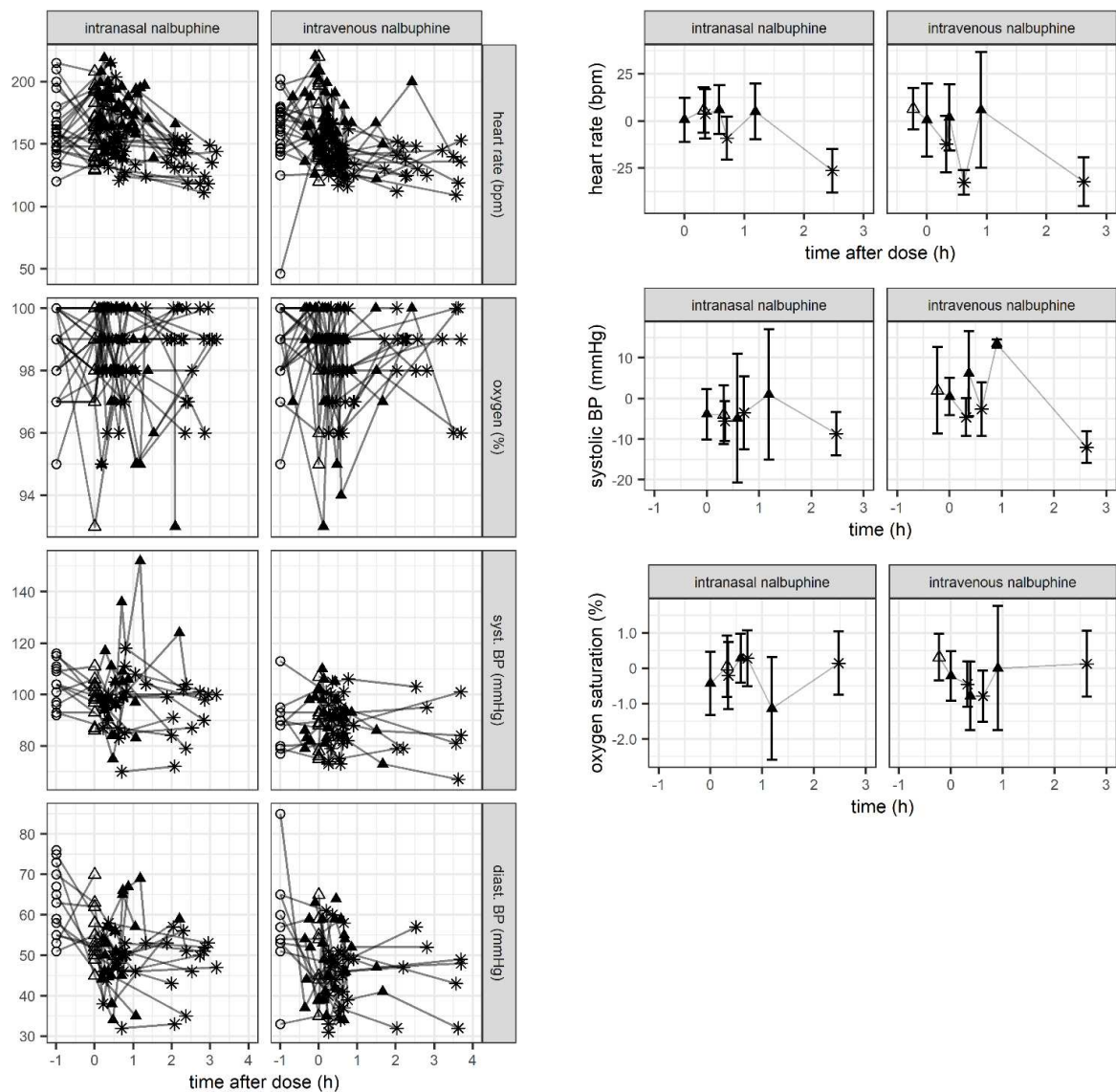


Supplemental Material



Supplementary Figure: left: Illustration of (vital signs (A-D) measured in all patients having received nalbuphine. Right: Data is illustrated as mean change from baseline with 95% confidence interval (error bars).

○: baseline ▲: establishment of venous accesses, urinary catheterization, lumbar puncture. Δ: nalbuphine administration. *: blood sampling for pharmacokinetic assessment.

Supplementary Table: Supplement: Summary of Neonatal Infant Pain Score (NIPS) for all 52 patients who received nalbuphine as indicator of pain control (baseline, during establishment of venous access, urinary catheterization and lumbar puncture) and tolerability of route of administration (during nalbuphine administration) *

	Baseline	Establishing venous access		Nalbuphine administration (intravenous and intranasal)		Urinary Catheterization		Lumbar puncture	
		iv group N (%)	intranasal group N (%)	iv group N (%)	intranasal group N (%)	iv group N (%)	intranasal group N (%)	iv group N (%)	intranasal group N (%)
Neonatal Infant Pain Score (NIPS)									
number (%) of patients available for NIPS evaluation	43/52 (83%)	19/26 (73%)	21/26 (81%)	14/26 (54%)	21/26 (81%)	22/26 (85%)	20/26 (77%)	11/26 (42%)	14/26 (54%)
low <3 mild to no pain	33/43 (77%)	7/19 (37%)	7/21 (33%)	10/14 (71%)	14/21 (67%)	5/22 (23%)	7/20 (35%)	1/11 (9%)	4/14 (29%)
medium 3+4 moderate pain	5/43 (12%)	4/19 (21%)	1/21 (5%)	1/14 (7%)	1/21 (5%)	7/22 (32%)	3/20 (15%)	1/11 (9%)	2/14 (14%)
high > 4 severe pain	5/43 (12%)	8/19 (42%)	13/21 (62%)	3/14 (21%)	6/21 (29%)	10/22 (45%)	10/20 (50%)	9/11 (82%)	8/14 (57%)

N = number of patients. *Interventions for medical work up were carried out at 5 minutes before (iv)/after (intranasal) nalbuphine administration (establishment of venous access for blood sampling), and 20, and 35 minutes after drug administration (urinary catheterization and lumbar puncture, respectively).