vista monitoring system Norwood, Massachusetts,

USA) was initiated and two intravenous lines established, one for remifentanil infusion (using Perfusor fm B/Brown , Melsungen AG, Germany), the other for the administration of other medications and fluids.

Patients were randomly allocated (using envelope method) to one of the following groups: 1. A- 31 patient received 1μg/kg remifentanil bolus over 30 seconds immediately before the induction, followed by 0.15 μg/kg/min infusion that was stopped after the skin incision.

2. B- 27 patients received 1μg/kg remifentanil bolus over 30s immediately before the induction

3. C (control)- 19 patients did not receive remifentanil until delivery of the baby.

Anesthesia was induced with thiopentone, starting with 3 mg/kg, followed by additional 25 mg boluses until adequate dept of anesthesia has been reached (BIS values under 60, but not below 40); succinylcholine was administered in a dose 1.5 mg/kg. Anesthesia was maintained with 1-1.5% end-tidal sevoflurane and 50% nitrous oxide in oxygen. Further muscle relaxation has been provided with rocuronium 0.6 mg/kg. The lungs were mechanically ventilated to maintain end-tidal PCO_2 of 28-32 mmHg, with fresh gas flow of 6 l/min.

SAP, DAP, MAP (systolic, diastolic, main arterial pressure, respectively), HR (heart rate) and BIS were measured and recorded at basal time (T0) and 30 seconds after induction to anesthesia (T1), endotracheal intubation (T2), skin incision (T3), peritoneal incision (T4), delivery (T5) and also in 2 minutes intervals from the delivery until the end of operation.

After delivery, neonatologist blinded to group assignment assessed neonates and recorded the time to sustained respiration, Apgar score at 1^{st} and 5^{th} minute, neonatal heart rate (HR), SpO_2 and, if required, resuscitative measures (tactile stimulation, beg-mask ventilation, endotracheal intubation or naloxone administration). We took arterial and venous blood samples (in heparinized syringes) from a double-clamped umbilical cord, for blood gas analysis (using Gem Premier 3000 Blood Gas/ Electrolyte Analyzer, Model 5700, Instrumentation Laboratory Company, Bedford, Massachusetts, USA).

In the later course of the operation sevoflurane and remifentanil were titrated according to BIS values and presence/absence of signs of intraoperative surgical stress (autonomic, somatic, hemodynamic). Sevoflurane and nitrous oxide were discontinued at the moment of skin closure, residual neuromuscular block antagonized using neostigmine and atropine, and remifentanil infusion rate reduced to 0.07 μg/kg/min. The trachea was extubated when spontaneous respiratory rate reached >10 breaths/min, end- tidal CO_2<45 mmHg and the patient became responsive to verbal commands. Remifentanil infusion was then stopped. . The presence of intraoperative awareness was checked 2 and 24 hours after the operation by using Brisce questionnaire: What is the last thing you remember before you slept? What is the first thing you remember when you woke up? Do you remember anything between sleeping and waking up? Did you dream of anything during the sleep period of your operation? [5].

Our main goal was to compare between groups the remifentanil effect on changes of maternal hemodynamic values during I-D period and on neonatal outcome.

Our second goal was to study the influence of remifentanil on anesthetics consumption

Statistical analyses

The calculation of sample size showed that 15 patients per group would have 90% power with p<0.01 to detect a difference in SAP of 15 mmHg in response to intubation.

Statistical analysis was performed using SSPS statistic package, version 13. Normal distribution was evaluated with Kolmogorov-Smirnov test. Analysis of variance (ANOVA) was used for parameters comparison between three groups, with subsequent post hoc analysis. In cases of irregular data distribution Kruskal-Wallis test was utilized, with subsequent post hoc analysis with Mann Whitney U test. The Chi-square test was used to verify the relation between categorical variables. The statistic hypothesis was tested on the significance level for risk of α=0.05; the difference between samples was considered significant if p was <0.05.

RESULTS

Patient's characteristics and surgical details are summarized in Table1; no differences between groups have been observed.

The Tables 2-7 and Figure 1 represent serial hemodynamic values measured at T0 to T5. Baseline (Table 2) and postinductional values (Table 3) did not differ between groups except for SAP and HR (B vs C), but without clinical significance. After the intubation SAP, DAP, MAP and HR rose significantly in group C compared to A and B (Table 4).

After skin incision hemodynamic variables were still significantly higher in group C compared to A, but not compared to B – values in group B began to rise (Table 5).

After peritoneal incision significant difference in SAP, MAP and HR between groups A and C persisted. Significant difference in SAP, DAP and MAP between groups A and B also appeared (Table 6).

After delivery SAP and HR were still significantly higher in group C than in A and SAP and MAP significantly higher in B than in A (Table 7).

BIS values rose significantly after the intubation in all groups compared to preintubational values (from 46 to 66). In subsequent measurements BIS values were 58-67 and did not differ between groups.

Thiopentone dose used for induction in groups A and B was significantly lower than in C (Table 8). Sevoflurane consumption (Table 8) during I-D interval was significantly lower in group A compared to B and C, and lower in B compared to C. After the delivery until the end of the operation sevoflurane as well as remifentanil consumption was significantly lower in group A compared to B and C (Table 8).

During the operation there were no episodes of hypotension and bradycardia; blood loss and oxytocine consumption where in the average range, with no difference between groups. Maintenance of low remifentanil infusion after the end of surgery allowed smooth emergence from anesthesia without a delay in recovery – patients were extubated within 2-3 minutes after surgery. None of them complained of intraoperaitve awareness in an interview performed 2 and again 24h after the operation.

Neonatal outcome is presented in Table 9, with no differences between groups in any of estimated variables: 77,4% of neonates in group A, 81,5 % in group B and 73,7% in group C started breathing immediately after delivery. The rest of them needed only brief tactile stimulation (12.9%, 7.4%, 15.8% respectively) or bag mask ventilation (9.7%, 11.1%, 10.5% respectively) (χ_{kw}^2 =4.365; p=0.359%). Umbilical blood gas values were within normal range and did not demonstrate significant differences between groups (Table 10).

DISCUSSION

During the past two decades numerous authors reported the use of remifentanil during I-D period of caesarean section in order to attenuate maternal stress response to endotracheal intubation and surgical incision. Van de Velde [9], using 0.5 μg/kg remifentanil bolus followed by 0.2 μg/kg/min infusion until delivery, managed to attenuate maternal stress response, but brief respiratory depression was present in half of the newborns. Kee [7], using 1 μg/kg remifentanil bolus, provided attenuation of maternal BP and HR response, but 10% neonates needed naloxone. Behdad [11] accomplished reduction of SAP and DAP, but not HR, with a remifentanil bolus of 0.5 μg/kg, without neonatal respiratory depression. Draisci [6], using 0.5 μg/kg bolus plus 0.15 μg/kg/min remifentanil infusion, interrupted at the moment of peritoneal incision, observed partially obtunded neuroendocrine response to surgery, with lower Apgar scores at 1st minute, respiratory depression or required endotracheal intubation in 14% of neonates. It seems that initial 0.5 μg/kg bolus might have been insufficient to accomplish the attenuation of maternal stress response and, on the other hand, that remifentanil infusion, prolonged until peritoneal incision, caused neonatal respiratory depression (the time interval between peritoneal incision and delivery was only 2.8 min) [6]. Noskova [12], using 1μg/kg remifentanil, observed higher incidence in lower Apgar scores at first minute compared to control, possibly because of short I-D interval (4 min). Yoo [13] administered 1 μg/kg remifentanil and effectively attenuated hemodynamic response to intubation, but at the expense of maternal hypotension and greater need for neonatal resuscitative measures in the first minutes after delivery. Reduced catecholamine response compared to control was noted at the intubation, but not at delivery, so a single remifentanil dose did not manage to prevent catecholamine rise during the whole period. Hu et al measured umbilical arterial and venous remifentanil concentration at delivery and

proved rapid remifentanil metabolism in fetal circulation, but emphasized that it can be affected by the differences in dosing regimens [10].

Based on reported data, we created a dosing regimen of 1μg/kg remifentanil bolus given immediately before the induction, followed by 0.15 μg/kg infusion stopped after skin incision, in attempt to establish both safe and effective regimen that can be used in obstetric clinical practice during I-D period of caesarean section, and compared its maternal and neonatal effects with regimens of sole 1μg/kg remifentanil bolus and with remifentanil-free control (traditionally performed anesthesia during I-D period). We hypothesized that remifentanil infusion would provide hemodynamic stability during both endotracheal intubation and surgical incision. Earlier infusion interruption than in previous studies (after skin incision instead of at peritoneal incision or even at delivery) should leave enough time for remifentanil redistribution and metabolism in fetal circulation, thus diminishing the probability of neonatal respiratory depression.

Hemodynamic variables measured after the intubation in groups A and B were significantly lower than in group C. So both regimens attenuated cardiovascular response to endotracheal intubation, which is in accordance with previous reports [4,9,12-16]. The next measurement, performed after skin incision, already showed the difference: the significant difference in SAP, DAP, MAP and HR between groups B and C disappeared, but persisted in A compared to C. At the time of peritoneal incision and at the delivery measured hemodynamic variables were significantly lower in group A compared to both C and B group. It appears that remifentanil bolus plus infusion regimen (group A) effectively blunted cardiovascular response during entire I-D period whereas sole remifentanil bolus (group B), was not effective enough to provide hemodynamic stability in a period following intubation.

Synergism between remifentanil and anesthetics has been described in numerous studies [17-19]. Our results are in agreement with those data. Thiopentone dose was significantly lower in remifentanil groups than in control. Prolonged remifentanil infusion in group A provided significantly diminished sevoflurane requirements during I-D period, and also during the rest of operation. We believe that adequate analgesia, achieved in group A before the start of noxious stimulation and kept during surgical incision (preemptive approach), caused lower remifentanil consumption in a period from delivery until the end of the operation.

In our research remifentanil administration did not affect BIS values, which is in agreement with other reports [5,6,13,]. BIS values are the reflection of hypnotic drugs action on cerebral cortex, whereas opioids act primarily on subcortical level, and their sedative effects cannot be detected by BIS monitoring. When appropriate BIS level during remifentanil/sevoflurane-based anesthesia is considered, it is emphasized that attempts to maintain the target BIS of 40-60 would lead to an excessively deep level of anesthesia and 50-150% higher end-tidal sevoflurane concentration than actually needed [20]. BIS values in our research remained 58-68 throughout the whole operation. Nevertheless, even with reduced anesthetic consumption in remifentanil groups (especially in group A), the achieved hypnotic state was adequate, estimated by the absence of somatic, autonomic and hemodynamic responses to noxious stimuli, but also by the absence of explicit memory of operation period.

Our results did not demonstrate negative remifentanil effects on neonatal outcome. Opposite to the results from mentioned studies [6,7,9,12,13] all neonatal Apgar scores at 1st minute were $\geq$ 8; oxygen saturation and HR were within normal range and without differences between groups. Majority of neonates started breathing within few seconds after delivery; the rest of them needed only brief (up to one minute) tactile stimulation or beg mask ventilation. Similarly to other studies [6,7,12,13], we did not find differences in umbilical blood gas analysis, and all values were within normal range [21,22].

CONCLUSION

Our dosing regimen of remifentanil bolus given at the induction, followed by infusion interrupted after skin incision, effectively prevented significant rise in BP and HR during entire I-D period without compromising neonatal wellbeing and significantly diminished anesthetics consumption, so it can be considered effective as well as safe to use during induction-delivery period of caesarean section.

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Table 1. Parturients characteristics and surgical details

Characteristics	Group A n=31	Group B n=27	Group C n=19	F	p
Age (years) mean ± SD	31.74±4.46	31,22±5.22	30.89±1.04	0.202	0.818
Gestation (weeks) mean ± SD	38.94±0.72	39.04±1.09	39.47±0.90	2.162	0.122
Weight (kg) mean ± SD	77.19±13.27	82.37±9.52	79.26±11.84	2.216	0.918
I-D interval (minutes) mean ± SD	11.22±1.67	10.04±1.81	10.37±1.71	3.639	0.131
U-D interval (seconds) mean ± SD	57.39±18.93	58.00±14.92	60.42±22.25	0.165	0.848

F – ANOVA; I-D interval– induction–delivery interval; U-D interval – uterine incision – delivery interval

Table 2. Hemodynamic variables at T_0 (basal)

Variables	Group A n=31	Group B n=27	Group C n=19	F	p
SAP (mmHg) mean ±SD	132.42±15.05	132.19±10.53	131.74±10.08	0.018	0.982
DAP (mmHg) mean ±SD	83.90±11.61	83.81±9.78	77.63±12.07	2.246	0.113
MAP (mmHg) mean ±SD	100.48±14.08	100.11±9.28	96.47±11.58	0.818	0.445
HR (bps) mean ±SD	101.48±16.01	98.18±13.49	98.84±14.62	0.397	0.674

F – ANOVA; SAP – systolic arterial pressure; DAP – diastolic arterial pressure; MAP – main arterial pressure; HR – heart rate; bps – beats per minute

Table 3. Hemodynamic variables at T_1 (after induction)

Variables	Group A n=31	Group B n=27	Group C n=19	F	p	Post Hoc
SAP (mmHg) mean ±SD	110.03±14.16	107.14±12.59	116.89±9.93	3.364	0.004	c
DAP (mmHg) mean ±SD	67.93±10.99	71.28±10.51	75.31±14.60	2.313	0.106	
MAP (mmHg) mean ±SD	85.80±13.21	84.22±13.01	91.05±13.17	1.590	0.211	
HR (bps) mean ±SD	97.06±9.88	94.70±9.96	103.15±11.64	3.819	0.026	c

F-ANOVA; c (B *vs.* C); SAP – systolic arterial pressure; DAP – diastolic arterial pressure; MAP – main arterial pressure; HR – heart rate; bps – beats per minute

Table 4. Hemodynamic variables at T_2 (after intubation)

Variables	Group A n=31	Group B n=27	Group C n=19	F	p	Post Hoc
SAP (mmHg) mean ±SD	119.61±13.95	121.89±13.82	149.00±14.50	29.302	<0.001	b. c
DAP (mmHg) mean ±SD	75.71±12.93	81.56±10.65	98.21±15.01	18.750	<0.001	b. c
MAP (mmHg) mean ±SD	91.06±12.60	96.70±12.49	116.68±14.76	23.292	<0.001	b. c
HR (bps) mean ±SD	100.68±8.92	102.41±11.02	109.68±9.61	5.165	0.008	b. c

F – ANOVA; a (A *vs.* B); b (A *vs.* C); c (B *vs.* C); F-ANOVA; c (B *vs.* C); SAP – systolic arterial pressure; DAP – diastolic arterial pressure; MAP – main arterial pressure; HR – heart rate; bps – beats per minute

Table 5. Hemodynamic variables at T_3 (skin incision)

Variables	Group A n=31	Group B n=27	Group C n=19	F	p	Post Hoc
SAP (mmHg) mean ±SD	119.06±13.12	124.93±13.09	132.12±8.17	7.948	0.001	b
DAP (mmHg) mean ±SD	75.38±11.74	84.18±10.97	86.84±12.67	6.894	0.002	a. b
MAP (mmHg) mean ±SD	92.83±12.21	99.19±10.81	106.63±10.12	8.951	<0.001	b
HR (bps) mean ±SD	98.81±14.32	102.44±1.89	110.10±11.89	4.520	0.014	b

F – ANOVA; a (A *vs*. B); b (A *vs*. C). c (B *vs*. C); SAP – systolic arterial pressure (mmHg). DAP – diastolic arterial pressure (mmHg). MAP – main arterial pressure (mmHg). HR – heart rate; bps – beats per minute

Table 6. Hemodynamic variables at T_4 (peritoneal incision)

Variables	Group A n=31	Group B n=27	Group C n=19	F	p	Post Hoc
SAP (mmHg) mean ±SD	118.39±14.28	129.18±15.29	128.94±11.38	5.401	0.006	a. b
DAP (mmHg) mean ±SD	74.65±11.58	84.81±12.56	80.05±13.54	4.855	0.010	a
MAP (mmHg) mean ±SD	91.93±12.84	101.52±14.12	101.05±9.89	5.087	0.009	a. b
HR (bps) mean ±SD	96.61±12.76	100.96±12.76	105.89±10.63	3.410	0.038	b

F – ANOVA; a (A *vs.* B). b (A *vs.* C). c (B *vs.* C); SAP – systolic arterial pressure DAP – diastolic arterial pressure; MAP – main arterial pressure; HR – heart rate; bps – beats per minute

Table 7. Hemodynamic variables at T_5 (delivery)

Variables	Group A n=31	Group B n=27	Group C n=19	F	p	Post Hoc
SAP (mmHg) mean ±SD	116.06±13.93	125.52±9.08	124.31±9.26	5.843	0.004	a. b
DAP (mmHg) mean ±SD	68.55±9.99	76.29±12.82	73.05±16.55	2.663	0.076	
MAP (mmHg) mean ±SD	86.52±11.93	97.37±12.20	94.53±13.53	5.906	0.004	a
HR (bps) mean ±SD	91.61±11.59	93.11±11.59	100.95±10.88	3.619	0.032	b

F – ANOVA; a (A vs. B); b (A *vs*. C); c (B *vs*. C); SAP – systolic arterial pressure; DAP – diastolic arterial pressure; MAP – main arterial pressure; HR – heart rate; bps – beats per minute

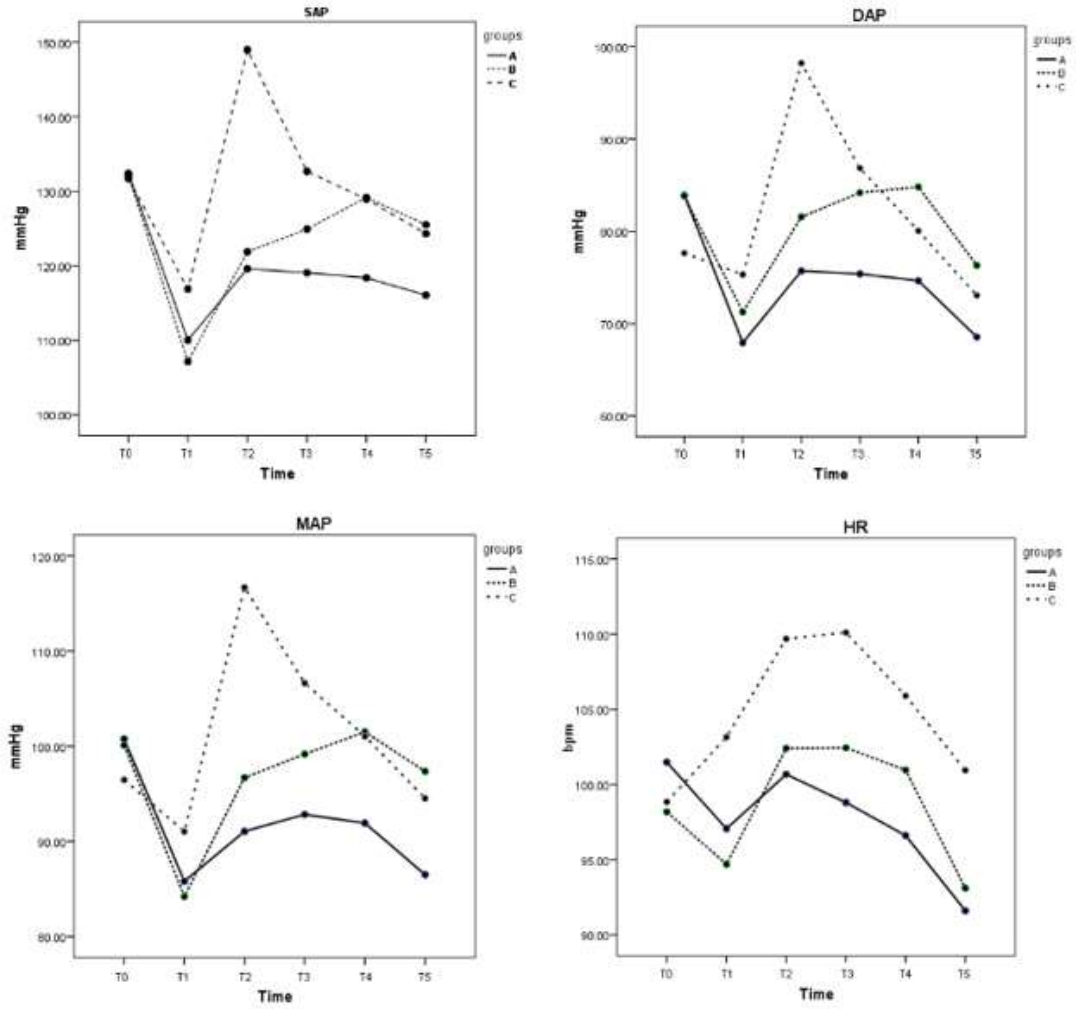

Figure 1. Serial systolic, diastolic, main arterial pressure and heart rate measurements – from T0 to T5

SAP – systolic arterial pressure; DAP – diastolic arterial pressure; MAP – main arterial pressure; HR – heart rate; T0 – basal values; T1 – induction of anesthesia; T2 – intubation; T3 – skin incision; T4 – peritoneal incision; T5 – delivery; group A – remifentanil bolus + infusion; group B – remifentanil bolus; group C – control

Table 8. Consumption of anesthetics

	Group A n =31	**Group B n=27**	**Group C n=19**	**χ_{KW}^2/ F***	**p**	**Post Hoc**
Thiopentone (mg/kg) at induction mean ±SD	4.74±0.64	4.72±0.62	5.63±0.72	13.495*	<0.001	b. c
Remifentanil consumption: D –end (µg/kg/min) mean ±SD	0.14±0.02	0.17±0.03	0.17±0.05	15.662	<0.001	a. b
Sevo consumption I-D (vol%) mean ±SD	1.29±0.24	1.50±0.00	1.59±0.17	27.890	<0.001	a. b. c
Sevo consumption D-end (vol%) mean ±SD	0.89±0.10	0.97±0.10	1.01±0.15	11.148	0.004	a. b

F – ANOVA; χ_{KW}^2 – Kruskal–Wallis test; a – A *vs*. B; b – A *vs*. C; c – B *vs*. C;

Remifentanil consumption: D-end (µg/kg/min) – remifentanil consumption from the delivery of baby until the end of operation in µg/kg/min; Sevo consumption I-D (vol%) – consumption of sevoflurane during induction – delivery period in vol%; Sevo consumption D-end (vol%) – consumption of sevoflurane from the delivery of baby to the end of the operation in vol%

Table 9. Newborns' characteristics

Characteristics	Group A n=31	Group B n=27	Group C n=19	χ_{KW}^2 / F*	p
Ap^1 mean±SD	8.81±0.55	8.81±0.48	8.63±0.49	2.969	0.227
Ap^5 mean±SD	9.03±0.31	8.93±0.26	8.89±0.32	2.972	0.226
SpO_2 (%) mean±SD	95.07±3.37	95.72±2.21	94.61±3.33	3.953	0.307
HR(bpm) mean±SD	141.48±9.93	138.13±14.35	140.50±12.51	3.423*	0.098

F – ANOVA; χ_{KW}^2- Kruskal-Wallis test; Ap^1 – Apgar score in 1st minute; Ap^5 – Apgar score in 5th minute; SpO_2 – hemoglobin oxygen saturation; HR – heart rate; bps – beats per minute

Table 10. Umbilical blood gas values

Gas values	Group A n=31	Group B n=27	Group C n=19	χ_{KW}^2 / F*	p
venous pH mean±SD	7.30±0.02	7.32±0.03	7.32±0.03	3.879	0.144
venous BD mmol/l mean±SD	5.06±2.00	4.07±1.61	5.08±1.38	2.757*	0.070
venous lactate (mmol/l) mean±SD	1.28±0.24	1.31±0.25	1.21±0.21	0.836*	0.438
arterial pH mean±SD	7.27±0.02	7.28±0.02	7.28±0.08	2.162	0.339
arterialBD (mmol/l) mean±SD	4.19±2.20	4.27±1.66	4.41±1.14	0.082*	0.921
arterial lactate (mmol/l) mean±SD	1.30±0.33	1.30±0.36	1.39±0.27	0.836*	0.438

F – ANOVA; χ_{KW}^2 – Kruskal–Wallis test

