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Original Article

Refeeding hypophosphataemia is more common in enteral than parenteral feeding in adult in patients

Sebastian Zeki*, Alison Culkin, Simon M. Gabe, Jeremy M. Nightingale

Lennard-Jones Intestinal Failure Unit, St. Mark's hospital, Watford Road, Harrow, Middlesex HA1 3UW, UK

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SUMMARY

Background & aims: Refeedinghypophosphataemia (RH) can result in sudden death. This study aimed to compare the incidence of RH between patients fed enterally and those fed parenterally.
Methods: The risk of RH in adult patients fed parenterally (PN) or nasogastrically (NG) was assessed by comparison of patient records with the UK NICE guidelines for refeeding syndrome, between December 2007 and December 2008. A fall in serum phosphate to less than 0.6 mmol/L was indicative of RH.
Results: Of 321 patients,92 were at risk of RH. Of these, 23 (25%) patients developed RH ($p = 0.003$). 18 (33%) of NG fed, 'at-risk' patients developed RH vs 5 (13%) fed parenterally ($p = 0.03$). Death within 7 days and RH were not associated. The sensitivity and specificity of the NICE criteria for defining patient's risk of RH was calculated: 0.76 and 0.50 respectively for NG feeding; 0.73 and 0.38 respectively for parenteral feeding.
Conclusion: Patients fed by NG tube and deemed at risk of RH are more likely to develop RH than patients fed by PN. The higher risk with NG feeding may be due to the incretin effect from absorption of glucose. The UK guidelines lack specificity.

1. Introduction

Refeeding syndrome was first observed in partially starved ex-prisoners of World War II war when they started to take food.[1,2] Oedema and sudden deaths were observed. The oedema is now thought to occur as the sodium/potassium pump in the cell membrane returns to normal function and so expels sodium from the cells causing a hyperosmolar extracellular environment that retains water. The sudden death may have related to hypophosphataemia and its effect in causing severe muscle weakness (respiratory and cardiac). The hypophosphataemia occurs due to insulin secretion (secondary to carbohydrate intake); insulin increases the cellular phosphate uptake so the serum level falls. Within the cell phosphate is vital for many cellular pathways including glycolysis and the decarboxcylic acid cycle. Other metabolic abnormalities are observed and include hypokalaemia, hypomagnesaemia, vitamin deficiencies (especially thiamine) and glucose intolerance.[2] While hypophosphataemia was first described in patients taking oral nutrition, it has also been described in patients given parenteral nutrition.[3,4] While the term refeeding syndrome is often used to denote the many metabolic problems, most studies rely upon a definition of hypophosphataemia[3] or a significant drop in phosphate[5]following feeding.

The UK National Institute For Clinical Excellence (NICE) have produced guidelines to help the clinician stratify a patient's risk of developing RH (Table 1). These largely relate to the degree of starvation before a patient is refed (Table 2). Although certain specific disease populations have also been studied as being at risk (cancer[6] elderly population.[7] anorexia, diabetic ketoacidosis[8–10]) the true incidence of RH is yet to be established in a general adult hospital population. It is also not clear from the literature whether hypophosphataemia is more likely to occur in patients who are fed enterally or parenterally although there has been a small study in patients with cancer[11]

Death related to RH was reported when the condition was first recognised[3] yet the incidence of death related to RH now is either uncommon or unrecognised. Several case reports have derived a higher morbidity in those with refeeding syndrome.[12–16]

2. Aims

The primary aim of the study was to determine the overall and comparative incidence of RH between enteral and parenteral feeding in general adult hospital in patients. Secondary aims included assessment of the number of patients progressing to RH in those deemed to be at risk according to UK NICE guidelines, to determine the mortality at one week of those with RH and to assess the sensitivity and specificity of the UK NICE guidelines for the development of RH.

* Tel.: +44 781 22 47 387.
E-mail address: sebastiz@hotmail.com (S. Zeki).

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Table 1
NICE Criteria for determining people at high risk of developing refeeding problems.

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

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

3. Materials and methods

Patients were retrospectively identified from patient records. Only patients above the age of 16 who had an initial in patient consultation at the hospital between the 1st December 2007 and the 1st December 2008 outside of the intensive care setting, were selected. The date of the initial consultation and establishment of initial feed were collected for each patient as was the initial route of feeding. The first method of feeding that was sustained for more than 24 h was recorded. Each patient's risk of developing RH before feeding was assessed by analysis of the patient's record. A patient was said to be at risk of developing RH if they satisfied the National Institute For Clinical Excellence criteria (Table 1). This risk was independently validated by a dietitian (AC) having been assessed by a gastroenterologist (SZ). A low electrolyte level prior to feeding was not included as a criterion, as the primary endpoint was a phosphate drop in patients who had a normal phosphate prior to feeding. For each patient the pathology database was questioned to establish whether the phosphate dropped from a normal level before feeding (NR 0.74–1.52 mmol/L) to <0.6 mmol/L within a week after the establishment of the initial feed. .The literature varies in terms of what values represent a significant hypophosphataemia. For this study a value between two previously published studies on the same topic was chosen.[17,18] One week was chosen as the assessment period as most refeeding occurs within 2–4 days, although a week was thought to increase sensitivity.[19]Only 5 parenteral and 5 NG fed patients had low phosphate levels prior to feeding and these were excluded from the study. Mortality data was obtained from the patient's record and was only recorded if the patient died within 1 week of being refed.

Fisher's exact test was used to examine the risk of RH and its occurrence. Fisher's exact test was also used to examine the association between RH and death within 7 days.

4. Results

Of all patients ($n = 321$, mean age 62yrs SD 18.3) fed by both parenteral and NG feeding routes, 92 (29%) were at risk of developing RH. 23 (25%) of these developed RH compared with 26 (11%) of those with no identified RH risk ($p = 0.003$). The overall incidence of developing RH in all assessed patients was $n = 49$ (15%).

4.1. NG fed patients (Fig. 1)

54 (33%) of the 168 nasogastrically fed patients (mean age 70 (16–99), SD 16.5) were deemed at risk of developing RH 18 (33%) of these developed RH; thus there was a significant association between being at risk of RH and developing it ($p = 0.02$). Of those patients who did refeed in the 'at-risk' group, 27% died at 7 days ($n = 5$). However this was not different to the 9 (25%) who died and did not develop RH in the 'at-risk' group ($p = 0.53$). 18 (16%) patients who were not considered at risk of RH developed it and 2 of these died within 7 days.

4.2. Parenterally fed patients (Fig. 2)

38 (25%) of all parenterally fed patients ($n = 153$, mean age 54 (19–86), SD 15.2) were at risk of RH. 5 (13%) of these developed RH; but there was no significant association between being at risk of RH and developing it ($p = 0.31$). No patients in the at risk group who developed RH died within 7 days. 8 (7%) of those not at risk of RH developed RH and none of these died within 7 days.

4.3. Comparison of RH between NG fed and parenterally fed patients

At risk patients in the naso-gastric group were more likely to develop RH ($n = 18$, 33%,) than parenterally fed patients ($n = 5$, 13%) ($p = 0.03$).

4.4. Death at 7 days

Overall death within a week was significantly more common in the NG fed group ($n = 22$ 13% dying within 7 days of starting a feed) compared to none in the parenterally fed group ($p < 0.001$). The analyses indicated no significant association between the development of RHS and death within 7 days ($p = 0.73$). This result held for all patients combined, and when parenteral and naso-gastric patients were examined separately.

4.5. Sensitivity and specificity of the NICE guidelines on refeeding syndrome

In the context of parenteral feeding, the NICE guidelines (Table 1) demonstrate a moderate specificity (0.76 (95% CI 0.69, 0.83) and a poor sensitivity (0.50 (95% CI 0.32, 0.67) for the development of RH if a patient is deemed to be at risk of developing the condition. For NG fed patients, the specificity is 0.73(95% CI 0.64, 080) with a poor sensitivity 0.38(95% CI 0.14, 0.68).

5. Discussion

This paper represents the largest retrospective study on refeeding in artificially fed adult hospital in patients. It shows that

Table 2
Sensitivity and Specificity of the NICE guidelines for the development of RH if a patient is at risk according to the NICE criteria.

		No. who did not develop RH	No. who did develop RH	Total	Specificity of NICE guidelines (95% CI)	Sensitivity of NICE guidelines (95% CI)
Nasogastric	Number at risk of RH according to NICE	36	18	54	0.76(0.69,0.83)	0.50(0.32,0.67)
	Number not at risk of RH according to NICE	96	18	114		
	Totals	132	36	168		
Parenteral	Number at risk of RH according to NICE	33	5	38	0.73(0.64,080)	0.38(0.14,0.68)
	Number not at Risk of RH according to NICE	97	8	105		
	Totals	130	13	143		