Examining the Relationship of Inflammatory Mediators Among Fetal Compartments

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Examining the Relationship of Inflammatory Mediators Among Fetal Compartments

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OBJECTIVE: Although cytokines have been shown to be important in both term and preterm labor, the source (ie, fetal or placental) of many cytokines is uncertain. Therefore, we evaluate the relationship of inflammatory mediators between the umbilical artery, umbilical vein, placenta, and amniotic fluid.

STUDY DESIGN: Twenty term, non-laboring patients without major maternal or fetal complications undergoing cesarean delivery were asked to provide samples during the immediate pre-operative and intra-operative period. Amniotic fluid was obtained intra-operatively via needle aspiration of the intact amniotic sac after hysterotomy. Fetal plasma from the umbilical artery and vein were sampled from a section of cord after delivery. A portion of the placenta was cultured under standard conditions for 24 hours. The supernatant was then collected. All fluids were analyzed for 27 inflammatory mediators using the Bio-Plex Array. We the compared the inflammatory mediator profile between compartments using Spearman correlation with P <0.05 required for significance. Mediator levels in the umbilical artery and vein were compared using the t-test.

RESULTS: Table 1 shows the number of cytokines (out of 27) that reached a significant correlation between the various fetal compartment combinations. There was a high degree of correlation between the umbilical artery and vein with 19 of the 27 reaching a significant correlation. When comparing median cytokine levels, only monocyte chemotactic protein-1 (MCP-1) was significantly different in the artery (196 pg/ml) when compared to the vein (123 pg/ml, P=0.01).

CONCLUSION: There is significant correlation of inflammatory mediators between the umbilical artery and vein, but not between the fetal circulation and amniotic fluid. The contribution of the placenta to the in-utero inflammatory milieu remains unclear as few cytokine levels were correlated with other compartments.

Background and Objective:

- Although cytokines and other inflammatory mediators have been shown to be important in both term and preterm labor, the source (ie, fetal or placental) of many cytokines is uncertain.
- We evaluate the relationship of inflammatory mediators between the umbilical artery, umbilical vein, placenta, and amniotic fluid.

Methods:

- Term, non-laboring patients without major maternal or fetal complications undergoing cesarean delivery were asked to provide samples during the immediate pre-operative and intra-operative period.
- Amniotic fluid was obtained intra-operatively via needle aspiration of the intact amniotic sac after hysterotomy.
- Fetal plasma from the umbilical artery and vein were sampled from a section of cord after delivery.
- A portion of the placenta was cultured under standard conditions for 24 hours. The supernatant was then collected.
- All fluids were analyzed for 27 inflammatory mediators using the Bio-Plex™ Array.
- We the compared the inflammatory mediator profile between compartments using Spearman correlation with P <0.05 required for significance.
- Mediator levels in the umbilical artery and vein were compared using the non-parametric t-test.

Results:

- Table 1 shows the number of cytokines (out of 27) that reached a significant correlation between various fetal compartment combinations.
- There was a high degree of correlation between the umbilical artery and vein with 19 of the 27 reaching a significant correlation.
- Table 2 contains the median cytokine levels for each compartment.
- When comparing median cytokine levels, only monocyte chemotactic protein-1 (MCP-1) was significantly different in the artery (196 pg/ml) when compared to the vein (123 pg/ml, P=0.01).

Conclusions:

- There is significant correlation of inflammatory mediators between the umbilical artery and vein, but not between the fetal circulation and amniotic fluid.
- The contribution of the placenta to the in-utero inflammatory milieu remains unclear as few cytokine levels were correlated with other compartments and there was little change in mediator levels between the umbilical artery and vein.
- It is possible that the culture methods altered placental mediator expression. Future studies will attempt to perform direct analysis of placental tissue.

Table 1. Inflammatory Mediator Correlation Among Compartments

Compartment	Amniotic Fluid	Umbilical Vein	Umbilical Artery	Placental Culture
Amniotic fluid		1	1	2
Umbilical Vein			19	5
Umbilical Artery				4
Placental Culture				

KEY: *Table indicates the number of inflammatory mediators (out of 27) that reached a significant correlation between the indicated compartments.*

Table 2. Median Inflammatory Mediator Levels by Compartment (pg/ml)

Compartment	Amniotic Fluid	Umbilical Vein	Umbilical Vein	Placental Culture
IL-1β	2.1	1.2	0.9	239.7
IL-1ra	930.3	167.6	104	5836.0
IL-2	Not detected	Not detected	Not detected	Not detected
IL-4	1.8	1.1	0.7	4.1
IL-5	3.4	0.9	0.6	0.9
IL-6	25.3	3.0	3.6	OOR>*
IL-7	12.6	2.7	3.7	4.2
IL-8	40.0	4.7	4.4	29855.7
IL-9	21.3	7.6	4.5	48.9
IL-10	1.9	1.9	1.7	239.5
IL-12	13.0	6.1	4.6	5.9
IL-13	5.1	2.4	2.2	53.6
IL-15	Not detected	8.0	7.5	21.6
IL-17	9.9	27.5	23.1	56.1
PDGF	37.1	241.8	257.4	93.8
Eotaxin	Not detected	45.6	51.8	20.3
FGF	13.7	46.0	26.3	181.2
G-CSF	99.4	43.7	42.9	OOR>*
GM-CSF	Not detected	100.2	100.2	263.7
IFN-γ	167.2	74.2	68.5	281.4
IP-10	390.4	187.6	273.8	16308.8
MCP-1	28.2	190.2	97.7	12803.9
MIP-1A	Not detected	Not detected	Not detected	5451.3
MIP-1B	6.2	81.4	84.1	13838.1
RANTES	22.5	1001.7	943.8	1178.5
TNA-α	Not detected	18.0	16.1	4044.5
VEGF	8.11	30.3	25.4	22.7

KEY: *Interleukin (IL), platelet derived growth factor (PDGF), fibroblast growth factor (FGF), granulocyte colony stimulating factor (G-CSF), granulocyte macrophage stimulating factor (GM-CSF), interferon gamma (IFN-γ), inducible protein-10 (IP-10), monocyte chemotactic protein-1 (MCP-1), macrophage inflammatory protein (MIP), tumor necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF), regulated on activation normal T cell expressed and secreted (RANTES);*
**Out of range, greater than the limit of the assay.*

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