X TÜRK ALMAN JİNEKOLOJİ KONGRESİ

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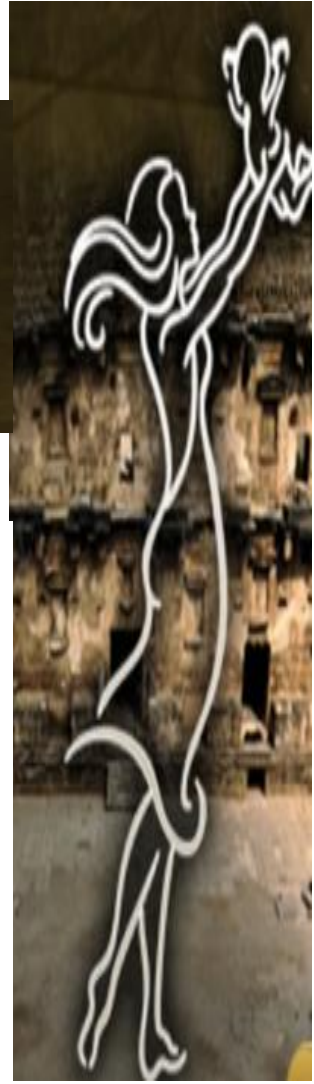

The impact of route of anesthesia on maternal and fetal ischemia modified albumin levels at cesarean section: a prospective randomized study

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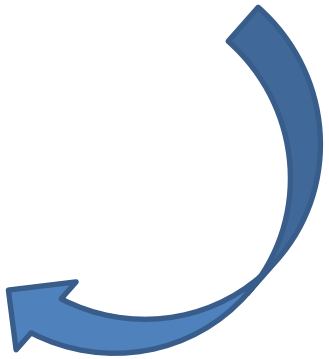
Ufuk University Faculty of Medicine
Obstetrics and Gynecology Department

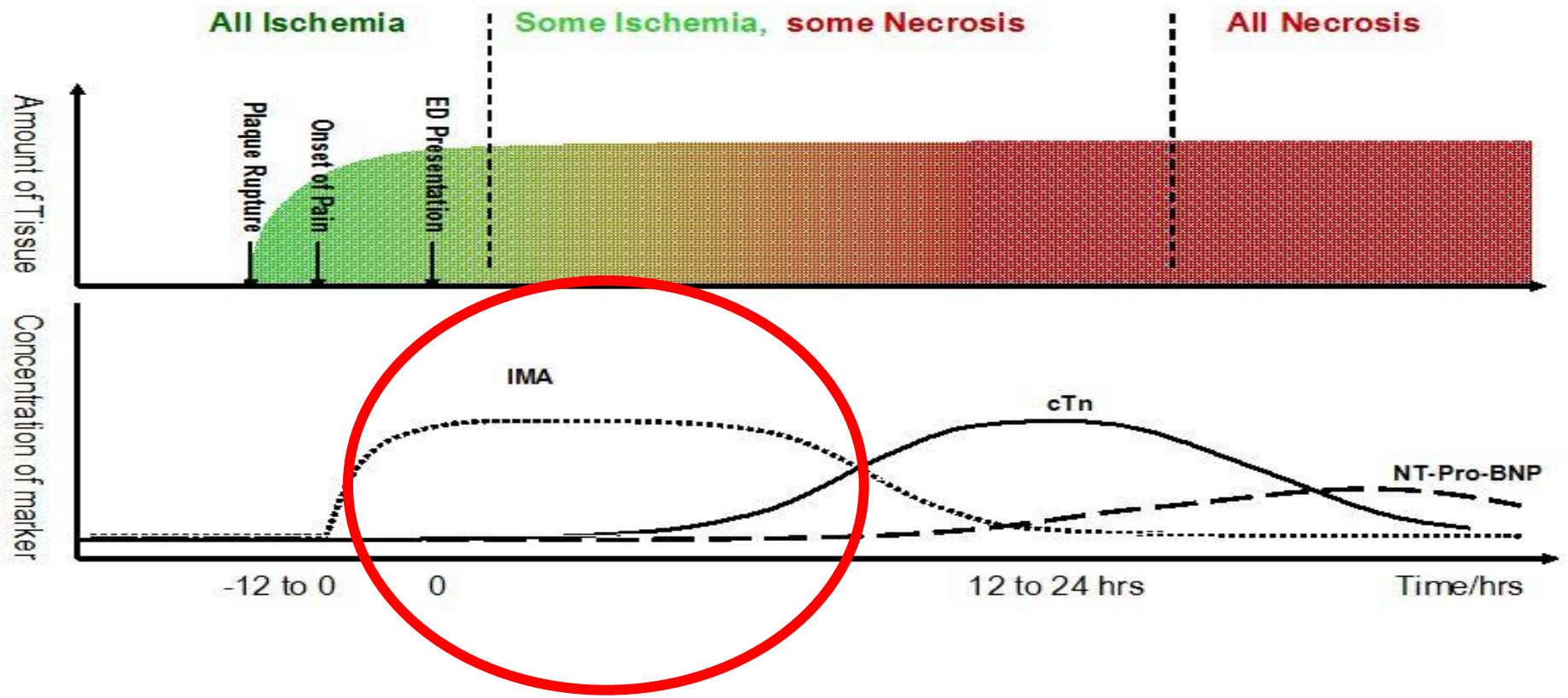
Ischemia Modified Albumin (IMA)

- During ischemia, N-terminus of albumin is altered; probably due to free-radical damage.

- This damage results with a new albumin which can not bi COBALT.

Ischemia Modified Albumin





Kinetic release of Ischemia modified albumin (IMA, dotted line) and other cardiac markers, cardiac troponin (cTn, solid line) and natriuretic peptide (NTproBNP, dashed line) [bottom panel], in relation to extent and timing of tissue damage [top panel].

D.C. Gaze, Biomarkers of Cardiac Ischemia

Laboratory Medicine

Update on Cardiac Biomarkers

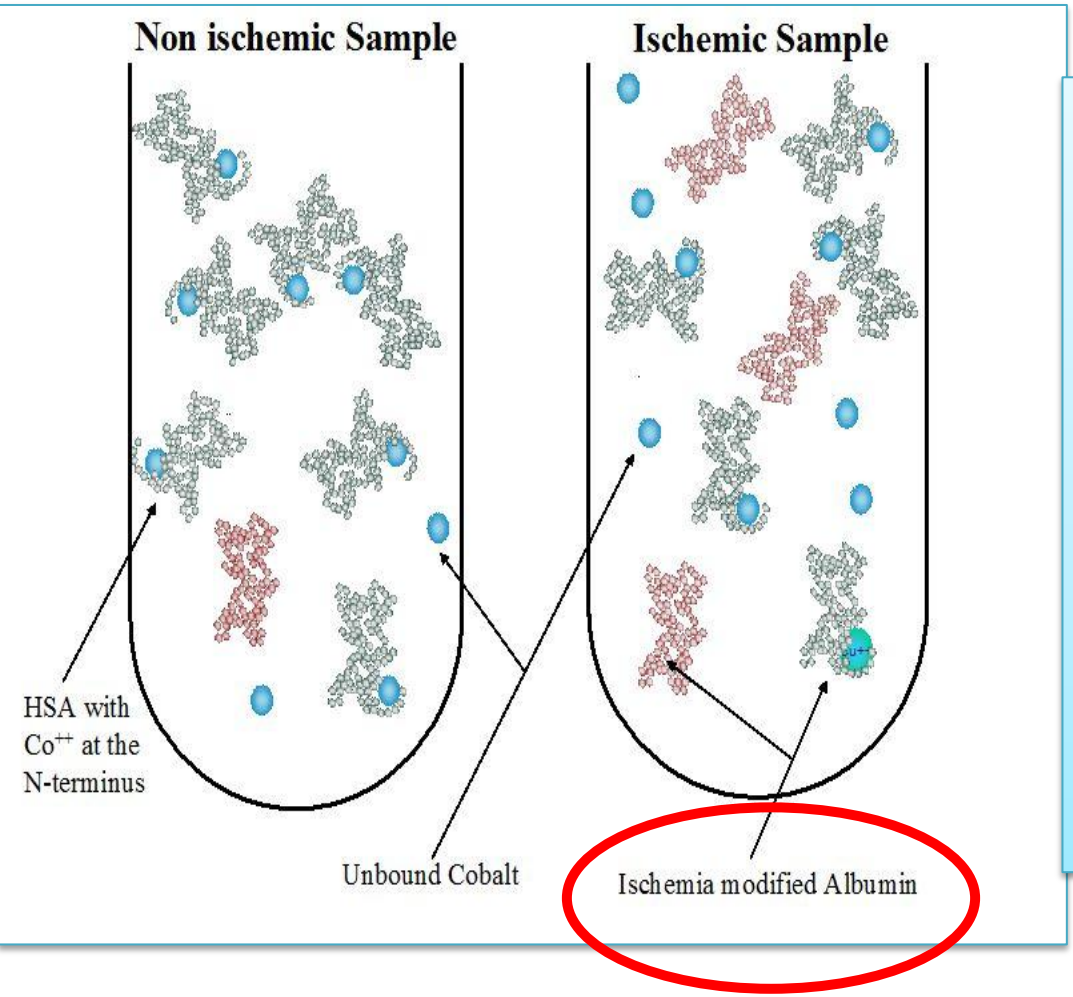
Eileen Carreiro-Lewandowski, MS, CLS(NCA) | Disclosures

Lab Med. 2006;37(10):598-605.

Markers of Ischemia

To date, only ischemia modified albumin (IMA) is approved by the FDA, using the albumin cobalt binding test (ACB), for assessment of myocardial ischemia. It was determined that an alteration in the N-terminus end of human serum albumin (HSA) occurs to a greater extent in patients experiencing ischemia. This damage is most likely due to damage caused by oxidative free radicals prevalent during ischemic events, and as a result, HSA demonstrates altered binding of trace metals resulting in IMA. There are 2 forms of IMA one in which HSA binds mostly copper, and a second form in which the damage to the N-terminus prevents metal binding. Patients without

IMA Measurement?



Albumin Cobalt Binding (ACB) assay:

A known amount of $CoCl_2$ is added to a serum sample.

DTT is added which binds unbound Co^{++}causing a colorimetric change read spectrophotometrically.

High IMA levels

- Carbon monoxide poisoning
- Congestive cardiac failure
- Chronic kidney disease
- Deep vein thrombosis
- Diabetes Mellitus
- Hypercholesterolemia
- Intermittent claudication
- Ischemic bowel
- Liver cirrhosis
- Neural tube defects

- Pleural effusion
- Polycystic ovary syndrome
- Polycythemia vera
- Pulmonary embolism
- Skeletal muscle ischemia
- Stroke
- β-thalassemia
- Testicular torsion
- Obesity

Gaze DC, Biomarkers of Cardiac ischemia

IMA in 'OB&GYN'

- **GYNECOLOGY**
  - **PCOS**
  - **Endometriosis**
  - **Laparoskopi**
  - **Uterine artery embolisation for myoma uteri**
- **OBTETRICS**
  - **IUGR**
  - **Preeclampsia**
  - **Habitual Abortus**
  - **Route of Delivery**

IMA in Obstetrics

European Journal of Obstetrics & Gynecology and Reproductive Biology 170 (2013) 348–351

Contents lists available at SciVerse ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Ischemia-modified albumin in pregnancy

Alberto Rossi [a], Nadia Bortolotti [b], Sara Vescovo [b], Irene Romanello [a,*], Leonardo Forzano [a], Ambrogio Pietro Londero [a], Guido Ambrosini [c], Diego Marchesoni [a], Francesco Curcio [b]

[a] *Obstetrics and Gynecology Department, University Hospital of Udine, Udine, Italy*
[b] *Clinical Analysis Institute, University Hospital of Udine, Udine, Italy*
[c] *Department of Obstetrics and Gynecology, University of Padua, Italy*

IMA levels in first trimester of pregnancies ending up with SGA fetuses, are higher than AGA fetuses.

Rossi et al, 2013

IMA in Obstetrics

European Journal of Obstetrics & Gynecology and Reproductive Biology 155 (2011) 209–212

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Assessment of ischemia-modified albumin level in patients with recurrent pregnancy loss during the first trimester

Suna Özdemir[a,*], Aysel Kıyıcı[b], Osman Balci[a], Halime Göktepe[a], Hümeyra Çiçekler[b], Çetin Çelik[a]

When compared to control pregnant subjects in first trimester, pregnant women with a history of 2 or more previous miscarriages have higher levels of IMA.

Ozdemir et al, 2011

IMA in Obstetrics

The Journal of Maternal-Fetal and Neonatal Medicine, March 2011; 24(3): 418–421

informa
healthcare

Ischemia-modified albumin as an oxidative stress marker in preeclampsia

YUSUF ÜSTÜN[1], YAPRAK ENGIN-ÜSTÜN[1], ÖZLEM ÖZTÜRK[2], IBRAHIM ALANBAY[3], & HALIL YAMAN[2]

[1]*Department of Obstetrics and Gynecology, School of Medicine, Inonu University, Malatya, Turkey,* [2]*Department of Biochemistry, Gulhane Military Medical Academy, Ankara, Turkey, and* [3]*Department of Obstetrics and Gynecology, Gulhane Military Medical Academy, Ankara, Turkey*

IMA levels at the time of diagnosis of preeclampsia are higher than control group.

IMA with a cut-off point of 0.31 identified women with preeclampsia with sensitivity 80% and spesificity 77%.

Ustun et al, 2011

IMA in Obstetrics

Available online at www.sciencedirect.com

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Clinica Chimica Acta 362 (2005) 155–160

ELSEVIER

www.elsevier.com/locate/clinchim

Ischemia-modified albumin levels in cord blood: A case-control study in uncomplicated and complicated deliveries

Alejandro Gugliucci [a,*], Ricardo Hermo [b], Carolina Monroy [a], Masahide Numaguchi [c], Satoshi Kimura [d]

IMA levels at cord blood of newborns from complicated deliveries are higher than uneventful ones.

Gugliucci et al, 2005

IMA in Obstetrics

The Journal of Maternal-Fetal and Neonatal Medicine, 2013; 26(5): 528–531

ISSN 1476-7058 print/ISSN 1476-4954 online
DOI: 10.3109/14767058.2012.743519

informa
healthcare

Maternal and umbilical cord ischemia-modified albumin levels in nonreassuring fetal heart rate tracings regarding the mode of delivery

Gamze S. Caglar[1], Yasemin Tasci[2], Umit Goktolga[2], Efser Oztas[1], Recai Pabuccu[1], Elif D. Ozdemir[1] & Rabia Seker[3]

[1]Ufuk University School of Medicine, Department of Obstetrics and Gynecology, Ankara, Turkey, [2]Ministry of Health, Etlik Zübeyde Hanım Womens Health Research Hospital, Department of Obstetrics and Gynecology, Ankara, Turkey, and [3]Ufuk University School of Medicine, Department of Biochemistry, Ankara, Turkey

Cord Blood IMA levels are higher in C/S group (Fetal distress or repeat C/S) compared to vaginal delivery.

Cord blood IMA levels are negatively correlated with 1st minute Apgar score.

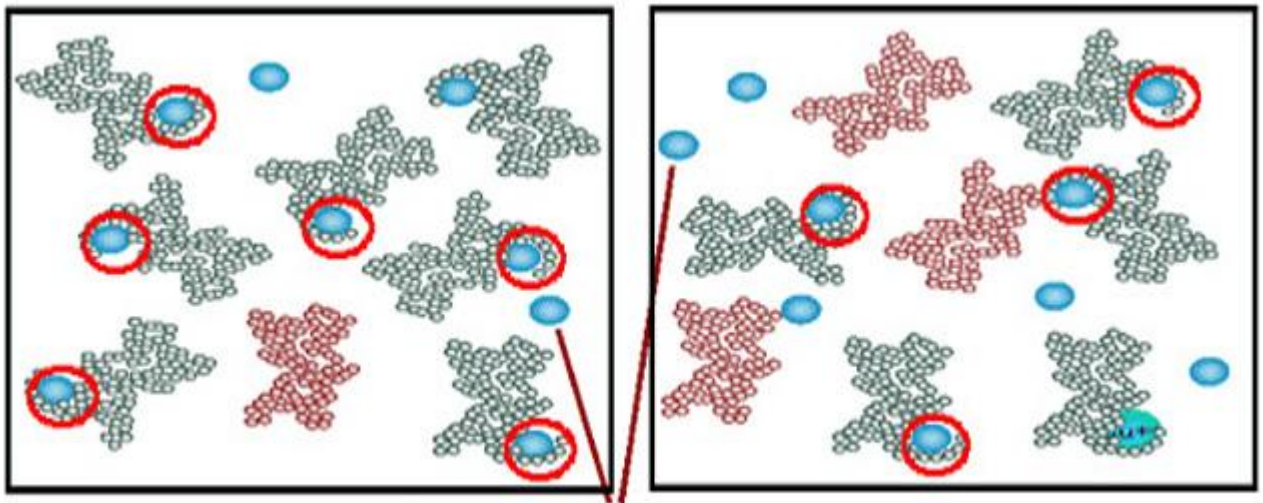
GS Caglar, 2013

Does route of anesthesia during cesarean section have an effect on maternal and cord blood IMA levels?

The impact of route of anesthesia on maternal and fetal ischemia modified albumin levels at cesarean section: a prospective randomized study

Aim:

- Does Route of anesthesia (regional or general) has an impact on maternal and fetal IMA levels?



Materials and Methods

- Prospective Randomised Study
- September 2011- July 2012,
- University Hospital.

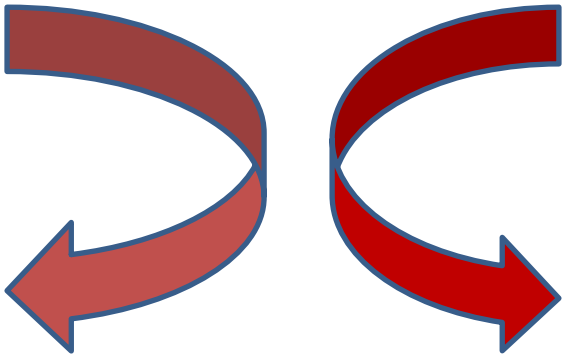
- N=72, Term gestation 37 -40 completed weeks.
- Cesarean section indication;
  - Previous cesarean section
  - Fetal malpresentation.

Materials and Methods

Exclusion Criteria;

- Complicated pregnancies,
- History of maternal cardiac symptoms,
- Smokers and alcohol consumers,
- Cases with abnormal albumin levels,
  (< 3.5 g/dL and > 5.5 g/dL),
- Multiple pregnancies,
- Contraindications of neuroaxial anesthesia.

37-40 week pregnant subjects
Cesarean section
N=72



General anesthesia
N=35

Regional anesthesia
N=37

Materials and Methods

Anesthesia

Operating room;

ECG, blood pressure, oxygen saturation (SpO2), and pulse rate.

2 L/min O2 inhalation by nasal cannulation.

Materials and Methods

- *General anesthesia;* 2–3 mg/kg propofol, 0.6 mg/kg rocuronium infusion & maintained by 50% O2–50% N2O, 1%–1.5% sevoflurane.

- *Regional anesthesia (Spinal);* 2 mL 0.5% hyperbaric bupivacaine was administered through L 2–3 or L 3–4 intervertebral space by a 25-gauge spinal needle.

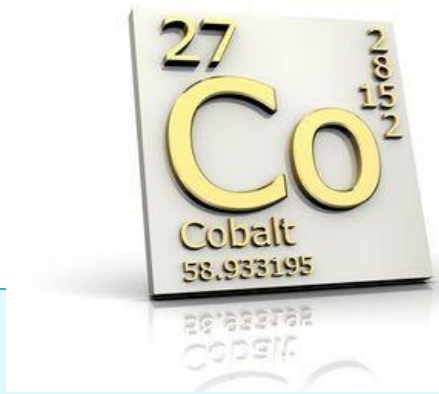
Materials and Methods

Samples;

- Maternal venous blood samples were taken at the 10th minute of induction.

- Cord blood was collected immediately after the delivery for umbilical cord acid base analyses, and an extra umbilical cord blood sample was taken for the analysis of fetal IMA.

Materials and Methods



- IMA concentrations were analyzed by colorimetric method in a spectrophotometer.
- Levels of IMA were given in Absorbance Units (ABSU).


150
120
90
60
30
0
200
150
100
50
0

Parameters	General anesthesia (n=35)	Regional anesthesia (n=37)	P-value
Age (years)			
Mean±SD	30.17±5.31	28.10±4.68	0.084
Gravidity			
Median (min–max)	2 (1–6)	2 (1–4)	0.087
Parity			
Median (min–max)	0 (0–4)	0 (0–2)	0.773
Gestational age at birth (weeks)			
Mean±SD	38.5±1.1	38.6±0.9	0.497
Time required for anesthesia[a] (min)			
Mean±SD	1.81±0.96	2.44±1.42	0.037[b]
Incision to delivery interval (min)			
Median (min–max)	2.5 (0–12)	3 (0–6)	0.121
Maternal IMA levels (ABSU)			
Mean±SD			
Fetal IMA levels (ABSU)			
Mean±SD			
Umbilical cord acid base parame			
pH			
Mean±SD	7.31±0.04	7.33±0.06	0.330
pO_2			
Mean±SD	17.48±8.40	17.21±6.70	0.881
pCO_2			
Mean±SD	51.97±6.65	50.51±8.43	0.420
BE			
Median (min–max)	−0.41(−5.5–2.8)	0.2 (−11.8–4.7)	0.575
Lactate			
Mean±SD	1.47±0.61	1.68±1.04	0.483

Significantly longer time required for anesthesia in Regional anesthesia group.

[a]Induction period in general anesthesia, time for regional anesthesia. [b]P<0.05. SD=standard deviation, IMA=ischemia modified albumin, ABSU=absorbance unit, pO_2=partial oxygen pressure, pCO_2=partial carbon dioxide pressure, BE=base excess.

Parameters	General anesthesia (n=35)	Regional anesthesia (n=37)	P-value
Age (years)			
Mean±SD	30.17±5.31	28.10±4.68	0.084
Gravidity			
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Parity			
Median (min–max)	0 (0–4)	0 (0–2)	0.773
Gestational age at			
Mean±SD			0.497
Time required for a			
Mean±SD			0.037[b]
Incision to delivery			
Median (min–ma			0.121
Maternal IMA level			
Mean±SD	0.99±0.19	0.80±0.27	0.001[b]
Fetal IMA levels (ABSU)			
Mean±SD	1.00±0.21	0.70±0.26	<0.001[b]
Umbilical cord acid base parameters			
pH			
Mean±SD	7.31±0.04	7.33±0.06	0.330
pO_2			
Mean±SD	17.48±8.40	17.21±6.70	0.881
pCO_2			
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Lactate			
Mean±SD	1.47±0.61	1.68±1.04	0.483

Umbilical cord acid- base parameters were similar between general and regional anesthesia groups.

[a]Induction period in general anesthesia, time for regional anesthesia. [b]P<0.05. SD=standard deviation, IMA=ischemia modified albumin, ABSU=absorbance unit, pO_2=partial oxygen pressure, pCO_2=partial carbon dioxide pressure, BE=base excess.

Parameters	General anesthesia (n=35)	Regional anesthesia (n=37)	P-value
Age (years)			
Mean±SD	30.17±5.31	28.10±4.68	0.084
Gravidity			
Median (min–m			
Parity			
Median (min–m			
Gestational age a			
Mean±SD			
Time required for			
Mean±SD			
Incision to delivery interval (min)			
Median (min–max)	2.5 (0–12)	3 (0–6)	0.121
Maternal IMA levels (ABSU)			
Mean±SD	0.99±0.19	0.80±0.27	0.001[b]
Fetal IMA levels (ABSU)			
Mean±SD	1.00±0.21	0.70±0.26	<0.001[b]
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pH			
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pCO_2			
Mean±SD	51.97±6.65	50.51±8.43	0.420
BE			
Median (min–max)	−0.41(−5.5–2.8)	0.2 (−11.8–4.7)	0.575
Lactate			
Mean±SD	1.47±0.61	1.68±1.04	0.483

Maternal and fetal cord IMA levels were significantly higher in general anesthesia group.

Time Median (min–max)	Systolic blood pressure (mm Hg)		P-value	Di								
	Group 1	Group 2										
0 min	130 (100–173)	126 (95–155)	0.012[a]									
1 min	130 (100–163)	124 (90–154)	0.040[a]									
2 min	124 (99–162)	116 (75–146)	0.016[a]									
3 min	125 (90–168)	111 (85–143)	0.050									
4 min	121 (90–175)	111 (67–169)	0.073	73 (49–104)	63 (38–94)	0.001[a]	99 (97–100)	100 (94–100)	0.051	93 (62–135)	91 (58–130)	0.989
5 min	117 (86–164)	110 (83–147)	0.143	72 (41–103)	60 (36–88)	0.004[a]	99 (97–100)	100 (73–100)	0.022[a]	99 (60–135)	91 (56–162)	0.848
10 min	122 (93–157)	112 (78–169)	0.244	71 (51–96)	65 (29–94)	0.004[a]	99 (94–100)	100 (75–100)	0.038[a]	88 (69–126)	92 (55–143)	0.918

[a]Statistically significant.

Neither the changes in systolic or diastolic blood pressures differed in the general and regional anesthesia groups.

Systolic blood pressure was significantly higher at 0, 1, and 2 min in the general anesthesia group.

Time Median (min–max)	Systolic blood pressure (mm Hg)		P-value	Diastolic blood pressure (mm Hg)		P-value	Saturation		P-value	Pulse rate		P-value
	Group 1	Group 2		Group 1	Group 2		Group 1	Group 2		Group 1	Group 2	
0 min	130 (100–173)	126 (95–155)	0.012[a]	80 (55–108)	76 (53–92)	0.220	99	99	0.141	95	99	0.344
1 min	130 (100–163)	124 (90–154)	0.040[a]	80 (53–97)	72 (44–98)	0.035[a]						
2 min	124 (99–162)	116 (75–146)	0.016[a]	76 (54–104)	63 (37–97)	<0.001[a]						
3 min	125 (90–168)	111 (85–143)	0.050	74 (42–104)	62 (42–91)	0.002[a]						
4 min	121 (90–175)	111 (67–169)	0.073	73 (49–104)	63 (38–94)	0.001[a]						
5 min	117 (86–164)	110 (83–147)	0.143	72 (41–103)	60 (36–88)	0.004[a]	99 (97–100)	100 (73–100)	0.022[a]	99 (60–135)	91 (56–162)	0.848
10 min	122 (93–157)	112 (78–169)	0.244	71 (51–96)	65 (29–94)	0.004[a]	99 (94–100)	100 (75–100)	0.038[a]	88 (69–126)	92 (55–143)	0.918

[a]Statistically significant.

Diastolic blood pressures were significantly higher in the general anesthesia group at all times (1, 2, 3, 4, 5 and 10 min) except initiation of anesthesia (0 min).

Time Median (min–max)	Systolic blood pressure (mm Hg)		P-value	Diastolic blood pressure (mm Hg)		P-value	Saturation		P-value	Pulse rate		P-value
	Group 1	Group 2		Group 1	Group 2		Group 1	Group 2		Group 1	Group 2	
0 min	130	126	0.012[a]	80	76	0.220	99	99	0.141	95	99	0.344
							(85–100)	(97–100)		(76–132)	(40–133)	
						35[a]	99	99	0.030[a]	100	96	0.972
							(96–100)	(96–100)		(65–132)	(62–133)	
						01[a]	99	99	0.044[a]	91	96	0.454
							(98–100)	(97–100)		(72–149)	(64–140)	
						02[a]	99	100	0.050	99	97	0.767
							(97–100)	(96–100)		(71–155)	(65–145)	
4 min	121	111	0.073	73	63	0.001[a]	99	100	0.051	93	91	0.989
	(90–175)	(67–169)		(49–104)	(38–94)		(97–100)	(94–100)		(62–135)	(58–130)	
5 min	117	110	0.143	72	60	0.004[a]	99	100	0.022[a]	99	91	0.848
	(86–164)	(83–147)		(41–103)	(36–88)		(97–100)	(73–100)		(60–135)	(56–162)	
10 min	122	112	0.244	71	65	0.004[a]	99	100	0.038[a]	88	92	0.918
	(93–157)	(78–169)		(51–96)	(29–94)		(94–100)	(75–100)		(69–126)	(55–143)	

Significantly higher values of SO2 were found at 1, 3, 5, and 10 min in the regional anesthesia group when compared with the general anesthesia group.

[a]Statistically significant.

Parameters	Maternal IMA		Fetal IMA	
	Correlation coefficient (r)	P-value	Correlation coefficient (r)	P-value
Maternal age	0.076	0.526	0.157	0.187
Gestational age	0.134	0.262	−0.091	0.448
Gravidity	0.181	0.129	0.310	0.008[a]
Parity	0.090	0.453	0.259	0.028[a]
Fetal birth weight	0.311	0.008[a]	0.237	0.045[a]

Gravidity, Parity and Fetal birth weight were positively correlated Fetal IMA levels.

Parameters	Maternal IMA		Fetal IMA	
	Correlation coefficient (r)	P-value	Correlation coefficient (r)	P-value
Time required for anesthesia[b]	-0.114	0.355	-0.131	0.285
Incision to delivery interval	-0.118	0.327	-0.296	0.012[a]

Time from incision to delivery was found to be positively correlated with Fetal IMA levels.

Discussion

- First study in literature;

Maternal and fetal IMA levels in different anesthesia types used for cesarean section in uncomplicated term gestations.

Route of Anesthesia;

- Maternal and fetal IMA levels in the general anesthesia group were found significantly higher compared to regional anesthesia.

IMA?

- A valuable marker in perinatology in the future?

Maternal;

- Higher maternal IMA levels with cesarean section compared to vaginal delivery.

  Caglar GS, Matern Fetal Neonatal Med. 2013

- Sham laparotomy group in animal models did not end up with an effect on IMA levels.

  Aran T, Eur J Obstet Gynecol Reprod Biol. 2010

Possible reason?

Muscle injury during the cesarean section?

Hypotension and blood pressure alterations?

Maternal;

- Higher Maternal IMA levels in general anesthesia group.
- Negative correlation between systolic blood pressure and cord IMA levels.

Possible reason?

Lower Sat O2 with general anesthesia?

Fetal;

- Gravidity, parity and fetal birth weight found to be positively correlated with fetal IMA levels.

This effect should be clarified before any further interpretations !

Fetal;

- Cord blood IMA levels from complicated deliveries are higher than uncomplicated deliveries.

  Gugliucci A, Clin Chim Acta. 2005
  Iacovidou N, Mediators Inflamm, 2008

- Complicated delivery causes an almost 50% increase in fetal cord blood IMA levels.

  Gugliucci A, Clin Chim Acta. 2005

Fetal;

- Fetal cord blood acid-base status were in normal range.
- Fetal cord IMA levels were higher in general anesthesia group.

IMA  Cord blood acid-base status

In conclusion;

The importance of normal acid-base status in cord blood but high IMA levels needs to be clarified with long term follow of these newborns.

O2 Saturation and systolic blood pressure should be strictly controlled during C/S under general anesthesia.

Thank you..