NICE or not so NICE Refeeding Guidelines

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Introduction



NEN STARVE IN MINNESOTA Comscientious objectors volunteer for strict hunder tests to study europe's food problem

FIGURE 2 Life magazine photograph of conscientious objectors during starvation experiment. July 30, 1945. Volume 19, Number 5, p. 43. Credit: Wallace Kirkland/Time Life Pictures/Getty Images.

Keys *et al.* (1950) In: The Biology of Human Starvation. Minneapolis, MN: University of Minnesota Press.

Death resulting from overzealous total parenteral nutrition: the refeeding syndrome revisited^{1, 2}

Roland L. Weinsier, M.D., Dr.P.H. and Carlos L. Krumdieck, M.D., Ph.D.

ABSTRACT Although cachectic patients are relatively well adapted to their calorically deprived state, they are prone to acute metabolic imbalances when infused with hypertonic solutions of dextrose and amino acids. Of particular concern is hypophosphatemia and its associated disorders of cardiac, pulmonary, hematological, and neuromuscular functions. This report describes two chronically malnourished but stable patients who were given aggressive total parenteral nutrition support, which was rapidly followed by acute cardiopulmonary decompensation associated with severe hypophosphatemia and other metabolic abnormalities. Despite attempts at correction, progressive multiple systems failure led to death. In light of the high prevalence of hospital malnutrition and the ready availability of total parenteral nutrition, attention is brought to these examples of how overzealous nutrition repletion can paradoxically precipitate deterioration in clinical status. *Am. J. Clin. Nutr.* 34: 393–399, 1981.

KEY WORDS Total parenteral nutrition, hyperalimentation, hypophosphatemia, hospital malnutrition, protein-calorie malnutrition, marasmus

Definition

- Metabolic and physiological problems of feeding malnourished patients
- Key factors involved
 - Glucose
 - Magnesium, Phosphate & Potassium
 - Vitamins (thiamine)
 - Fluid & sodium
- No internationally agreed definition making comparisons difficult
- Prevalence currently unknown

Starvation & Refeeding



Adapted from Stanga et al (2008) Eur J Clin Nutr. 62:687



Consequences

	Cardiac	Respiratory	Neuro- muscular
Phosphate	Altered myocardial function, Arrhythmia, congestive heart failure	Acute ventilatory failure	Lethargy, weakness, seizures, confusion, coma, paralysis, rhabdomyolysis
Potassium	Arrhythmia, cardiac arrest	Respiratory distress	Paralysis, weakness, rhabdomyolysis
Magnesium	Arrhythmia, tachycardia	Respiratory depression	Ataxia, confusion, muscle tremors, weakness, tetany
Thiamine	Congestive heart failure & lactic acidosis		Wernicke-Korsakoff syndrome, muscle weakness

National Institute for Health and Clinical Excellence

Issue date: February 2006

Nutrition support in adults

Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition

D Grade Evidence

Clinical Guideline 32 Developed by the National Collaborating Centre for Acute Care

National Collaborating Centre for Acute Care, Feb 2006. Nutrition support in adults oral nutrition support, enteral tube feeding and parenteral nutrition

Patients at High Risk (NICE 2006)

- Patient has one or more of the following:
 - BMI <16kg/m²
 - Unintentional weight loss >15% over 3-6 months
 - Little or no nutritional intake for >10 days
 - Low levels of potassium, phosphate or magnesium prior to feeding

OR

- Patient has two or more of the following:
 - BMI less than 18.5kg/m²
 - Unintentional weight loss >10% over 3-6 months
 - Little or no nutritional intake for >5 day
 - A history of alcohol abuse or drugs including insulin, chemotherapy, antacids & diuretics

D Grade Evidence

How to feed patients at risk (NICE 2006)

High risk

- Consider starting nutrition support at a maximum of 10kcal/kg increasing levels slowly to meet or exceed needs by 4 -7 days
- Consider restoring circulatory volume and monitoring fluid balance and overall clinical status closely

• Extreme high risk

Consider using only 5 kcal/kg/day and monitoring cardiac rhythm continually in these patients

D Grade Evidence

How to feed patients at risk (NICE 2006)

Consider providing immediately

before and during the first 10 days of feeding:

- Oral thiamine 200-300 mg/day
- Vitamin B co strong 1or 2 tablets tds OR
- Full dose intravenous vitamin B preparation <u>if necessary</u>
- A balanced multivitamin/trace element supplement

Consider providing oral, enteral or intravenous supplements of:

- Potassium = 2 4mmol/kg/day
- Phosphate = 0.3 0.6mmol/kg/day
- Magnesium = IV 0.2 or oral 0.4mmol/kg/day
 - (unless pre-feeding plasma levels are high)
- Pre feeding correction of low plasma levels unnecessary

D Grade Evidence

Other Guidelines

Reference	Energy	Protein	Electrolytes	Fluid	Micro nutrients
Solomen & Kirby (1990) <i>JPEN,</i> 14:90	20kcal/kg	1.2-1.5g	_	_	
Dewar & Horvath (2001) <i>A Pocket</i> <i>Guide to Clinical</i> <i>Nutrition</i>	20kcal/kg	_	Replenish as required	_	Thiamine IV 48hrs → Oral & Forceval
Crook <i>et al</i> (2001) <i>Nutrition.</i> 7:632	20kcal/kg	1.2-1.5g	Replenish as required	_	Thiamine IV 48hrs \rightarrow Oral
Kraft <i>et al</i> (2005) <i>Nutr Clin Pract.</i> 20:625	25% of requirements	_	10 -15mmol of PO4/1000kcal Replenish as required	<1L/d	Thiamine IV 50- 100mg/d or 100mg PO 5-7d & multivitamin
Stanga <i>et al</i> (2008) <i>Eur J Clin Nutr.</i> 62:687	10kcal/kg 50-60% CHO 30-40% Fat	10-20%	KCL: 1-3mmol/kg Mg 0.3-0.4mmol/kg PO4 0.5-0.8mmol/kg Na <1mmol/kg	20- 30ml/kg	100% Thiamine IV 200- 300 for 72hrs

Attitudes to NICE Refeeding Guidelines

- Unpublished survey of HCP
- 44% of doctors followed the guidance vs. 70% of dietitians
- 39% thought guidance was safe practice
- 36% thought excessively cautious
- Obstacle to providing adequate nutrition
- Other never seen refeeding despite providing 100% requirement from day 1

Dietetic Practice in Refeeding

- Questionnaire including 3 case studies
- 30.8% response rate, 89.8% had read NICE
- 66.9% changed practice based on NICE
- 89.5% do not wait for normal biochemistry
- Feed increased over 3-4 days
- 75% supplement electrolytes reactively
- Current practice is inconsistent but 20kcal/kg common
- Common themes: lack of evidence, overcautious & exacerbate malnutrition vs. better safe than sorry
- Clinical Judgment
- Advice on supplementation confusing or difficult to follow and often impractical.

Wagstaff (2011) JHND 24:505

Marsipan Report (2010)

- Joint report Royal College of Physicians & Royal College of Psychiatrists working group
- Recommendation 8
- The key tasks of the in patient team are to:
 - safely re-feed the patient
 - avoid re-feeding syndrome caused by too rapid re-feeding
 - avoid underfeeding syndrome caused by too cautious rates of re-feeding

Refeeding in Anorexia Nervosa

- 33 in-patients with anorexia nervosa
 - Mean BMI 11.3±0.7kg/m²,REE 777±145kcal/d
- Treatment:
 - Oral/enteral thiamine & B vitamins bd before feeding
 - IV 5-10% glucose ~20-40ml/hr (n=29)
 - NG feeding over 24 hr (n=30), ONS (n=3)

Gentile et al (2010) Clin Nutr 29:627

Refeeding in Anorexia Nervosa

	Time								
	Day 0	7 days	15 days	30 days					
Measured kcal/expenditure — kcal/day	776 ± 145								
Enteral feeding regimen — kcal/day	806 ± 269	1002 ± 270	1133 ± 420	1154 ± 420					
Oral diet — kcal/day	431 ± 331 (25) ^b	707 ± 320	890 ± 314	1162 ± 387					
Glucose ^c kcal/day — i.v. ^d infusion	$171 \pm 56 (29)$	$186 \pm 91 \ (28)$	$189 \pm 113~(21)$	$194 \pm 88 (15)$					
Phosphate mEq/day — i.v./oral	39.9 ± 24.8 (26)	$45.0\pm 32.0(25)$	$46.5\pm 32.0(23)$	$32.5\pm26.9(23)$					
Potassium mEq/day — i.v./oral	33.0 ± 19.2 (21)	$29.9 \pm 13.9 (16)$	$29.7 \pm 20.9 (15)$	$20 \pm 8.2 \ (16)$					
Body weight – kg	29.1 ± 3.2	30.3 ± 3.8	31.35 ± 2.8	32.3 ± 2.9					
$BMI^{f} - kg/m^{2}$	11.3 ± 0.7	11.8 ± 0.7	12.2 ± 0.9	12.6 ± 0.9					
Δ Body weight ^g – kg	0	1.2 ± 1.3	2.3 ± 1.8	3.2 ± 2.2					

Day 1

NG feeding & glucose & oral food = Total kcal day 1 => 40kcal/kg Majority supplemented with IV/oral phosphate (n=26) & potassium (n=21) and occasionally magnesium (n=3)

Gentile et al (2010) Clin Nutr 29:627

Refeeding Audit

Aims

• Determine the overall & comparative incidence of refeeding hypophosphataemia (RH) between EN & PN

 Assessment of the number of patients progressing to RH in those deemed at risk according to NICE (2006)

- Determine mortality at one week of those with RH
- Assess sensitivity & specificity of NICE guidelines

Method

- Retrospective study using dietetic record cards
- Inclusion: All patients referred for EN or PN over a 12 month period
- Exclusion: Serum phosphate of <0.6mmol/L & ICU
- Refeeding hypophosphatemia: ↓ in serum phosphate to <0.6mmol/L during the first 7 days of feeding

Results – Enteral



(Fisher's exact test)

• Significant association between being at risk of RH and developing RH (p=0.02)

 No difference in mortality between those deemed at risk of RH and developing RH compared to those who did not develop RH (p=0.53)

Results – Parenteral



 No significant associations between being at risk of RH and developing RH (p=0.31)

Results

- Death was more common in EN compared to PN (p<0.001)
- No association between developing RH and death in EN and/or PN (p=0.73)
- At risk EN patients more likely to develop RH than PN (p=0.003)

Specificity & Sensitivity

- Specificity measures the proportion of negatives which are correctly identified (i.e. the % of patients correctly identified as not experiencing RH)
- Sensitivity measures the proportion of actual positives which are correctly identified as such (i.e. the % of patients correctly identified as experiencing RH)

Parenteral

- Moderate specificity (0.76) & poor sensitivity (0.5)

Enteral

- Moderate specificity (0.73) & poor sensitivity (0.38)

Discussion

- A third of patients were at risk of RH using NICE criteria
- A quarter developed RH but more common in EN
- Possible causes include:
 - Inadequate phosphate in enteral feeds
 - Lack of prophylactic supplementation
 - Poor absorption in the gut
 - Incretin effect? ↑ Insulin secretion from enteral vs. parenteral delivery of glucose
 - Experienced Nutrition Team prescribing PN
- RH may be common but not association with mortality

Occurrence of Refeeding

- Prospective cohort study
- 243 patients starting EN or PN
- 133 at risk of refeeding
- Predictors of refeeding (sensitivity of 67%):
 - Poor intake for >10 days
 - Weight loss of >15%
 - Low serum magnesium
- No deaths attributable to refeeding.
- Rare survivable phenomena
- Starvation is the most reliable predictor

Rio et al (2013) BMJ Open:3:e002173. doi:10.1136



The Challenge

Buddha & Goldilocks





Thank you for your attention

Case Study

- Male age 27
- Crohn's disease diagnosed 2000
- SB resection 2002 & 2009
- Previous EN via PEG
- Resistant to medical intervention
- BO x 2/day semi formed
- Ht 1.88, Wt = 49kg, O/E oedema ~6kg
- Est dry wt 43kg, est BMI=12.2kg/m²
- Usual wt 55kg 3/12 ago, % wt loss 21.8%
- TST <5th, MAMC <5th, Handgrip 21kg <85% normal

Risk of Refeeding

Patients with any one of the following:	Yes	No
BMI <16kg/m ²		
Unintentional weight loss >15% in 3-6/12		
Very little or no food for > 10 days		
Low levels of K, PO4 or Mg before feeding		
Patients with 2 or more of the following:	Yes	No
BMI <18.5kg/m ²		
Unintentional weight loss >10% in 3-6/12		
Very little or no food for > 5 days		
History of alcohol, insulin, chemotherapy, antacids or diuretics		

Biochemistry

Date	WCC	Na	К	Cr	Urea	CRP	ALT	AP	Bili	Alb	Са	Mg	PO4
19/9/12	4.2	137	3.3	41	2.7	59	18	148	4	7	1.85	<0.27	0.87
20/9/12	3.7	137	2.6	41	2.3	-	22	174	5	7	1.80	0.43	0.86

Receiving IV fluids with electrolytes (40mmol Mg & 80mmol KCL) IV Thiamine given before feeding as enteral route compromised

Risk of Refeeding

Patients with any one of the following:	Yes	No
BMI <16kg/m ²	V	
Unintentional weight loss >15% in 3-6/12	٧	
Very little or no food for > 10 days		X
Low levels of K, PO4 or Mg before feeding	۷	
Patients with 2 or more of the following:	Yes	No
BMI <18.5kg/m ²	۷	
Unintentional weight loss >10% in 3-6/12	۷	
Very little or no food for > 5 days	۷	
History of alcohol, insulin, chemotherapy, antacids or diuretics		Х

Calculated PN Requirements

- BMR = 1233kcal + stress 0% (apyrexic & CRP 59) + activity 20% = 247kcal = Total = 1480kcal
- N₂ = 0.3g/kg = 12.9g/day
- Fluid = 35ml/kg = 1505ml
- GOR = 991kcal
- Sodium 1-1.5mmol/kg = 43-65mmol
- Potassium 1-1.5mmol/kg = 43-65mmol
- Calcium 0.1-0.15mmol/kg = 4.3-6.5mmol
- Magnesium 0.1-0.2mmol/kg = 4.3-8.6mmol
- Phosphate 0.5-0.7mmol/kg = 21.5-30mmol

Requirements

	Calculated requirements	NICE	Prescribed
Energy (kcal)	1480	215	1400
Kcal/kg	?	5	32
Glucose (kcal)	991	?	400
Lipid (kcal)	?	?	1000
Nitrogen (g)	12.9	6.5	9
K (mmol)	43-65	86-172	100
Ca (mmol)	4.3-6.5	?	6
PO4 (mmol)	21.5-30	12.9-25.8	30
Mg (mmol)	4.3-8.6	4.3-8.6	30

PN & Biochemistry

Date	N2	Glucose	Lipid	Na	K	Mg	Ca	PO4	Volume	Rate
21/9/12	9	400	1000	60	100	30	6	30	1500	24
24/9/12	9	800	571	60	100	30	6	30	1500	24
27/9/12	9	1000	571	60	80	30	6	30	1500	16

Date	WCC	Na	К	Cr	Urea	CRP	ALT	AP	Bili	Alb	Ca	Mg	PO4
19/9/12	4.2	137	3.3	41	2.7	59	18	148	4	7	1.85	<0.27	0.87
20/9/12	3.7	137	2.6	41	2.3	-	22	174	5	7	1.80	0.43	0.86
21/9/12	4.1	135	4.2	41	1.1	63	24	162	7	12	1.46	-	0.70
22/9/12	3.1	132	4.0	45	0.8	100	18	146	5	9	2.14	0.98	0.94
23/9/12	3.0	134	4.3	46	1.1	103	15	148	6	8	2.23	1.02	1.11
24/9/12	-	131	4.1	42	1.1	95	-	-	-	-	-	0.78	-
26/9/12	5.3	134	4.9	45	1.4	104	16	309	7	8	-	0.54	1.14

Outcome

- At extreme high risk of refeeding according to NICE but did not refeed
- 50:50 mix of lipid:glucose
- Electrolytes improved before feeding
- BG 4.2-5.9mmol/L
- Biochemical vs. symptomatic refeeding
- Recommendation: Kcal/kg → Glucose kcal/kg