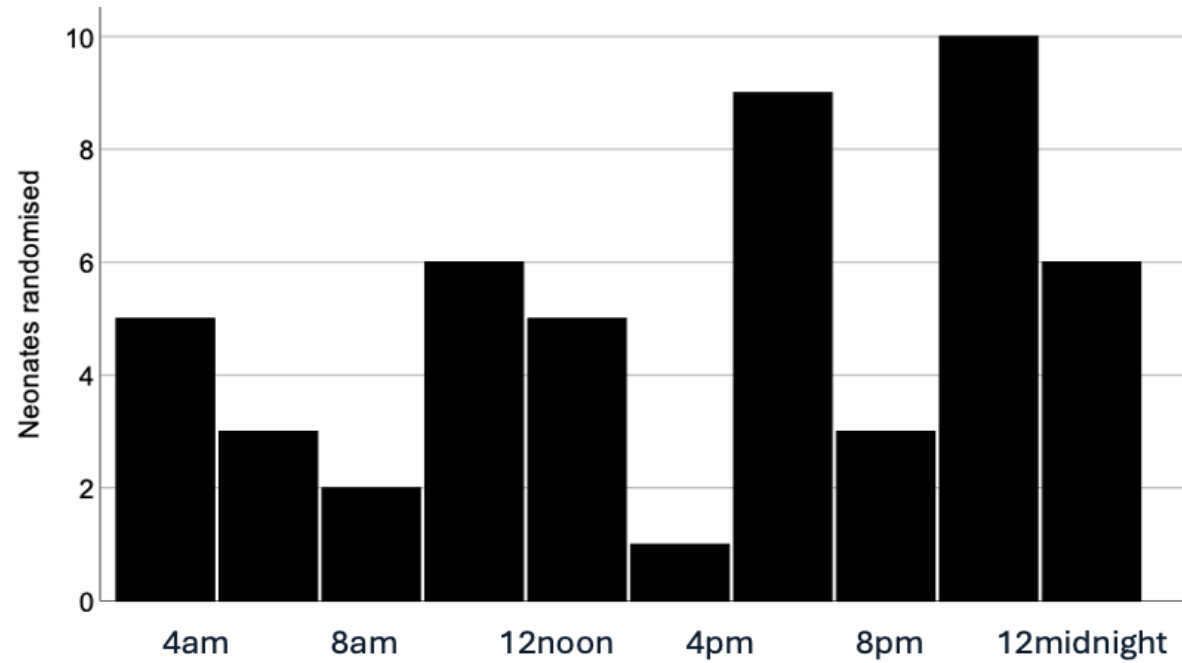
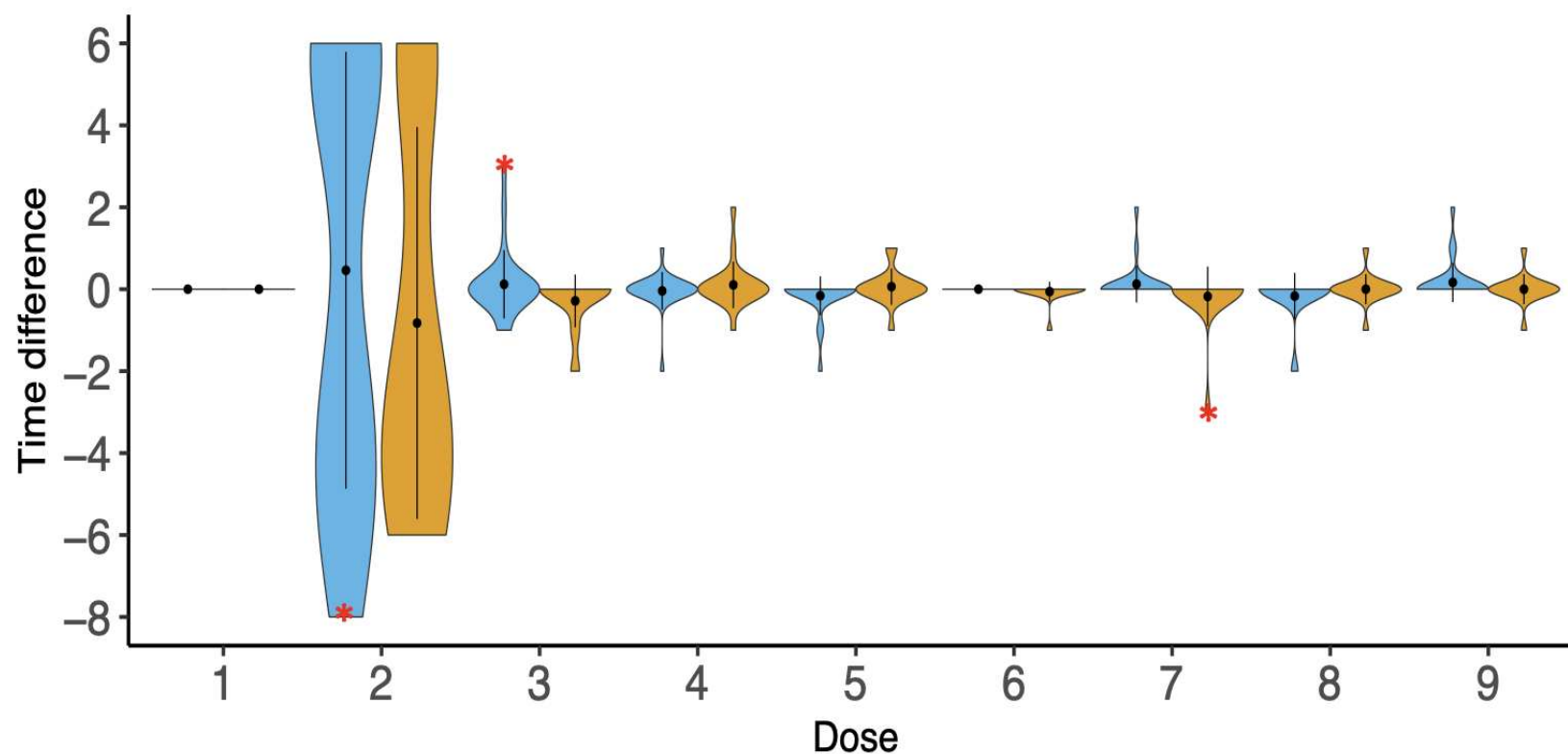


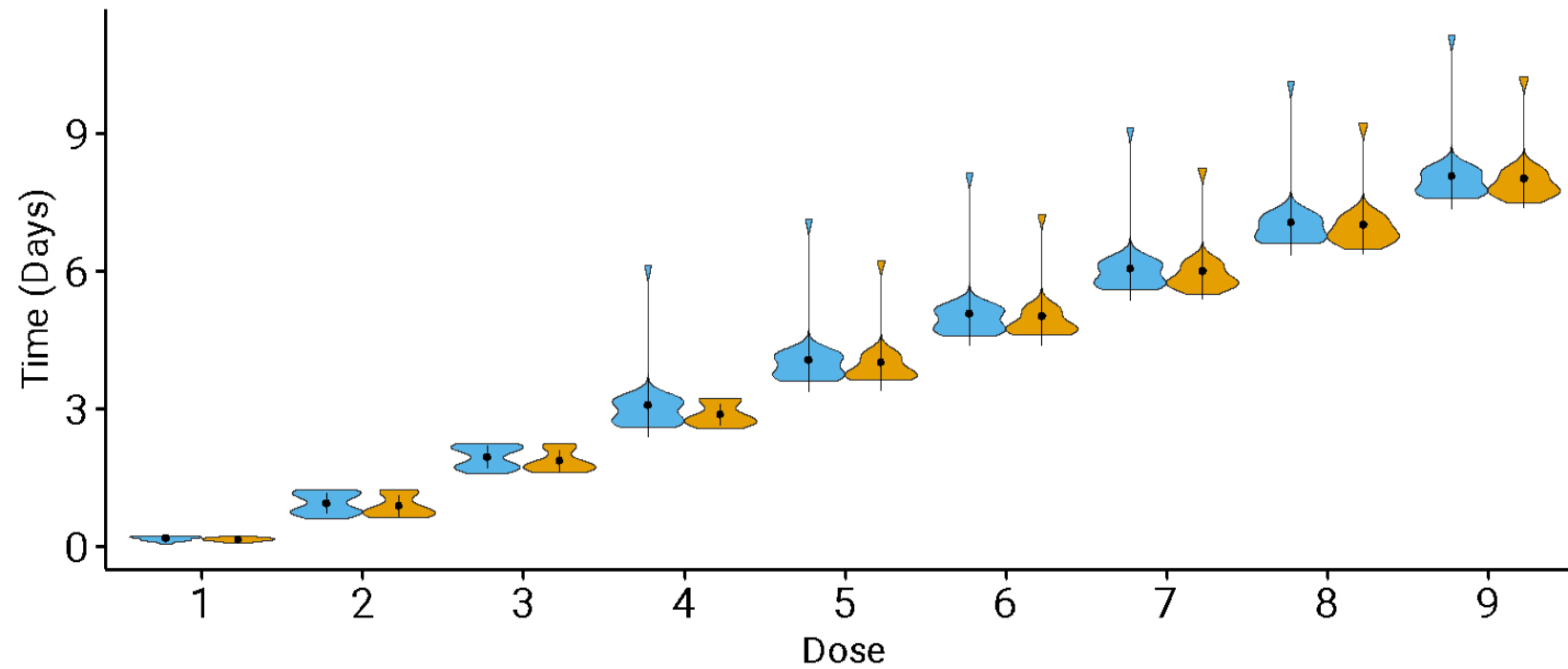
Supplementary figure 1. Time of randomisation demonstrating recruitment occurring round the clock without any systematic bias.



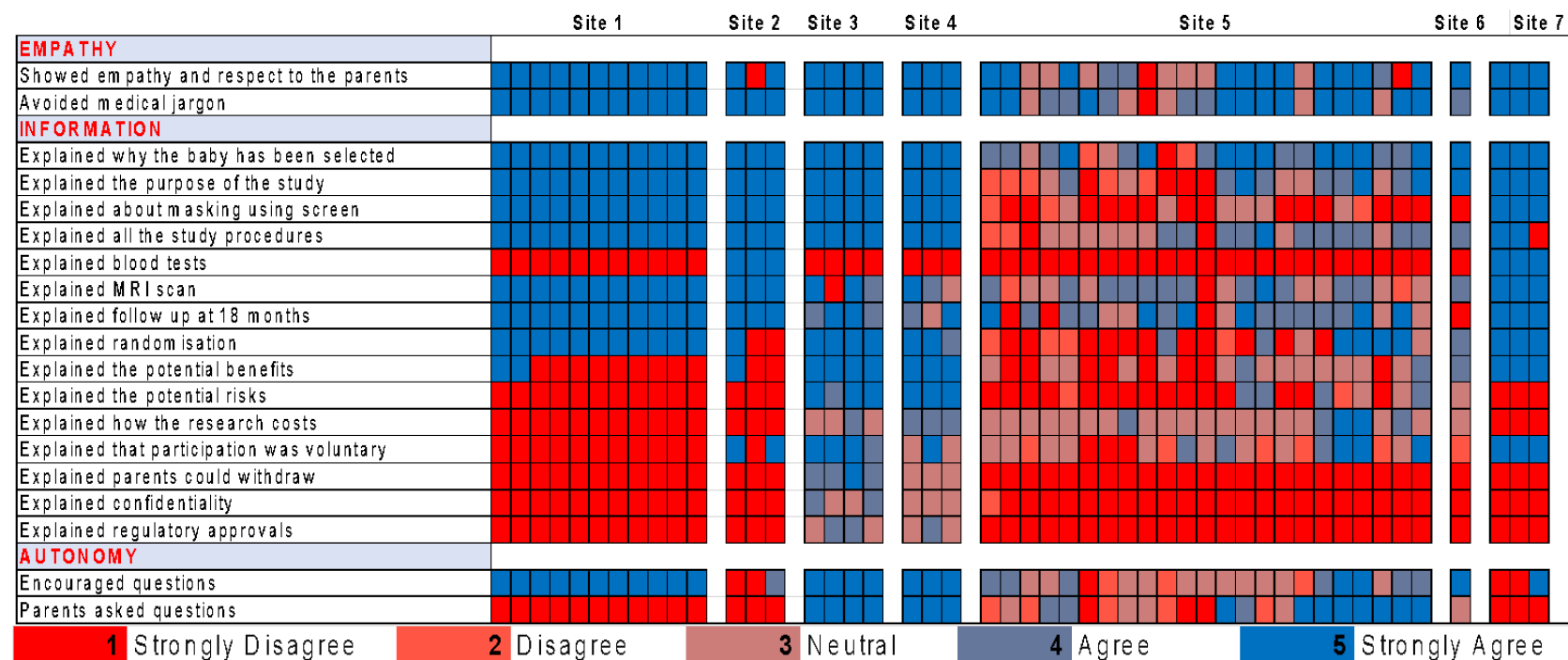
Supplementary figure 2. Scheduled and actual time of intervention amongst erythropoietin (blue) and placebo groups (orange). 0 indicates that the intervention was administered exactly at the scheduled time, plus numbers indicates intervention was given later than the scheduled time and minus indicate intervention was given earlier than the scheduled time. Red star (1 in erythropoietin and 2 in placebo) indicate if it was given outside ± 2 hours of the scheduled time (protocol deviations). In addition, one neonate had the fourth dose omitted and another had the fifth dose omitted due to nursing staff unavailability (not shown in the plot below). Both were in the erythropoietin group. An additional dose was given on day 10 so that the neonates received a total cumulative dose of 4500U/kg.



Supplementary figure 3. Age at intervention. Violin plots display median and range of age at the time of erythropoietin (blue) and placebo (orange) groups.



Supplementary figure 4. Analysis of the audio-visual records of informed consent. Likert scores under the empathy, information and autonomy domains for each participating site is color coded.



Supplementary table 1. Expanded modified Sarnat Staging and certification process.

CATEGORIES (TOTAL 6)	SIGNS OF NEONATAL ENCEPHALOPATHY (NE) IN EACH CATEGORY			
	NORMAL	MILD NE	MODERATE NE	SEVERE NE
1. Level of consciousness				
	Alert, Responsive to external stimuli (state dependent, eg. post feeds)	Hyper-alert, has a stare, jitteriness, high-pitched cry, exaggerated responds to minimal stimuli, inconsolable	Lethargic	Stupor/coma
2. Spontaneous activity				
	Changes position when awake	Normal or decreased	Decreased activity	No activity
3. Posture				
	Predominantly flexed when quiet	Mild flexion of distal joints (fingers, wrist usually)	Moderate flexion of distal joint, Complete extension	Decerebrate
4. Tone				
	Strong flexor tone in all extremities + strong flexor hip tone	Normal or slightly increased peripheral tone	Hypotonia (focal or general) or Hypertonia	Flaccid Rigid
5. Primitive reflexes (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Suck	Strong, easily elicited	Weak, poor	Weak but has a bite	Absent
Moro	Complete	Partial response, Low threshold to elicited	Incomplete	Absent
6. Autonomic system (Circle only the highest level in each sign; The maximum score is only one in any one category)				
Pupils	In dark: 2.5-4.5 mm. In light: 1.5-2.5 mm.	Mydriasis	Constricted	Deviation/ dilated/ non-reactive to light
Heart rate	100-160 bpm	Tachycardia (HR > 160)	Bradycardia (HR < 100)	Variable HR
Respiration	Regular respirations	Hyperventilation (RR > 60/min)	Periodic breathing	Apnea or requires ventilator
TOTAL SCORE				

The level of encephalopathy will be assigned based on which level of signs (moderate or severe) predominates among the 6 categories. If moderate and severe signs are equally distributed, the designation is then based on the highest level in Category #1: The level of consciousness. Infant who has seizure will be Moderate or Severe NE depending on the neurologic exam. Seizure with normal or mild NE or moderate NE on neurologic exam will be "Moderate NE". Seizure with severe NE will be "Severe NE".

Supplementary table 2. Laboratory parameters and clinical support on day 1

	Erythropoietin (N=26)		Placebo (N=24)	
	n	Summary	n	Summary
Haemoglobin, g per L	8	158 ± 23	8	169 ± 32
Hb <120 per L	8	1 (13%)	8	0 (0%)
Hb >220g per L	8	0 (0%)	8	0 (0%)
White blood cells per µL	8	22311 ± 9807	8	21343 ± 9294
WBC <5000 or >15,000	8	5 (63%)	8	7 (88%)
Platelets, 10 ⁹ per L	8	201 ± 81	8	210 ± 50
Platelets <100 x10 ⁹ per L	8	1 (13%)	8	0 (0%)
CRP >10 mg per L	2	0 (0%)	2	0 (0%)
pH	10	7.36 ± 0.14	8	7.13 ± 0.18
pCO ₂ , mm of Hg	9	18.8 [14.4, 27.6]	8	32.5 [20.7, 67.9]
Base excess (mEq/L)	10	-10.9 ± 4.4	8	-14.8 ± 6.3
Lowest blood sugar, mg per dL	11	84 [73, 102]	7	82 [64, 96]
Lowest Blood sugar <40 mg / dl	11	0 (0%)	7	0 (0%)
Highest blood sugar, mg per dL	13	98 [90, 149]	12	93 [86, 103]
Highest blood sugar >125 mg / dL	13	4 (31%)	12	1 (8%)
Prothrombin time, seconds	1	16.3 ± 0.0	0	-
Activated partial thromboplastin time, s	1	28.5 ± 0.0	0	-
International normalised ratio (INR)	1	1.3 ± 0.0	0	-
INR > 1.2	1	1 (100%)	0	-
Inotropes (any)	26	17 (65%)	24	16 (67%)
Dopamine	26	14 (54%)	24	13 (54%)
Dobutamine	26	0 (0%)	24	2 (8%)
Adrenaline	26	5 (19%)	24	4 (17%)
Noradrenaline	26	0 (0%)	24	2 (8%)
Hydrocortisone	26	0 (0%)	24	1 (4%)
Other	26	2 (8%)	24	1 (4%)
Breathing support				
None	26	0 (0%)	24	0 (0%)
Oxygen	26	0 (0%)	24	0 (0%)
CPAP	26	4 (15%)	24	4 (17%)
Invasive ventilation	26	23 (88%)	24	20 (83%)
Sedation (any)	26	2 (8%)	24	2 (8%)
Chloral hydrate	26	0 (0%)	24	0 (0%)
Fentanyl	26	1 (4%)	24	1 (4%)
Morphine	26	1 (4%)	24	0 (0%)
Melatonin	26	0 (0%)	24	0 (0%)
Other	26	0 (0%)	24	1 (4%)
Anticonvulsants (any)	26	13 (50%)	24	10 (42%)
Phenobarbitone	26	11 (42%)	24	9 (38%)
Phenytoin	26	2 (8%)	24	2 (8%)
Levetiracetam	26	3 (12%)	24	4 (17%)
Clonazepam	26	0 (0%)	24	0 (0%)
Midazolam	26	3 (12%)	24	1 (4%)
Others	26	0 (0%)	24	0 (0%)
Sedation and/or anti-convulsant (any)	26	14 (54%)	24	11 (46%)
Clinical seizures	26	9 (35%)	24	8 (33%)
Antibiotics	26	22 (85%)	24	22 (92%)
Fluids therapy				
IVF	26	25 (96%)	24	23 (96%)
IVF and NG feeds	26	1 (4%)	24	0 (0%)
NG feeds	26	0 (0%)	24	1 (4%)
Other	26	3 (12%)	24	1 (4%)

Summary statistics are: mean ± standard deviation, median [inter-quartile range] or number (percentage)

Supplementary table 3. Laboratory parameters and clinical support on day 2

	Erythropoietin (N=26)		Placebo (N=24)	
	n	Summary	n	Summary
Haemoglobin, g per L	8	148 ± 29	8	143 ± 31
Hb <120g per L	8	1 (13%)	8	1 (13%)
Hb >220g per L	8	0 (0%)	8	0 (0%)
White blood cells per µL	8	18018 ± 9538	8	19998 ± 4540
WBC <5000 or >15,000	8	5 (63%)	8	6 (75%)
Platelets, 10 ⁹ per L	8	178 ± 53	8	107 ± 46
Platelets <100 x10 ⁹ per L	8	0 (0%)	8	5 (63%)
CRP >10 mg per L	4	2 (50%)	3	2 (67%)
pH	6	7.25 ± 0.25	7	7.17 ± 0.24
pCO ₂ , mm of Hg	6	26.1 [21.9, 35.2]	7	40.3 [30.0, 70.6]
Base excess (mEq/L)	10	-12.0 ± 4.5	7	-8.4 ± 10.8
Lowest blood sugar, mg per dL	10	90 [78, 94]	9	79 [74, 94]
Lowest Blood sugar <40 mg / dl	10	0 (0%)	9	0 (0%)
Highest blood sugar, mg per dL	11	100 [88, 150]	9	98 [92, 102]
Highest blood sugar >125 mg / dL	11	4 (36%)	9	1 (11%)
Prothrombin time, seconds	1	43.0 ± 0.0	1	22.8 ± 0.0
Activated partial thromboplastin time, seconds	0	-	0	-
International normalised ratio (INR)	1	3.3 ± 0.0	1	1.7 ± 0.0
INR > 1.2	1	1 (100%)	1	1 (100%)
Inotropes (any)	26	18 (69%)	24	15 (63%)
Dopamine	26	15 (58%)	24	12 (50%)
Dobutamine	26	3 (12%)	24	4 (17%)
Adrenaline	26	7 (27%)	24	7 (29%)
Noradrenaline	26	1 (4%)	24	1 (4%)
Hydrocortisone	26	0 (0%)	24	2 (8%)
Other	26	2 (8%)	24	2 (8%)
Breathing support				
None	26	0 (0%)	24	2 (8%)
Oxygen	26	2 (8%)	24	3 (13%)
CPAP	26	3 (12%)	24	3 (13%)
Invasive ventilation	26	21 (81%)	24	16 (67%)
Sedation (any)	26	2 (8%)	24	2 (8%)
Chloral hydrate	26	0 (0%)	24	0 (0%)
Fentanyl	26	1 (4%)	24	1 (4%)
Morphine	26	1 (4%)	24	0 (0%)
Melatonin	26	0 (0%)	24	0 (0%)
Other	26	0 (0%)	24	1 (4%)
Anticonvulsants (any)	26	14 (54%)	24	11 (46%)
Phenobarbitone	26	12 (46%)	24	10 (42%)
Phenytoin	26	3 (12%)	24	2 (8%)
Levetiracetam	26	5 (19%)	24	5 (21%)
Clonazepam	26	0 (0%)	24	0 (0%)
Midazolam	26	4 (15%)	24	1 (4%)
Others	26	0 (0%)	24	0 (0%)
Sedation and/or anti-convulsant (any)	26	15 (58%)	24	12 (50%)
Clinical seizures	26	4 (15%)	24	5 (21%)
Antibiotics	26	25 (96%)	24	23 (96%)
Fluids therapy				
IVF	26	18 (69%)	24	13 (54%)
IVF and NG feeds	26	7 (27%)	24	9 (38%)
NG feeds	26	1 (4%)	24	2 (8%)
Other	26	2 (8%)	24	1 (4%)

Summary statistics are: mean ± standard deviation, median [inter-quartile range] or number (percentage)

Supplementary table 4. Laboratory parameters and clinical support on day 3

	Erythropoietin (N=25)		Placebo (N=21)	
	n	Summary	n	Summary
Haemoglobin, g per L	8	165 ± 21	7	161 ± 48
Hb <120g per L	8	0 (0%)	7	1 (14%)
Hb >220g per L	8	0 (0%)	7	1 (14%)
White blood cells per μ L	8	14018 ± 5873	6	7854 ± 4377
WBC <5000 or >15,000	8	3 (38%)	6	1 (17%)
Platelets, 10^9 per L	8	191 ± 72	7	132 ± 88
Platelets <100 x 10^9 per L	8	1 (13%)	7	0 (0%)
CRP >10 mg per L	4	2 (50%)	7	4 (57%)
pH	6	7.35 ± 0.19	5	7.34 ± 0.16
pCO ₂ , mm of Hg	5	29.0 [23.6, 47.0]	5	28.6 [27.8, 32.3]
Base excess (mEq/L)	5	-8.5 ± 5.6	5	-7.5 ± 7.8
Lowest blood sugar, mg per dL	7	83 [68, 92]	4	83 [79, 97]
Lowest Blood sugar <40 mg / dl	7	1 (14%)	4	0 (0%)
Highest blood sugar, mg per dL	9	106 [102, 124]	6	99 [84, 104]
Highest blood sugar >125 mg / dL	9	2 (22%)	6	1 (17%)
Prothrombin time, seconds	1	9.8 ± 0.0	1	18.6 ± 0.0
Activated partial thromboplastin time, seconds	1	27.3 ± 0.0	0	-
International normalised ratio (INR)	1	0.9 ± 0.0	1	1.5 ± 0.0
INR > 1.2	1	0 (0%)	0	1 (100%)
Inotropes (any)	25	17 (68%)	21	12 (57%)
Dopamine	25	14 (56%)	21	11 (52%)
Dobutamine	25	2 (8%)	21	4 (19%)
Adrenaline	25	9 (36%)	21	2 (10%)
Noradrenaline	25	1 (4%)	21	5 (24%)
Hydrocortisone	25	3 (12%)	21	1 (5%)
Other	25	1 (4%)	21	1 (5%)
Breathing support				
None	25	1 (4%)	21	3 (14%)
Oxygen	25	1 (4%)	21	2 (10%)
CPAP	25	4 (16%)	21	3 (14%)
Invasive ventilation	25	19 (76%)	21	13 (62%)
Sedation (any)	25	1 (4%)	21	1 (5%)
Chloral hydrate	25	0 (0%)	21	0 (0%)
Fentanyl	25	1 (4%)	21	1 (5%)
Morphine	25	0 (0%)	21	0 (0%)
Melatonin	25	0 (0%)	21	0 (0%)
Other	25	0 (0%)	21	0 (0%)
Anticonvulsants (any)	25	13 (52%)	21	11 (52%)
Phenobarbitone	25	13 (52%)	21	10 (48%)
Phenytoin	25	3 (12%)	21	3 (14%)
Levetiracetam	25	5 (20%)	21	5 (24%)
Clonazepam	25	0 (0%)	21	0 (0%)
Midazolam	25	1 (4%)	21	0 (0%)
Others	25	0 (0%)	21	0 (0%)
Sedation and/or anti-convulsant (any)	25	14 (56%)	21	12 (57%)
Clinical seizures	25	1 (4%)	21	2 (10%)
Antibiotics	25	24 (96%)	21	20 (95%)
Fluids therapy				
IVF	25	15 (60%)	21	11 (52%)
IVF and NG feeds	25	8 (32%)	21	9 (43%)
NG feeds	25	1 (4%)	21	1 (5%)
Other	25	2 (8%)	21	2 (10%)

Summary statistics are: mean ± standard deviation, median [inter-quartile range] or number (percentage)

Supplementary table 5. Laboratory parameters and clinical support on day 4.

	Erythropoietin (N=25)		Placebo (N=17)	
	n	Summary	n	Summary
Haemoglobin, g per L	3	139 ± 29	3	159 ± 27
Hb <120g per L	3	1 (33%)	3	0 (0%)
Hb >220g per L	3	0 (0%)	3	0 (0%)
White blood cells per µL	3	9257 ± 4409	3	15467 ± 5859
WBC <5000 or >15,000	3	1 (33%)	3	1 (33%)
Platelets, 10 ⁹ per L	3	149 ± 134	3	142 ± 108
Platelets <100 x 10 ⁹ per L	3	1 (33%)	3	1 (33%)
CRP >10 mg per L	3	1 (33%)	1	0 (0%)
pH	4	7.45 ± 0.14	2	7.42 ± 0.15
pCO ₂ , mm of Hg	4	24.5 [16.7, 36.3]	2	27.7 [17.9, 37.4]
Base excess (mEq/L)	3	-4.1 ± 1.1	2	-6.3 ± 0.9
Lowest blood sugar, mg per dL	7	72 [68, 89]	4	76 [71, 95]
Lowest Blood sugar <40 mg / dl	7	1 (14%)	4	0 (0%)
Highest blood sugar, mg per dL	10	97 [72, 98]	5	91 [88, 94]
Highest blood sugar >125 mg / dL	10	1 (10%)	5	0 (0%)
Prothrombin time, seconds	2	26.2 ± 18.1	0	-
Activated partial thromboplastin time, seconds	0	-	0	-
International normalised ratio (INR)	1	1.0 ± 0.0	0	-
INR > 1.2	1	1 (100%)	0	-
Inotropes (any)	25	14 (56%)	17	6 (35%)
Dopamine	25	11 (44%)	17	6 (35%)
Dobutamine	25	1 (4%)	17	1 (6%)
Adrenaline	25	5 (20%)	17	2 (12%)
Noradrenaline	25	1 (4%)	17	2 (12%)
Hydrocortisone	25	3 (12%)	17	0 (0%)
Other	25	2 (8%)	17	0 (0%)
Breathing support				
None	25	2 (8%)	17	3 (18%)
Oxygen	25	4 (16%)	17	1 (6%)
CPAP	25	3 (12%)	17	5 (29%)
Invasive ventilation	25	16 (64%)	17	8 (47%)
Sedation (any)	25	1 (4%)	17	0 (0%)
Chloral hydrate	25	0 (0%)	17	0 (0%)
Fentanyl	25	1 (4%)	17	0 (0%)
Morphine	25	0 (0%)	17	0 (0%)
Melatonin	25	0 (0%)	17	0 (0%)
Other	25	0 (0%)	17	0 (0%)
Anticonvulsants (any)	25	14 (56%)	17	7 (41%)
Phenobarbitone	25	14 (56%)	17	7 (41%)
Phenytoin	25	3 (12%)	17	1 (6%)
Levetiracetam	25	4 (16%)	17	3 (18%)
Clonazepam	25	0 (0%)	17	0 (0%)
Midazolam	25	0 (0%)	17	0 (0%)
Others	25	0 (0%)	17	0 (0%)
Sedation and/or anti-convulsant (any)	25	15 (60%)	17	7 (41%)
Clinical seizures	25	1 (4%)	17	1 (6%)
Antibiotics	25	22 (88%)	17	15 (88%)
Fluids therapy				
IVF	25	11 (44%)	17	6 (35%)
IVF and NG feeds	25	9 (36%)	17	10 (59%)
NG feeds	25	2 (8%)	17	1 (6%)
Other	25	5 (20%)	17	3 (18%)

Summary statistics are: mean ± standard deviation, median [inter-quartile range] or number (percentage)