

Management of preterm labour: Overview of systematic reviews on tocolytic treatment

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WHY TO RESEARCH IN PRETERM BIRTH

- ❑ BIRTH BEFORE 37 COMPLETED WEEKS
- ❑ 5-11% OF BIRTHS AND NOT DECLINE
- ❑ MAJOR CAUSE OF MORBIDITY AND MORTALITY
- ❑ 45.8% OF ALL CAUSES OF DEATH BETWEEN BIRTH AND 1 YEAR OF AGE
- ❑ 33% OF PRETERM ARE BORN BEFORE 34 WEEKS OF GESTATION
- ❑ LARGE VARIETY OF INTERVENTIONS FOR TREATMENT
- ❑ BENEFITS FOR PROLONGATION PREGNANCY
- ❑ TOCOLYTIC AGENTS

OVERVIEW

- ❑ OBJECTIVES
- ❑ SEARCH: Cochrane Library
- ❑ INTERVENTIONS
- ❑ OUTCOMES: Maternal
Infant/child
Health services
- ❑ RESULTS : 14 SR (72 RCT; 7504 women)
Outcomes: maternal; neonatal (3 broad categories)
Interventions: acute and maintenance tocolysis

MATERNAL OUTCOMES

Tocolytic Agent	SR (RCTs)	Comparison	Outcome	No. of RCTs with outcome	No. women included	RR/WMD*	95% CI
Betamimetics	1 (11)	Placebo	Discont. for side effects	5	1081	11.38	5.21 - 24.86
Betamimetics Maintenance	1 (8)	Placebo	Discont. for side effects	2	141	2.71	0.11 - 64.79
			Readmission to hospital	4	335	1.11	0.76 - 1.62
	1 (3)	Magnesium sulphate	Discont. for side effects	2	100	0.90	0.24 - 3.46
			Readmission to hospital	1	50	1.09	0.60 - 1.99
CCB	1 (12)	Other	Adverse drug reaction	8	717	0.32	0.24 - 0.41
			Discont. for side effects	10	833	0.14	0.05 - 0.36
	1 (9)	Betamimetics	Adverse drug reaction	5	426	0.40	0.30 - 0.55
			Discont. for side effects	7	542	0.09	0.02 - 0.38
CCB Maintenance	1 (1)	No treatment	Readmission to hospital	1	64	4.00	0.47 - 33.86
Atosiban	1 (2)	Placebo	Discont. for side effects	2	613	4.02	2.05 - 7.85
	1 (4)	Betamimetics	Adverse drug reaction	2	486	0.86	0.72 - 1.03
			Discont. for side effects	4	1034	0.04	0.02 - 0.11
Atosiban	1 (1)	Placebo	Adverse drug reaction	1	512	1.55	1.33 - 1.81
SO4Mg	1 (11)	Other	Discont. for side effects	10	838	0.63	0.37 - 1.90
	1 (9)	High quality RCTs	Discont. for side effects	5	457	9.16	2.48 - 33.90
	1 (4)	Placebo/NT**	Discont. for side effects	4	310	1.59	0.57 - 4.41
SO4Mg Maintenance	1 (3)	Placebo/NT**	Adverse drug reaction	1	133	1.88	1.11 - 3.20
			Diarrhoea	1	133	7.67	2.41 - 24.41
	1 (3)	Other	Discont. for side effects	2	100	1.11	0.29 - 4.23
			Readmission to hospital	2	100	1.01	0.63 - 1.65
COX inhibitors	1 (3)	Placebo	Adverse drug reaction	3	101	1.58	0.66 - 3.78
			Postpartum	1	34	3.94	0.95 - 16.99
	1 (8)	Other	Adverse drug reaction	7	629	0.22	0.15 - 0.33
			Discont. for side effects	5	355	0.07	0.02 - 0.29
Nitric oxide donors	1 (1)	Placebo	Adverse drug reaction	1	33	4.03	0.94 - 17.22
	1 (4)	Other	Adverse drug reaction	24	2398	0.47	0.37 - 0.61
Hydration	1 (2)	Bed rest	Maternal death	0	0	NE	NE
Combination of tocolytics	1 (7)	Ritodrine + SO4Mg vs Ritodrine	Adverse drug reaction	1	41	7.79	1.11 - 54.80
		Ritodrine + Indomethacine vs Ritodrine	Adverse drug reaction	1	208	1.00	0.65 - 1.53
			Recurrence of labour	1	208	1.00	0.54 - 1.05
Terbutaline pump maintenance	1 (2)	Placebo	Discont. for side effects	2	79	1.15	0.68 - 1.95
		Oral terbutaline	Discont. for side effects	1	30	3.00	0.72 - 12.95

NEONATAL OUTCOMES

Tocolytic Agent	SR (RCTs)	Comparison	Outcome	No. of Trials with outcome	No. women included	RR/WMD*	95% CI
Betamimetics	1 (11)	Placebo	Birth <48 hs trial entry	10	1209	0.63	0.53 - 0.75
			RDS	8	1239	0.87	0.71 - 1.08
			Perinatal death	11	1332	0.84	0.46 - 1.55
CCB	1 (12)	Other	Birth < 7 days trial entry	4	453	0.76	0.60 - 0.97
			RDS	9	763	0.63	0.46 - 0.88
			Perinatal mortality	10	820	1.42	0.61 - 3.31
	1 (9)	Betamimetics	Birth <48 hs trial entry	6	470	0.72	0.53 - 0.97
			RDS	7	552	0.64	0.45 - 0.91
			Perinatal mortality	7	529	1.39	0.60 - 3.24
Atosiban	1 (2)	Placebo	Birth <48 hs trial entry	1	112	1.17	0.99 - 1.37
			Birthweight	2	692	-138.31	-248.76 - -27.86
			Infant death	1	583	6.15	1.39 - 27.22
	1 (4)	Betamimetics	Birth <48 hs trial entry	4	1033	0.98	0.68 - 1.41
			Birthweight	2	575	1.96	1.15 - 3.35
			Perinatal death	3	836	0.66	0.24 - 1.83
SO4Mg	1 (11)	Other	Birth <48 hs trial entry	11	881	0.85	0.58 - 1.25
			RDS	5	437	1.12	0.99 - 1.27
			Total deaths	7	727	2.82	1.20 - 6.62
	1 (9)	High quality RCTs	Birth <48 hs trial entry	5	513	0.87	0.61 - 1.24
			RDS	4	403	1.09	0.96 - 1.23
			Total deaths	4	454	1.84	0.67 - 5.06
	1 (4)	Placebo/NT	Birth <48 hs trial entry	3	190	0.57	0.28 - 1.15
			RDS	3	289	1.09	0.98 - 1.22
			Total deaths	3	292	1.74	0.63 - 4.77

NEONATAL OUTCOMES

COX inhibitors	1 (3)	Placebo	Birth <37 weeks	1	36	0.21	0.07 - 0.62
			Birthweight	2	67	716.34	425.52 - 1007.16
			Perinatal mortality	3	106	0.80	0.25 - 2.58
	1 (8)	Other	Birth <37 weeks	3	168	0.53	0.31 - 0.94
			RSD	6	503	1.08	0.66 - 1.76
			Perinatal mortality	8	660	1.46	0.57 - 3.74
Nitric oxide donors	1 (1)	Placebo	Birth <48 hs trial entry	1	33	3.06	0.74 - 12.63
			RSD	1	33	0.36	0.07 - 1.78
			Neonatal death	1	33	0.94	0.05 - 16.37
	1 (4)	Other	Birth <37 weeks	3	391	0.53	0.35 - 0.81
			Neonatal death	2	382	1.03	0.18 - 6.02
Hydration	1 (2)	Bed rest	Birth < 37 weeks	2	228	1.09	0.71 - 1.68
			NICU admission	1	118	0.99	0.46 - 2.16
			Perinatal mortality	0	0	Not estimable	Not estimable

Combination of tocolytics	1 (7)	Ritodrine + SO4Mg vs Ritodrine	Birth < 37 weeks	1	63	0.62	0.38 - 1.01
		Ritodrine + Indomethacine vs Ritodrine	Birth < 37 weeks	1	208	0.77	0.61 - 0.97
			RDS	1	153	0.51	0.05 - 5.47
			Perinatal mortality	1	208	1.00	0.65 - 1.53

NEONATAL OUTCOMES

Betamimetics Maintenance	1 (8)	Placebo	Birth <48 hs trial entry	1	200	0.78	0.30 - 2.10
			RDS	5	577	1.10	0.61 - 1.98
			Perinatal death	6	681	2.41	0.86 - 6.74
	1 (3)	Other	Birth <37 weeks	2	100	1.02	0.58 - 1.79
			RDS	1	50	2.01	0.19 - 20.67
			Perinatal death	1	50	0.03	0.01 - 3.97
Terbutaline pump maintenance	1 (2)	Placebo	Birth < 37 weeks	1	52	1.17	0.79 - 1.73
			RDS	2	79	0.82	0.23 - 2.93
	Oral terbutaline	Birthweight	1	30	484.00	-25.00 - 993.00	
		RDS	1	30	1.00	0.16 - 6.20	
CCB Maintenance	1 (1)	No treatment	Birth <37 weeks	1	74	1.01	0.73 - 1.37
			RDS	1	74	1.01	0.22 - 4.64
Atosiban Maintenance	1 (1)	Placebo	Birth < 37 weeks	1	510	0.89	0.71 - 1.12
			RDS	1	557	1.06	0.66 - 1.70
			Perinatal death	1	512	0.77	0.21 - 2.83
SO4Mg Maintenance	1 (3)	Placebo/NT	Preterm birth	1	50	0.85	0.47 - 1.51
			RDS	1	50	3.00	0.13 - 70.30
			Perinatal mortality	1	50	5.00	0.25 - 99.16
	1 (3)	Other	Preterm birth	2	100	0.98	0.56 - 1.72
			NICU admission	1	137	0.98	0.53 - 1.80
			Perinatal mortality	1	50	5.00	0.25 - 99.16

CONCLUSIONS

- ❑ CHALLENGE: PREVENTION PRETERM DELIVERY AND LBW
- ❑ OVERALL GOAL: TO REDUCE MORBIMORTALITY
- ❑ NO CLEAR CONCLUSIONS CAN BE DRAWN ABOUT WHICH TOCOLYTIC AGENT, IF ANY, IS THE BEST TREATMENT FOR PRETERM LABOUR
- ❑ RITODRINE
- ❑ PLACEBO-CONTROLLED TRIALS
- ❑ FURTHER WELL DESIGNED RCT OF TOCOLYTIC THERAPY ARE NEEDED, ANY SUCH TRIAL WOULD HAVE A PLACEBO ARM TO ALLOW APPROPRIATE INTERPRETATION

THANKS!!!

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