

Quality of sleep

Linear mixed-effects model

nlme::lme(quality_of_sleep ~ allocation + day + allocation:day + random = ~1|participant)

Coefficients	Estimate (95% CI)
Intercept (placebo, night 1)	4.0 (3.3 to 4.8)
Dexamethasone	1.2 (0.1 to 2.3)
Dexamethasone + dexmedetomidine	1.5 (0.4 to 2.6)
Night 2	3.0 (2.1 to 3.9)
Night 3	3.3 (2.4 to 4.3)
Dexamethasone : night 2	-2.4 (-3.7 to -1.1)
Dexamethasone+Dexmedetomidine : night 2	-2.3 (-3.6 to -1.0)
Dexamethasone : night 3	-1.5 (-2.9 to -0.2)
Dexamethasone+Dexmedetomidine : night 3	-1.5 (-2.8 to -0.2)
Random effect (participant)	Standard deviation 1.3

Estimated marginal means

emmeans::emmeans(lme, c("allocation", "day"))

Allocation	Day	Marginal means (95% CI)
Placebo	1	4.0 (3.3 to 4.8)
Dexamethasone	1	5.2 (4.4 to 6.0)
Dexamethasone+dexmedetomidine	1	5.5 (4.7 to 6.3)
Placebo	2	7.1 (6.3 to 7.8)
Dexamethasone	2	5.9 (5.1 to 6.7)
Dexamethasone+dexmedetomidine	2	6.2 (5.4 to 7.0)
Placebo	3	7.4 (6.6 to 8.1)
Dexamethasone	3	7.0 (6.2 to 7.8)
Dexamethasone+dexmedetomidine	3	7.4 (6.6 to 8.2)

Opioid consumption

Linear mixed-effects model

nlme::lme(opioid ~ allocation + day + allocation:day + random = ~1|participant)

Coefficients	Estimate (95% CI)
Intercept (placebo, day 1)	26 (19 to 33)
Dexamethasone	-18 (-28 to -8)
Dexamethasone + dexmedetomidine	-15 (-25 to -6)
Day 2	-4 (-11 to 2)
Day 3	-8 (-15 to -2)

Dexamethasone : Day 2	22 (12 to 32)
Dexamethasone+Dexmedetomidine : Day 2	15 (6 to 25)
Dexamethasone : Day 3	16 (7 to 26)
Dexamethasone+Dexmedetomidine : Day 3	14 (5 to 24)
Random effect (participant)	Standard deviation 16

Estimated marginal means

emmeans::emmeans(lme, c("allocation", "day"))

Allocation	Day	Marginal means (95% CI)
Placebo	1	26 (19 to 33)
Dexamethasone	1	8 (1 to 15)
Dexamethasone+dexmedetomidine	1	11 (3 to 18)
Placebo	2	22 (15 to 29)
Dexamethasone	2	26 (19 to 33)
Dexamethasone+dexmedetomidine	2	22 (15 to 29)
Placebo	3	18 (11 to 25)
Dexamethasone	3	16 (9 to 23)
Dexamethasone+dexmedetomidine	3	17 (10 to 24)

Pain at rest

Linear mixed-effects model

nlme::lme(pain_rest ~ allocation + day + allocation:day + random = ~1|participant)

Coefficients	Estimate (95% CI)
Intercept (placebo, day 1)	4.2 (3.5 to 4.9)
Dexamethasone	-1.2 (-2.2 to -0.2)
Dexamethasone + dexmedetomidine	-2.2 (-3.2 to -1.2)
Day 2	-1.2 (-1.9 to -0.4)
Day 3	-2.5 (-3.3 to -1.8)
Dexamethasone : Day 2	1.3 (0.2 to 2.4)
Dexamethasone+Dexmedetomidine : Day 2	1.9 (0.9 to 3.0)
Dexamethasone : Day 3	1.8 (0.7 to 2.9)
Dexamethasone+Dexmedetomidine : Day 3	2.5 (1.4 to 3.6)
Random effect (participant)	Standard deviation 1.5

Estimated marginal means

emmeans::emmeans(lme, c("allocation", "day"))

Allocation	Day	Marginal means (95% CI)
Placebo	1	4.2 (3.5 to 4.9)
Dexamethasone	1	2.9 (2.2 to 3.7)

Dexamethasone+dexmedetomidine	1	2.0 (1.3 to 2.7)
Placebo	2	3.0 (2.3 to 3.7)
Dexamethasone	2	3.0 (2.3 to 3.8)
Dexamethasone+dexmedetomidine	2	2.8 (2.0 to 3.5)
Placebo	3	1.7 (1.0 to 2.4)
Dexamethasone	3	2.2 (1.5 to 3.0)
Dexamethasone+dexmedetomidine	3	2.0 (1.2 to 2.7)

Average pain

Linear mixed-effects model

nlme::lme(pain_average ~ allocation + day + allocation:day + random = ~1|participant)

Coefficients	Estimate (95% CI)
Intercept (placebo, day 1)	4.0 (3.4 to 4.6)
Dexamethasone	-2.0 (-2.9 to -1.1)
Dexamethasone + dexmedetomidine	-2.5 (-3.4 to -1.6)
Day 2	-0.8 (-1.5 to -0.1)
Day 3	-1.3 (-2.0 to -0.6)
Dexamethasone : Day 2	2.9 (2.0 to 3.9)
Dexamethasone+Dexmedetomidine : Day 2	2.8 (1.9 to 3.8)
Dexamethasone : Day 3	2.0 (1.0 to 3.0)
Dexamethasone+Dexmedetomidine : Day 3	2.4 (1.5 to 3.4)
Random effect (participant)	Standard deviation 1.4

Estimated marginal means

emmeans::emmeans(lme, c("allocation", "day"))

Allocation	Day	Marginal means (95% CI)
Placebo	1	4.0 (3.3 to 4.6)
Dexamethasone	1	2.0 (1.4 to 2.7)
Dexamethasone+dexmedetomidine	1	1.4 (0.8 to 2.1)
Placebo	2	3.2 (2.5 to 3.8)
Dexamethasone	2	4.1 (3.5 to 4.8)
Dexamethasone+dexmedetomidine	2	3.5 (2.8 to 4.1)
Placebo	3	2.7 (2.1 to 3.3)
Dexamethasone	3	2.7 (2.0 to 3.4)
Dexamethasone+dexmedetomidine	3	2.6 (1.9 to 3.2)

Worst pain

Linear mixed-effects model

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nlme::lme(pain_worst~ allocation + day + allocation:day + random = ~1|participant)
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Coefficients	Estimate (95% CI)
Intercept (placebo, day 1)	7.1 (6.3 to 8.0)
Dexamethasone	-3.1 (-4.3 to -1.9)
Dexamethasone + dexmedetomidine	-4.0 (-5.3 to -2.8)
Day 2	-1.7 (-2.6 to -0.8)
Day 3	-2.9 (-3.8 to -2.0)
Dexamethasone : Day 2	3.8 (2.4 to 5.1)
Dexamethasone+Dexmedetomidine : Day 2	4.2 (2.9 to 5.6)
Dexamethasone : Day 3	3.4 (2.1 to 4.7)
Dexamethasone+Dexmedetomidine : Day 3	3.9 (2.6 to 5.2)
Random effect (participant)	Standard deviation 1.8

Estimated marginal means

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emmeans::emmeans(lme, c("allocation", "day"))
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Allocation	Day	Marginal means (95% CI)
Placebo	1	7.2 (6.3 to 8.0)
Dexamethasone	1	4.1 (3.2 to 5.0)
Dexamethasone+dexmedetomidine	1	3.1 (2.2 to 4.0)
Placebo	2	5.4 (4.6 to 6.3)
Dexamethasone	2	6.1 (5.2 to 7.0)
Dexamethasone+dexmedetomidine	2	5.6 (4.8 to 6.5)
Placebo	3	4.2 (3.4 to 5.1)
Dexamethasone	3	4.5 (3.7 to 5.4)
Dexamethasone+dexmedetomidine	3	4.1 (3.2 to 4.9)

Quality of sleep night 3	7.0 [6.0 to 9.0]	8.0 [6.0 to 9.0]	8.0 [6.0 to 9.0]	0.0 (-1.0 to 1.0) P = 0.815	0.0 (-1.0 to 1.0) p = 0.620	0.0 (-1.0 to 1.0) p = 0.831
Pain at 72 hours	2.0 [0.0 to 3.5]	1.5 [0.0 to 3.8]	1.0 [0.0 to 3.0]	0.0 (-1.0 to 1.0) P = 0.668	0.0 (0.0 to 1.0) p = 0.503	0.0 (-1.0 to 1.0) p = 0.811
Average pain from 48 to 72 hours	2.0 [1.0 to 4.0]	2.5 [1.0 to 4.0]	3.0 [2.0 to 4.0]	0.0 (-1.0 to 1.0) P = 0.562	0.0 (-1.0 to 1.0) p = 0.627	0.0 (-1.0 to 1.0) p = 0.980
Worst pain from 48 to 72 hours	4.0 [2.0 to 7.0]	5.0 [2.0 to 6.0]	4.0 [2.0 to 6.0]	0.0 (-1.0 to 1.0) P = 0.853	0.0 (-1.0 to 2.0) p = 0.626	0.0 (-2.0 to 1.0) p = 0.577
Cumulative opioid consumption from 0 to 72 hours	25 [5 to 78]	38 [15 to 78]	65 [25 to 97]	-20 (-45 to 0) P = 0.017	-15 (-40 to 5) p = 0.166	-8 (-25 to 10) p = 0.325

Table of median [interquartile range] for each outcome. Pairwise comparisons are Hodges-Lehmann pseudomedian estimates with 95% confidence intervals and p-value from a van Elteren test with adjustment for site. DXDM = dexamethasone + dexmedetomidine, DX = dexamethasone.