

Comparison: Routine application of chlorhexidine to the umbilical cord stump compared with dry cord care or usual care

Source: Chlorhexidine Umbilical Review Group. Efficacy and safety of umbilical cord cleansing with chlorhexidine in neonates – an individual participant data (IPD) meta-analysis (in preparation).

Certainty assessment							No of patients		Effect		Certainty (GRADE)	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine application of chlorhexidine to the umbilical cord stump	Dry cord care or usual care	Relative (95% CI)	Absolute (95% CI)		
Neonatal mortality (ITT analysis)												
5	randomized trials	not serious	not serious	serious ^a	not serious	none	1562/70 491 (2.2%)	1464/65 829 (2.2%)	OR 0.90 (0.78 to 1.04)	2 fewer per 1000 (from 5 fewer to 1 more)	⊕⊕⊕○ MODERATE	CRITICAL
Neonatal mortality (ITT analysis) – mortality rate ≥ 30 per 1000 live births												
3	randomized trials	not serious	serious ^b	serious ^c	serious ^d	none	1091/33 696 (3.2%)	980/27 589 (3.6%)	OR 0.83 (0.68 to 1.03)	6 fewer per 1000 (from 11 fewer to 1 more)	⊕○○○ VERY LOW	CRITICAL
Neonatal mortality (ITT analysis) – mortality rate < 30 per 1000 live births												
2	randomized trials	not serious	not serious	not serious	not serious	none	471/36 522 (1.3%)	484/38 240 (1.3%)	OR 0.99 (0.79 to 1.25)	0 fewer per 1000 (from 3 fewer to 3 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal mortality (ITT analysis) by place of birth – home												
5	randomized trials	not serious	serious ^b	serious ^e	serious ^d	none	1032/44 621 (2.3%)	845/39 049 (2.2%)	OR 0.86 (0.68 to 1.09)	3 fewer per 1000 (from 7 fewer to 2 more)	⊕○○○ VERY LOW	CRITICAL
Neonatal mortality (ITT analysis) by place of birth – facility												
5	randomized trials	not serious	not serious	serious ^e	not serious	none	432/25 000 (1.7%)	430/25 644 (1.7%)	OR 0.95 (0.81 to 1.10)	1 fewer per 1000 (from 3 fewer to 2 more)	⊕⊕⊕○ MODERATE	CRITICAL
Neonatal mortality (ITT analysis) – non-hygienic applications to umbilical cord stump												
5	randomized trials	not serious	not serious	serious ^a	not serious	none	173/11 294 (1.5%)	338/16 523 (2.0%)	OR 0.63 (0.50 to 0.79)	7 fewer per 1000 (from 10 fewer to 4 fewer)	⊕⊕⊕○ MODERATE	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine application of chlorhexidine to the umbilical cord stump	Dry cord care or usual care	Relative (95% CI)	Absolute (95% CI)		
Neonatal mortality (ITT analysis) – no non-hygienic applications to umbilical cord stump												
5	randomized trials	not serious	not serious	serious ^a	not serious	none	1562/70 491 (2.2%)	1464/65 829 (2.2%)	OR 0.89 (0.77 to 1.03)	2 fewer per 1000 (from 5 fewer to 1 more)	⊕⊕⊕○ MODERATE	CRITICAL
Post-24-hour neonatal mortality (ITT analysis)												
5	randomized trials	not serious	not serious	serious ^a	not serious	none	994/69 923 (1.4%)	949/65 314 (1.5%)	OR 0.91 (0.82 to 1.02)	1 fewer per 1000 (from 3 fewer to 0 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Omphalitis (ITT analysis) – moderate omphalitis												
5	randomized trials	not serious	not serious	serious ^a	not serious	none	2263/71 570 (3.2%)	3405/66 372 (5.1%)	OR 0.77 (0.71 to 0.83)	11 fewer per 1000 (from 14 fewer to 9 fewer)	⊕⊕⊕○ MODERATE	CRITICAL
Omphalitis (ITT analysis) – severe omphalitis												
5	randomized trials	not serious	serious ^b	serious ^a	not serious	none	1311/71 570 (1.8%)	2067/66 372 (3.1%)	OR 0.55 (0.39 to 0.76)	14 fewer per 1000 (from 19 fewer to 7 fewer)	⊕⊕○○ LOW	CRITICAL
Possible serious bacterial infection (PSBI) (ITT analysis) – any PSBI												
5	randomized trials	not serious	serious ^b	serious ^a	not serious	none	6846/71 719 (9.5%)	8057/66 223 (12.2%)	OR 0.91 (0.76 to 1.10)	10 fewer per 1000 (from 26 fewer to 11 more)	⊕⊕○○ LOW	CRITICAL
PSBI – more specific PSBI												
5	randomized trials	not serious	serious ^b	serious ^a	not serious	none	1868/71 719 (2.6%)	2103/66 223 (3.2%)	OR 0.91 (0.75 to 1.11)	3 fewer per 1000 (from 8 fewer to 3 more)	⊕⊕○○ LOW	CRITICAL
PSBI – more severe PSBI												
5	randomized trials	not serious	serious ^b	not serious ^a	not serious	none	2030/76 889 (2.6%)	1941/61 053 (3.2%)	OR 0.93 (0.83 to 1.10)	2 fewer per 1000 (from 5 fewer to 3 more)	⊕⊕⊕○ MODERATE	CRITICAL

CI: confidence interval; ITT: intention to treat; OR: odds ratio.

a. 80% of births occurred at home, 30% of babies were of low birthweight, three trials with infant mortality rate $\geq 30/1000$ (downgraded by one level for the combination of these factors).

b. Statistical heterogeneity ($I^2 \geq 60\%$).

c. 80% of births occurred at home, 30% of babies were of low birthweight (downgraded by one level for the combination of both factors).

d. Wide confidence interval crossing the line of no effect.

e. 30% of babies were of low birthweight, three trials with infant mortality rate of $\geq 30/1000$ (downgraded by one level for the combination of these factors).