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Table 2-online: **Criteria and Management of Feeding Intolerance.**

Signs of feeding intolerance		**Management*** **
Gastric aspirate prior to the feeding	**Other signs** of feeding intolerance**	
1a*) if both ≤2 ml **and** ≤1/3 of previous feed volume	None	Refeed aspirate as part of total volume, continue feeding
1b*) if ≤2 ml **but** >1/3 of previous feed volume or if >2 ml **but** <1/3 of previous feed volume	None	Check infant, then may refeed aspirate as part of total volume, and continue feeding. Or may hold feeding and resume in 3 hours.
2) if >2 ml and > 1/3 of previous feed volume	None	Stop feeding and recheck gastric aspirate in 3 hours. Resume feeding when conditions revert to 1 above.
3) Irrespective	Present	Stop feeding, perform appropriate evaluation**** and resume when infant stable and conditions revert to (1) above.

* if continuous naso or orogastric feedings are used, check for residuals every 3 – 4 hours. Tolerate residuals of ≤ 2ml or < 2 hours worth of feeds (whichever is more.)

** **Other signs** will include one or more of the following:
a) blood stained gastric aspirate;
b) vomiting ≥ 1/3 of the previous feed volume;
c) abdominal distension, discoloration or tenderness;
d) visible bowel loops
e) bloody stool;
f) KUB showing signs of intestinal dilatation;
g) metabolic acidosis or new thrombocytopenia;
h) Evidence that the child is not well: apnea (new onset or increasing frequency), respiratory distress, lethargy, poor perfusion, temperature instability, etc.

*** Recommendations: If residuals are bile stained or >1/3 feed volume, consider checking feeding tube placement, placing the infant prone or right side down; consider glycerin suppository if >18 hours since last stool; if recurrent episodes occur after a recent feeding advance, consider returning to the previously tolerated feeding volume

**** Evaluation of significant feeding intolerance to be performed by the primary clinical team according to the standard practice: (e.g., physical exam, X-ray, CBC, cultures, etc).

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Table 4; online. Demographics of Ibuprofen, Indomethacin, and Total Populations: univariate analyses

Demographic and Risk variables:	**Ibuprofen Population**		**Indomethacin Population**		**Total Population**	
	Fasting (*npo*) n=24	**Feeding n=16**	**Fasting (*npo*) n=72**	**Feeding n=65**	**Fasting (*npo*) n=96**	**Feeding n=81**
Study drug-indomethacin, %	0	0	100	100	75	80
Multiple birth, %	38	25	42	20 [a]	41	21 [a]
Rupture of membranes >18h, %	22	19	17	24	18	23
Preterm labor, %	75	63	65	78 [b]	68	75
Maternal Diabetes, %	8	0	10	8	9	6
Chorioamnionitis, %	25	13	10	11	14	11
Preeclampsia, %	29	38	18	14	21	19
Betamethasone (>6hr), %	83	53 [a]	70	71	74	68
Betamethasone (>24hr), %	63	40	55	57	57	54
Antenatal antibiotics, %	63	50	46	56	50	55
Birthweight-gm, mean (SD)	875 (186)	818 (164)	872 (212)	867 (173)	873 (205)	857 (171)
Birthweight categories:						
≤700 gm, %	17	31	26	17	24	20
701-1000 gm, %	54	50	42	62	45	59
1001-1250 gm, %	29	19	32	22	31	21
Gestation-wk, mean (SD)	26.5 (1.9)	26.3 (1.8)	26.2 (2.1)	26.2 (1.8)	26.3 (2.0)	26.2 (1.8)
SGA, %	13	6	8	3	9	4
5 min Apgar <4, %	8	13	8	12	8	12
Male sex, %	42	25	42	57 [b]	42	51
Caucasian, %	63	44	59	48	60	47 [b]
RDS, %	75	100 [a]	89	92	85	94 [b]
Surfactant, %	88	100	85	80	85	84
RSS at 24 hours-unit, mean (SD)	1.8 (1.0)	2.6 (2.7)	1.9 (1.1)	1.9 (1.2)	1.9 (1.1)	2.0 (1.6)
Vasopressors needed prior to enrollment, %	8	0	6	8	6	6
Prophylactic Indomethacin prior to enrollment, %	4	13	25	26	20	23
Hydrocortisone prior to enrollment, %	4	0	6	6	5	5
UAC present at enrollment, %	46	56	42	31	43	36
UVC present at enrollment, %	50	50	47	28 [a]	48	32 [a]
RSS at enrollment, mean	1.6	1.9	2.1	2.1	2.0	2.0

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(SD)	(0.9)	(1.3)	(2.1)	(2.1)	(1.9)	(2.0)
Number of contiguous initial study drug courses						
1-course, %	63	56	72	75	70	72
2-courses, %	29	38	25	25	26	27
3-courses, %	8	6	3	0	4	1
PDA failed to close after initial drug treatment, %	54	75	59	58	57	62
Additional study drug given during feeding advance, %	13	19	10	5	10	7
Ligation during feeding advance, %	29	31	14	19	18	21
Ligation during hospitalization, %	33	38	21	36 [b]	24	36 [b]
Age at 1st feeding-days, mean (SD)	4.7 (3.8)	3.8 (1.7)	4.9 (3.8)	3.5 (2.7) [a]	4.9 (3.8)	3.5 (2.6) [a]
Maximum enteral volume prior to study-ml/kg/d, mean (SD)	11.4 (12.5)	9.3 (11.3)	12.6 (14.9)	17.1 (16.7) [b]	12.3 (14.3)	15.6 (16.0)
Age at study entry-days, mean (SD)	5.3 (2.8)	5.5 (2.6)	6.7 (4.1)	6.9 (4.2)	6.4 (3.8)	6.6 (4.0)
Milk type-breast milk, %	92	75	81	86	83	84

[a] = $p<0.05$
[b] = $p<0.10$

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Table 6; online. Effect of "feeding" versus "fasting (*npo*)" on neonatal outcomes: univariate analyses

	Ibuprofen Population		**Indomethacin Population**		**Total Population**	
	Fasting (*npo*) n=24	**Feeding n=16**	**Fasting (*npo*) n=72**	**Feeding n=65**	**Fasting (*npo*) n=96**	**Feeding n=81**
Feeding Related Outcomes:						
Age when taking 120 ml/k/d-days, mean (SD)	25.8 (10.1)	24.7 (9.6)	23.4 (9.4)	20.8 (8.3) [b]	24.0 (9.6)	21.6 (8.7) [b]
Actual Number of days to reach 120 ml/k/d, mean (SD)	15.4 (8.1)	13.4 (8.4)	12.3 (7.6)	9.5 (5.9) [a]	13.1 (7.8)	10.3 (6.6) [a]
Difference between Actual and Ideal number of days to reach 120 ml/k/d), mean (SD)	7.5 (7.4)	4.9 (8.7)	4.7 (6.9)	2.5 (5.5) [a]	5.5 (7.1)	3.0 (6.3) [a]
Feeding advance delayed by feeding intolerance or NEC, %	46	38	38	21 [a]	40	24 [a]
Feeding advance delayed by "other" causes, %	54	56	41	59 [a]	44	59 [b]
NEC/perforation prior to reaching 120 ml/k/d, %	4	6	4	0 [b]	4	1
NEC/perforation ANY TIME during hospitalization, %	8	25	14	6	13	10
Age when central venous line removed-days, mean (SD)	30.1 (13)	26.2 (18)	30 (32)	27 (21)	30 (28)	27 (21)
infection during feeding advance, %	42	13 [a]	31	29	34	26
infection any time during hospitalization, %	54	31	42	48	45	44
Other Morbidities:						
ICH gr III or IV, %	8	6	7	5	7	5
PVL or hydrocephalus, %	13	6	6	6	7	6
BPD, %	43	50	33	57 [a]	36	56 [a]
ROP-treated, %	9	13	3	11 [b]	4	12 [b]
Death, %	4	6	8	5	7	5
Death or BPD, %	43	50	38	59 [a]	39	58 [a]
Death, NEC or BPD,	52	63	40	61 [a]	43	61 [a]

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%						

[a] = p<0.05
[b] = p<0.10
Definitions: Age, Postnatal age (day of birth = 0 days); *Necrotizing enterocolitis*, Bell's classification ≥II (treated medically or surgically) and "spontaneous perforations" occurring before 7 days of life; *Infection*, any culture positive infection (bacteremia, pneumonia, urinary tract infection, meningitis); *ICH*, intracranial hemorrhage ≥ Grade III; *PVL*, cystic periventricular leukomalacia diagnosed by ultrasound; *BPD*, Bronchopulmonary Dysplasia: the need for supplemental oxygen to maintain oxygen saturation >90% at 36 weeks corrected age; *ROP*, stage 2 with plus disease or stage 3 treated with either laser or bevacizumab; *Feeding advance delayed by "other" causes*, percent of the population that had their feeding advance interrupted or delayed by one or more of the following causes: a) PDA ligation, b) sepsis workup, recurrent apneas, respiratory deterioration, c) hypotension requiring inotropes, or d) blood transfusions.

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