Pregnancy and lactation during long-term total parenteral nutrition: A case report and literature review

Ailsa Borbolla Foster¹, Steven Dixon², J Tyrrell-Price^{2,3}
and Johanna Trinder¹

Abstract

There is a paucity of clinical data regarding the management of pregnancy and lactation in women requiring long-term total parenteral nutrition with complex nutritional needs. This case report and literature review highlights common challenges in care and presents evidence which can guide the obstetrician's approach to care.

Keywords

Crohn's disease, high-risk pregnancy, total parenteral nutrition

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Introduction

Knowledge regarding the management of pregnancy during long-term total parenteral nutrition (TPN) is sparse with a recent systematic review identifying only 15 case reports in this setting.¹ TPN and associated underlying medical conditions may be associated with subfertility, miscarriage or patient concerns regarding reproduction, further contributing to a lack of data on this topic.

Case history

LM, a 37-year-old primigravid non-smoker, had a history of ileocolonic Crohn's disease complicated by small bowel stricturing disease. In 2008, she underwent laparotomy, ileocaecal resection and extensive small bowel resection after developing steroid-dependent disease and subacute obstruction with no response to anti-tumour necrosis factor therapy. Only 70 cm of jejunum remained, leading to intestinal failure (IF) and subsequently she was commenced on TPN. She suffered several central venous catheter (CVC) losses from CVC-associated thrombosis previously requiring episodes of anticoagulation with warfarin. Implications of her medical condition on pregnancy had been discussed with the gastroenterology team, although formal obstetric pre-pregnancy counselling had not been arranged. Spontaneous pregnancy was achieved during clinical remission three years after ceasing long-term azathioprine at which time her body mass index (BMI) was stable at 17. Oral diet was thought to amount to 1500 kCal with uncertain absorption, and her long-standing TPN prescription was as shown in Table 1.

Management

Tertiary level care was provided jointly by gastroenterology, dietetics and maternal medicine, and key antenatal clinical assessments are outlined in Table 2. At her first antenatal visit, a full blood panel was requested as shown in Table 2 to identify biochemical or nutritional abnormalities related to her underlying medical condition or treatment. Enoxaparin 40 mg daily was commenced in view of her history of CVC-associated thrombosis. The initial antenatal care plan included monthly antenatal visits from 20 weeks and at least fortnightly from 28 weeks with maternal weight assessment and ultrasound assessment of fetal growth at each visit. In addition, she was to continue regular

contact with the dietetics and gastroenterology teams on a two to four weekly basis with detailed ongoing assessment of nutritional needs. It was anticipated that TPN requirements would need to increase in the third trimester, but assessment would be made at each antenatal visit based primarily on maternal weight gain and blood results. In the absence of fistulating perianal disease, the initial plan was for a vaginal delivery particularly in view of previous extensive abdominal surgery. Emesis persisting through the second trimester, together with increasing calorific requirements, was felt to underlie a fall in maternal weight at 25 weeks and a modest increase in TPN script was prescribed as described in Table 2. Baseline tests showed a mild pre-existing transaminitis previously attributed to long-term TPN as shown in Figure 1. Reinvestigation was prompted by asymptomatic deterioration in liver chemistry at 29 weeks, leading to a presumed diagnosis of intrahepatic cholestasis of pregnancy (ICP) and ursodeoxycholic acid (UDCA) was commenced.²

She presented at 31 + 2 weeks with an antepartum haemorrhage thought to be due to a marginal abruption and 12 mg bethamethasone was given due to a risk of preterm delivery. Detailed ultrasound was not performed as she laboured spontaneously shortly thereafter. Forceps delivery of a live male infant was performed with birthweight on the 19th centile for gestation. Postpartum recovery was uneventful with combined expressed breast milk and formula feeding instituted shortly after birth due to prematurity. By neonatal discharge on day 26, exclusive breastfeeding had been established and was being maintained at six-week follow-up with acceptable maternal and neonatal weight parameters.

¹Department of Obstetrics and Gynaecology, University Hospitals Bristol NHS Foundation Trust, Bristol, UK

²Department of Gastroenterology, University Hospitals Bristol NHS Foundation Trust, Bristol, UK

³Bristol Nutrition Biomedical Research Unit, University Hospitals Bristol NHS Foundation Trust, Bristol UK

Corresponding author:

Ailsa B Foster, Department of Obstetrics and Gynaecology, St Michael's Hospital, University of Bristol NHS Foundation Trust, Southwell Street, Bristol BS2 8EG, UK.

Email: ailsa.jordan@gmail.com

Table 1. Pre-pregnancy TPN prescription.

Constituent	Non-lipid TPN (Three days/week) Volume (ml)	Lipid TPN (Two days/week) Volume (ml)
Synthamin 9EF	1000	1000
Sodium chloride 30%	14	16
Calcium chloride 1 mmol/ml	8	8
Potassium chloride 15%	10	10
Ascorbic acid 10%	2	2
Additrac	10	10
Solivito N	1 vial in 10 ml sterile water	1 vial in 10 ml vitalipid
Water	10	0
Magnesium sulphate 50%	5	5
Glucose 20%	500	0
Sodium glycerophosphate 21.6%	4	0
Glucose 50%	550	650
Intralipid 10%	0	20
Vitalipid N adult	0	20
Total content		
Volume	2113 ml	2321 ml
Lipid	0 kCal	682 kCal
Nitrogen	9.1 g	14 g
Glucose	1500 kCal	1300 kCal
Sodium	79.82 mmol	82.08 mmol
Potassium	20 mmol	20 mmol
Calcium	8 mmol	8 mmol
Magnesium	10 mmol	10 mmol
Phosphate	4 mmol	9.3 mmol
Chloride	129.82 mmol	152.08 mmol
Acetate	44 mmol	68 mmol
Zinc	100 µmol	100 µmol
Selenium	0.4 µmol	0.4 µmol
Iron	20 µmol	20 µmol
Copper	20 µmol	20 µmol
Folic acid	0 mg	0 mg

Discussion

Home TPN is rare with point prevalence of 5.6 cases per million with 18.9% of patients being of child-bearing age.³ This case report highlights some of the management challenges in pregnancy.

Calorific requirements

There is increasing evidence demonstrating both short- and long-term impact on offspring of maternal undernutrition in pregnancy, particularly reduced growth potential of offspring, increased risk of preterm delivery and sensitization of infants to the development of chronic adult metabolic disease.⁴ However, clear recommendations regarding calorific requirements have proved challenging to produce. Whilst UK guidelines for women of normal BMI recommend a 200 kCal increase in daily intake within the third trimester,⁵ there remains

uncertainty regarding requirements for women who enter pregnancy underweight.⁵⁻⁷ Physiologic insulin resistance increases in advancing pregnancy due to antagonism by placental hormones; therefore, the risk of hyperglycaemia with TPN rises. This could produce effects on pregnancy similar to gestational diabetes and as such capillary blood glucose monitoring and insulin supplementation may be indicated.⁸ Provision of lipid TPN as a significant calorie source rather than only for prevention of essential fatty acid deficiency may minimise hyperglycaemia, but concerns in pregnancy include an association with placental fatty infiltration and preterm delivery in animal studies where lipids accounted for more than 50% of calorific intake, as well as pulmonary complications in preterm neonates exposed to lipid infusions.^{8,9} In view of these findings, it has been suggested that lipids should compose less than 30% of the calorific requirements during pregnancy.⁸ In this case, an increase in TPN requirements at 25 weeks was responded to by increasing the lipid component in an attempt to minimise risk of hyperglycaemia. A fasting glucose tolerance test performed three weeks after this change remained negative and in the absence of glycosuria at any further antenatal visit, capillary blood glucose monitoring was not performed.

Guidelines suggest an additional dietary intake of 330 kCal/day for the first six months of exclusive breastfeeding, although fat stores accumulated during pregnancy in well-nourished women may cover part of the initial energy needs.¹⁰ As weight gain in pregnancy may be compromised in women on TPN, it would seem prudent to ensure increased calorific intake during lactation to minimise maternal weight loss and compromise to milk supply. In this case, the TPN script was not amended for lactation because of concerns around parenteral nutrition-associated liver disease (PNALD), and there were no postnatal concerns regarding neonatal weight gain or maternal weight loss which were closely monitored. An individualised approach with support from lactation and nutrition specialists is recommended.

Nutrient requirements

IF is frequently associated with deficiencies in iron, B₁₂ and fat-soluble vitamins as well as minerals such as calcium, magnesium and zinc due to compromised absorption from the gastrointestinal tract.¹¹ General obstetric guidelines advise modest oral supplementation of thiamine, riboflavin, folate and Vitamins A, C and D; however, increased dietary intake for most nutrients is not required due to more efficient utilisation and absorption during pregnancy.⁴⁻⁶ Such adaptations are likely suboptimal in patients with IF and pre-existing nutritional deficiencies may be exacerbated by changes in maternal physiology and fetal demands. Parenteral preparations of combination trace elements and vitamins are readily available; however, pregnancy requirements are not clearly defined and intravenous administration may be compromised by adverse drug reactions, lack of compatibility with certain TPN preparations and loss of vitamins after compounding.¹¹ In this case, vitamin and mineral levels were normal in the first trimester; therefore, at 25 weeks, routine pre-pregnancy supplementation regimens were continued.

Liver dysfunction secondary to TPN

PNALD affects almost half of adult TPN patients.¹² Mechanisms are not fully understood but patterns of dysfunction include steatosis, cholestasis, biliary stasis and increased risk of cholelithiasis.¹³ Full investigation of changes in the biochemical liver picture during pregnancy is warranted to exclude significant obstetric and non-obstetric causes. Although a provisional diagnosis of ICP was made in this case and bile acids improved with UDCA therapy, diagnosis remained challenging in the context of pre-existing PNALD, the finding of a gallstone on imaging and ongoing rise in alanine transaminase

Table 2. Summary of key antenatal assessments.

Weeks	Wt (kg)	Maternal investigations	Fetal investigations	Management issues
12	46.0	Haemoglobin 124 g/L Ferritin 474 µg/L Vitamin D/B ₁₂ /A/E levels normal Calcium/magnesium/zinc normal	Routine fetal ultrasound normal Low risk combined first trimester screening result	Continue pre-pregnancy TPN prescription
21	48.2	Haemoglobin 114 g/L Ferritin 303 µg/L	Routine anomaly ultrasound normal	Nutrition team teach husband to administer TPN in case patient unable to self-care peripartum
25	43.9	Vitamin D/B ₁₂ /A/E levels normal Calcium/magnesium/zinc normal	Ultrasound: normal growth on 20th centile	Increase TPN prescription: - Additional lipid bag as per Table 1 to make three days/week - Average increase 257 kCal/day
29	50.7	Haemoglobin 108 g/L Ferritin 238 µg/L 75 g Glucose tolerance test normal Ultrasound: 30 mm gallstone at bladder neck Other investigations for underlying liver disease normal	Ultrasound: falling fetal abdominal circumference to 10th centile, other growth parameters normal on 20th centile	Ursodeoxycholic acid commenced at 10 mg/kg/day (250 mg twice daily)
31	51.4	Haemoglobin 113 g/L Ferritin 192 µg/L	Ultrasound: appropriate abdominal circumference growth, decreasing centiles for head and femur measurements, borderline increased resistance in umbilical artery Doppler studies.	—

Note: Liver function test results are shown in Figure 1.

Figure 1. Key liver function test results over the course of pregnancy.

Note: laboratory reference ranges for pregnancy: Alanine transaminase (ALT) 6–32 IU/L; bile acids <10 µmol/L; bilirubin second trimester 1.7–13.7 µmol/L, third trimester 1.7–18.8 µmol/L. Alkaline phosphatase (ALP) omitted as within normal pregnancy range throughout.

despite treatment. An association with long-term TPN and ICP has been previously described¹ and it would seem feasible that patients already experiencing a degree of PNALD may be more susceptible. As serial bile acid measurements have not been reported in the context of either pregnant or non-pregnant TPN, a role for increased surveillance in this patient cohort remains unclear.

Catheter issues

Randomised controlled trials have not identified benefit in the use of daily low-molecular weight heparin to prevent venous thromboembolic events related to CVCs for TPN, but current European guidelines support the use in patients at increased risk.¹⁴ The relative thrombophilic

state of pregnancy may increase risk, particularly in this case where a previous thrombotic event had occurred, and as such prophylactic enoxaparin was administered from initial obstetric review until six weeks after delivery.

Fetal outcomes

A recent small systemic review provided reassuring figures for fetal outcomes in TPN-dependent women.¹ In this case, the underlying cause for preterm delivery remains a little unclear. Fetal growth restriction and preterm delivery can, in general, be attributed to maternal, fetal or placental factors. With regard to maternal factors, there were no clinical features to suggest a flare of underlying inflammatory bowel disease and weight gain and nutritional parameters appeared to be within expected ranges. No specific fetal factors were apparent, but ultrasound Doppler interrogation had revealed possible early markers of placental insufficiency with borderline increased resistance in umbilical artery Doppler studies. Although it has been suggested that, similar to other inflammatory conditions, poor outcomes in inflammatory bowel disease patients may reflect underlying placental pathology, at present there is minimal evidence to support this, and one study has demonstrated no association between adverse perinatal outcome and placental inflammation.¹⁵ In view of multiple factors that may affect fetal growth, including low maternal pre-pregnancy weight, poor pregnancy weight gain, macro- and micronutrient deficiencies and potential risk of placental inflammatory pathology, regular growth ultrasounds are warranted in TPN-dependent women.

Conclusion

The association between low pre-pregnancy BMI and poor weight gain in pregnancy with adverse perinatal outcomes have been well described; yet, data remain scarce regarding outcome of pregnancy in women on TPN with many case reports dating from the 1980s and few describing impact on lactation. Significant developments in TPN provision and delivery now allow far greater flexibility to minimise the risk of maternal nutritional compromise, and the validity of nutritional status assessment has greatly improved over traditional dietary intake measures alone with the development of biochemical analyses using biochemical markers.¹⁶ As such, this report builds on previously published data by incorporating more up-to-date aspects of TPN delivery and nutritional assessment as well as reporting success in achieving and maintaining exclusive breastfeeding. In line with previous publications, this case report highlights the overall good maternal and fetal outcomes for pregnancy in TPN-dependent women cared for by an integrated highly specialised multidisciplinary team within a tertiary care setting.

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