

Effects of prenatal oral L-arginine on birth outcomes: a meta-analysis

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Supplementary Tables

Supplementary Table 1. Results of meta-analysis and subgroup and meta-regression analysis (dichotomous outcomes)

IUGR neonates (499 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	<i>I</i> ² (%)	<i>P</i> - value
Total population (<i>n</i> = 7)	0.676	0.464, 0.986	52.2	-
Region				
Europe (<i>n</i> = 6)	0.691	0.466, 1.024	58.8	0.55
Developed countries (<i>n</i> = 6)	0.691	0.466, 1.024	58.8	0.55
Population				
(High risk of) pre-eclampsia/hypertension: include (<i>n</i> = 4)	0.850	0.600, 1.202	22.0	0.51
(High risk of) pre-eclampsia/hypertension: exclude (<i>n</i> = 3)	0.613	0.350, 1.071	59.6	-
IUGR fetuses: include (<i>n</i> = 3)	0.72	0.361, 1.436	82.5	0.95
IUGR fetuses: exclude (<i>n</i> = 4)	0.641	0.414, 1.005	0.0	-
Intervention				
3 g/day (<i>n</i> = 6)	0.656	0.513, 0.839	60.0	0.89
Control				
Placebo (<i>n</i> = 6)	0.849	0.636, 1.133	0.0	0.14
Study quality				
Random sequence generation: (probably) yes (<i>n</i> = 7)	0.676	0.464, 0.986	52.2	-
Allocation concealment: (probably) yes (<i>n</i> = 6)	0.849	0.636, 1.133	0.0	0.14
Baseline difference: (probably) no (<i>n</i> = 6)	0.670	0.435, 1.034	60.0	0.89
Risk of bias: low (<i>n</i> = 6)	0.849	0.636, 1.133	0.0	0.14

Pre-term birth (625 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	<i>I</i> ² (%)	<i>P</i> - value
Total population (<i>n</i> = 3)	0.499	0.345, 0.845	32.2	-
Region				
Latin America (<i>n</i> = 2)	0.426	0.275, 0.659	18.3	0.68

Developing countries (<i>n</i> = 2)	0.426	0.275, 0.659	18.3	0.68
Population				
(High risk of) pre-eclampsia/hypertension: include (<i>n</i> = 3)	0.499	0.345, 0.845	32.2	-
IUGR foetuses: exclude (<i>n</i> = 3)	0.499	0.345, 0.845	32.2	-
Intervention				
4 – 14 g/day (<i>n</i> = 2)	0.521	0.358, 0.756	27.6	0.79
Control				
Placebo (<i>n</i> = 2)	0.413	0.081, 2.119	60.5	-
Study quality				
Random sequence generation: (probably) yes (<i>n</i> = 3)	0.499	0.345, 0.845	32.2	-
Allocation concealment: (probably) yes (<i>n</i> = 3)	0.499	0.345, 0.845	32.2	-
Baseline difference: (probably) no (<i>n</i> = 2)	0.426	0.275, 0.845	18.3	-
Risk of bias: low (<i>n</i> = 3)	0.499	0.345, 0.845	32.2	-

Abortion (493 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	<i>I</i> ² (%)	<i>P</i> - value
Total population (<i>n</i> = 2)	0.616	0.157, 2.415	0.0	-
Intervention				
Amount: 4 – 14 g/day (<i>n</i> = 2)	0.616	0.157, 2.415	0.0	-
Study quality				
Random sequence generation: (probably) yes (<i>n</i> = 2)	0.616	0.157, 2.415	0.0	-
Allocation concealment: (probably) yes (<i>n</i> = 2)	0.616	0.157, 2.415	0.0	-
Baseline difference: (probably) no (<i>n</i> = 2)	0.616	0.157, 2.415	0.0	-
Risk of bias: low (<i>n</i> = 2)	0.616	0.157, 2.415	0.0	-

Infection (110 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	<i>I</i> ² (%)	<i>P</i> - value
Total population (<i>n</i> = 2)	1.039	0.431, 2.508	0.0	-
Region				
Europe (<i>n</i> = 2)	1.039	0.431, 2.508	0.0	-
Developed countries (<i>n</i> = 2)	1.039	0.431, 2.508	0.0	-
Population				
IUGR foetuses: include (<i>n</i> = 2)	1.039	0.431, 2.508	0.0	-
Intervention				
Energy before birth: 3 kg (<i>n</i> = 2)	1.039	0.431, 2.508	0.0	-
Control				
Placebo (<i>n</i> = 2)	1.039	0.431, 2.508	0.0	-
Study quality				

Random sequence generation: (probably) yes ($n = 2$)	1.039	0.431, 2.508	0.0	-
Allocation concealment: (probably) yes ($n = 2$)	1.039	0.431, 2.508	0.0	-
Baseline difference: (probably) no ($n = 2$)	1.039	0.431, 2.508	0.0	-
Risk of bias: low ($n = 2$)	1.039	0.431, 2.508	0.0	-

RDS (160 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	I^2 (%)	P- value
Total population ($n = 3$)	0.460	0.241, 0.878	63.2	-
Region				
Europe ($n = 2$)	0.338	0.202, 0.567	0.0	0.26
Developed countries ($n = 2$)	0.338	0.202, 0.567	0.0	0.26
Population				
(High risk of) pre-eclampsia/hypertension: exclude ($n = 2$)	0.486	0.163, 1.446	75.0	0.83
IUGR foetuses: include ($n = 3$)	0.460	0.241, 0.878	63.2	-
Intervention				
Amount: 3 g/day ($n = 3$)	0.460	0.241, 0.878	63.2	-
Control				
Placebo ($n = 2$)	0.338	0.202, 0.567	0.0	0.27
Study quality				
Random sequence generation: (probably) yes ($n = 3$)	0.460	0.241, 0.878	63.2	-
Allocation concealment: (probably) yes ($n = 3$)	0.460	0.241, 0.878	63.2	-
Baseline difference: (probably) no ($n = 3$)	0.460	0.241, 0.878	63.2	-
Risk of bias: low ($n = 3$)	0.460	0.241, 0.878	63.2	-

ICH (110 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	I^2 (%)	P- value
Total population ($n = 2$)	1.494	0.852, 2.620	0.0	-
Region				
Europe ($n = 2$)	1.494	0.852, 2.620	0.0	-
Developed countries ($n = 2$)	1.494	0.852, 2.620	0.0	-
Population				
IUGR foetuses: include ($n = 2$)	1.494	0.852, 2.620	0.0	-
Intervention				
Amount: 3 g/day ($n = 3$)	1.494	0.852, 2.620	0.0	-
Control				
Placebo ($n = 2$)	1.494	0.852, 2.620	0.0	-
Study quality				
Random sequence generation: (probably) yes ($n = 2$)	1.494	0.852, 2.620	0.0	-

Allocation concealment: (probably) yes ($n = 2$)	1.494	0.852, 2.620	0.0	-
Baseline difference: (probably) no ($n = 2$)	1.494	0.852, 2.620	0.0	-
Risk of bias: low ($n = 2$)	1.494	0.852, 2.620	0.0	-

NICU admission (129 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	I^2 (%)	P - value
Total population ($n = 2$)	0.638	0.302, 1.534	24.6	-
Study quality				
Random sequence generation: (probably) yes ($n = 2$)	0.638	0.302, 1.534	24.6	-
Allocation concealment: (probably) yes ($n = 2$)	0.638	0.302, 1.534	24.6	-
Baseline difference: (probably) no ($n = 2$)	0.638	0.302, 1.534	24.6	-
Risk of bias: low ($n = 2$)	0.638	0.302, 1.534	24.6	-

Caesarean section (493 mother–neonate pairs)	Relative risk			Meta-regression
Category (number of studies)	Mean	95% CI	I^2 (%)	P - value
Total population ($n = 2$)	1.027	0.919, 1.147	0.0	-
Study quality				
Random sequence generation: (probably) yes ($n = 2$)	1.027	0.919, 1.147	0.0	-
Allocation concealment: (probably) yes ($n = 2$)	1.027	0.919, 1.147	0.0	-
Baseline difference: (probably) no ($n = 2$)	1.027	0.919, 1.147	0.0	-
Risk of bias: low ($n = 2$)	1.027	0.919, 1.147	0.0	-

CI, confidence interval; ICH, intracranial hemorrhage; IUGR, intrauterine growth retardation; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome.

Supplementary Table 2. Results of meta-analysis and subgroup and meta-regression analysis (continuous outcomes)

Birthweight (g) (755 mother–neonate pairs)	Difference			Meta-regression
Category (number of studies)	Mean	95% CI	I^2 (%)	P - value
Total population ($n = 8$)	101.411	15.51, 187.32	50.1	-
Region				
Europe ($n = 5$)	103.931	-60.54, 268.39	23.0	0.86
Latin America ($n = 2$)	85.002	-11.04, 287.04	74.0	0.59
Developing countries ($n = 3$)	97.667	-7.24, 202.58	77.2	0.87
Developed countries ($n = 5$)	103.931	-60.54, 268.39	23.0	-
Population				
(High risk of) pre-eclampsia/hypertension: include ($n = 4$)	160.587	-38.09, 359.27	62.1	0.70

(High risk of) pre-eclampsia/hypertension: exclude ($n = 4$)	128.370	105.22, 121.53	0.0	-
IUGR foetuses: include ($n = 4$)	130.051	106.85, 153.26	18.2	0.51
IUGR foetuses: exclude ($n = 4$)	38.151	-38.15, 114.46	42.8	-
Intervention				
3 g/day ($n = 6$)	131.676	108.66, 154.69	0.0	0.023
4 – 14 g/day ($n = 2$)	-4.263	-88.67, 80.14	0.0	-
Control				
Placebo ($n = 6$)	148.239	24.07, 272.41	14.4	0.85
Study quality				
Random sequence generation: (probably) yes ($n = 8$)	101.411	15.51, 187.32	50.1	-
Allocation concealment: (probably) yes ($n = 8$)	101.411	15.51, 187.32	50.1	-
Baseline difference: (probably) no ($n = 8$)	101.411	15.51, 187.32	50.1	-
Risk of bias: low ($n = 8$)	101.411	15.51, 187.32	50.1	-

Birth length (cm) (511 mother–neonate pairs)	Difference			Meta-regression
	Mean	95% CI	I^2 (%)	P- value
Category (number of studies)				
Total population ($n = 2$)	0.156	-0.427, 0.739	3.9	-
Population				
(High risk of) pre-eclampsia/hypertension: include ($n = 2$)	0.156	-0.427, 0.739	3.9	-
IUGR foetuses: exclude ($n = 2$)	0.156	-0.427, 0.739	3.9	-
Study quality				
Random sequence generation: (probably) yes ($n = 2$)	0.156	-0.427, 0.739	-	-
Allocation concealment: (probably) yes ($n = 2$)	0.156	-0.427, 0.739	-	-
Baseline difference: (probably) no ($n = 2$)	0.156	-0.427, 0.739	-	-
Risk of bias: low ($n = 2$)	0.156	-0.427, 0.739	-	-

Gestational age (weeks) (723 mother–neonate pairs)	Difference			Meta-regression
	Mean	95% CI	I^2 (%)	P- value
Category (number of studies)				
Total population ($n = 5$)	0.347	0.030, 0.663	0.0	-
Region				
Europe ($n = 3$)	0.109	-0.625, 0.843	10.5	0.64
Developing countries ($n = 2$)	0.402	0.050, 0.752	0.0	0.64
Developed countries ($n = 3$)	0.109	-0.625, 0.843	10.5	-
Population				
(High risk of) pre-eclampsia/hypertension: include ($n = 2$)	0.436	0.093, 0.779	0.0	0.28
(High risk of) pre-eclampsia/hypertension: exclude ($n = 3$)	-0.169	-0.992, 0.655	0.0	-
IUGR foetuses: include ($n = 3$)	-0.169	-0.992, 0.655	0.0	0.28
IUGR foetuses: exclude ($n = 2$)	0.436	0.093, 0.779	0.0	-

Intervention				
3 g/day (<i>n</i> = 3)	0.162	−0.647, 0.970	10.2	0.85
4 – 14 g/day (<i>n</i> = 2)	0.380	0.036, 0.724	0.0	-
Study quality				
Random sequence generation: (probably) yes (<i>n</i> = 5)	0.347	0.030, 0.663	0.0	-
Allocation concealment: (probably) yes (<i>n</i> = 4)	0.417	0.081, 0.753	0.0	0.31
Baseline difference: (probably) no (<i>n</i> = 5)	0.346	0.030, 0.663	0.0	-
Risk of bias: low (<i>n</i> = 4)	0.417	0.081, 0.753	0.0	0.31

Apgar score (1155 mother–neonate pairs)	Difference			Meta-regression
Category (number of studies)	Mean	95% CI	<i>I</i> ² (%)	<i>P</i> - value
Total population (<i>n</i> = 7)	0.146	−0.031, 0.323	81.1	-
Region				
Europe (<i>n</i> = 5)	0.247	−0.212, 0.705	84.1	0.77
Latin America (<i>n</i> = 2)	0.088	−0.107, 0.282	83.8	0.77
Developing countries (<i>n</i> = 2)	0.088	−0.107, 0.282	83.8	0.77
Developed countries (<i>n</i> = 5)	0.247	−0.212, 0.705	84.1	-
Population				
(High risk of) pre-eclampsia/hypertension: include (<i>n</i> = 4)	0.375	0.065, 0.684	89.3	0.14
(High risk of) pre-eclampsia/hypertension: exclude (<i>n</i> = 3)	−0.012	−0.123, 0.100	31.4	-
IUGR foetuses: exclude (<i>n</i> = 6)	−0.034	−0.012, 0.081	82.7	0.21
Intervention				
3 g/day (<i>n</i> = 4)	0.401	−0.090, 0.892	86.4	0.30
4 – 14 g/day (<i>n</i> = 3)	0.045	−0.168, 0.258	77.8	-
Time of Apgar score				
1 minute after delivery (<i>n</i> = 3)	0.319	−0.164, 0.802	79.2	0.57
5 minutes after delivery (<i>n</i> = 4)	0.086	−0.120, 0.292	80.9	-
Study quality				
Random sequence generation: (probably) yes (<i>n</i> = 7)	0.146	−0.031, 0.323	81.1	-
Allocation concealment: (probably) yes (<i>n</i> = 7)	0.146	−0.031, 0.323	81.1	-
Baseline difference: (probably) no (<i>n</i> = 7)	0.146	−0.031, 0.323	81.1	-
Risk of bias: low (<i>n</i> = 7)	0.146	−0.031, 0.323	81.1	-

CI, confidence interval; IUGR, intrauterine growth retardation.