TAÍS DAIENE RUSSO HORTENCIO

NUTRIÇÃO PARENTERAL – COMPLICAÇÕES METABÓLICAS EM PACIENTES PEDIÁTRICOS HOSPITALIZADOS E MUDANÇAS NA PRÁTICA CLÍNICA EM PACIENTES DOMICILIARES NO CANADÁ

PARENTERAL NUTRITION - METABOLIC COMPLICATIONS IN PEDIATRIC HOSPITALIZED PATIENTS AND CHANGES IN CLINICAL PRACTICE IN HOME PATIENTS IN CANADA

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Tese apresentada à Faculdade de Ciências Médicas da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título: Doutora em Ciências, área de concentração Saúde da Criança e do Adolescente.

Thesis submitted to Medical school of University of Campinas in partial fulfillment of the requirements of the degree of Doctor of Sciences, concentration area Children and Adolescent Health.

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CO-ORIENTADOR: PROF. DR ROBERTO JOSÉ NEGRÃO NOGUEIRA

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RESUMO

Introdução

O desenvolvimento da nutrição parenteral (NP) na década de 1960 e sua subsequente utilização na prática clínica tem tido um enorme impacto sobre os pacientes com numerosas doenças para as quais a nutrição foi impossível por outra via. Mas, esta nova tecnologia tem riscos associados, incluindo o desenvolvimento de distúrbios metabólicos, superalimentação e complicações infecciosas.

Método

Foram realizados dois estudos. O primeiro estudo teve como objetivo avaliar, em uma coorte histórica de pacientes pediátricos no Brasil que receberam NP individualizada e exclusiva, a prevalência de hipofosfatemia, hipocalemia e hipomagnesemia em até 48 horas antes do início da infusão de NP (P1), do 1° ao 4° dia (P2); 5° ao 7° dia (P3) e, investigar se a infusão de caloria e proteína e também a desnutrição foram relacionadas com esses distúrbios.

O segundo estudo foi feito no Canadá. Trata-se de um estudo retrospectivo e multicêntrico, avaliando pacientes sob nutrição parenteral domiciliar (NPD), prospectivamente inseridos no *Home Parenteral Nutrition Registry* (HPN Registry) nos períodos: 2005-2008 ou 2011-2014. Mudanças na demografia, indicações para NPD, prescrição, avaliação nutricional, acesso vascular e número de infecção de cateter por 1000 dias de cateter foram avaliados.

Resultados

A desnutrição esteve presente em 32,8% dos 119 pacientes avaliados no primeiro estudo, 66,4% estavam em unidade de terapia intensiva pediátrica (UTI Ped), 13,5% morreram.

O período de maior prevalência de distúrbios minerais foi o P1 54 (45,3%), no P2 = 35 (31,8%), no P3 = 4 (3,57%). Hipocalemia esteve relacionada à desnutrição OR 2,79 (95% CI 1,09-7,14) p = 0,045. Nos primeiros sete dias, foram infundidas calorias inferior à quantidade recomendada pelas recomendações atuais em até 84,9% dos pacientes e proteína adequada em até 75,7%. Proteína infundida acima da recomendação nos primeiros quatro dias foi relacionada com hypomagnesaemia OR: 5,66 (IC 95% 1,24 - 25,79) p = 0,033.

No estudo canadense, comparando os períodos 2011-2014 com 2005-2008, as indicações para a NPD mudaram significativamente com o aumento da proporção de pacientes com câncer (37,9% versus 16,7%) e diminuição da síndrome do intestino curto (32% versus 65,5%). A taxa de infecção de cateter diminuiu de 1,58 para 0,97 por 1.000 dias de cateter; o uso de cateter tunelizado diminuiu de 64,3% para 38,0% e a proporção de cateteres centrais de inserção periférica (PICC) aumentou de 21,6% para 52,9%. Além disso, houve uma redução no número e dias de internações relacionadas à NPD, e mudanças na prescrição de energia, proteína e oligoelementos.

Conclusão

Hipofosfatemia, hipocalemia e hipomagnesemia foram eventos frequentes, sendo a individualização ferramenta primordial para gerenciá-los. Pacientes desnutridos tiveram maior chance de desenvolver hipocalemia e os que receberam proteína acima da recomendação tiveram mais chances de desenvolver hipomagnesemia.

Os resultados sugerem uma mudança no perfil demográfico e acesso venoso no Canadá, com melhora na infecção de cateter, hospitalizações relacionadas à NPD, e prescrições.

Palavras-chaves: nutrição parenteral domiciliar, nutrição parenteral, minerais

ABSTRACT

Introduction:

The development of parenteral nutrition (PN) in the 1960s and its subsequent use in clinical practice has had a huge impact on patients with numerous diseases for which nutrition was impossible by other route. But, this new technology has associated risks, including the development of metabolic disorders, overfeeding, and infectious complications.

Methods

We conducted two studies The first study aims to evaluate in a historical cohort of pediatric patients, the prevalence of hypophosphatemia, hypokalemia and hypomagnesaemia until 48th hours before beginning PN infusion (P1), from 1st–4th day (P2); 5th–7th day (P3) of PN infusion and, investigate if malnutrition, calories, and proteins infusion were correlated to these disorders.

In Canada, a retrospective study evaluating patients who were prospectively entered in the registry either in 2005–2008 or in 2011–2014 was done. Changes in patient demography, indications for Home Parenteral Nutricion (HPN), regimen, nutritional assessment, vascular access, and number of line sepsis per 1000 catheter days were evaluated.

Results

Malnutrition was present 32.8% of 119 patients participants from the first study, 66.4% were in pediatric intensive care unit (PICU), 13.5% died. The P1 was the period of highest prevalence mineral disorders 54 (45.3%), P2 had 35 (31.8%) and, P3=4 (3.57%).

Hypokalemia events were related to malnutrition OR 2.79 (95% CI 1.09-7.14) p = 0.045. In the first seven days, infused calories were below the amount recommended by current guidelines in up to 84.9% of patients and protein infused was adequate in up to 75.7%. Protein infused above recommendation was related to hypomagnesaemia OR: 5,66 (95% CI 1,24 – 25,79) p=0,033.

In 2011–2014 compared with 2005–2008, indications for HPN changed significantly with an increased proportion of patients with cancer (37.9% versus 16.7%) and decreased short bowel syndrome (32% versus 65.5%). The line sepsis rate decreased from 1.58 to 0.97 per 1,000 catheter days; tunnelled catheters decreased as the most frequently chosen vascular access method from 64.3% to 38.0% and the proportion of peripherally inserted central catheters (PICC) increased from 21.6% to 52.9%. In addition, there was a reduction in number, and days of hospitalizations related to HPN, and changes in the prescription of energy, proteins, and trace elements were noted.

Conclusion

Hypophosphatemia, hypokalemia and hypomagnesemia were frequent events, being individualization primary tool to manage them. Malnourished patients were more likely to develop hypokalemia, and patients receiving protein above the recommendation were more likely to develop hypomagnesemia.

Results suggest a shift in patient demography and line access in Canada, with improvement in line sepsis, hospitalizations and HPN prescriptions.

Key words: home parenteral nutrition, parenteral nutrition, minerals

SUMÁRIO

DEDICATÓRIA

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“ Para ter algo que você nunca teve, é preciso fazer algo que você nunca fez”.

Chico Xavier

LISTA DE ABREVIATURAS E SIGLAS

Português

CVC: cateter venoso central

EMTN: equipe multiprofissional de terapia nutricional

EUA: Estados Unidos da América

GI: gastrointestinal

HC: hospital de clínicas

IMC: índice de massa corporal

NP: nutrição parenteral

NPc: NP cíclica

NPD: nutrição parenteral domiciliar

NPp: NP por via periférica

PICC: cateter central de inserção periférica

SIC: síndrome do intestino curto

SR: síndrome da realimentação

UTI: unidade de terapia intensiva

UTI Ped: unidade de terapia intensiva pediátrica

Inglês

ASPEN: American Society for Parenteral and Enteral Nutrition

AuSPEN: Australasian Society for Parenteral and Enteral Nutrition

CDC: Centers For Disease Control and Prevention

CI: confidence interval

DNA: desoxyribonucleic acid

ESPEN: European Society for Clinical Nutrition and Metabolism

HPN Registry: Home Parenteral Nutrition Registry

NSMT: nutritional support multidisciplinary team

OR: odds-ratio

PICC: peripherally inserted central catheter

PICU: pediatric intensive care unit

PN: parenteral nutrition

RNA: ribonucleic acid

TPN: total PN

UHN: University Health Network

W/A: weight/age

WHO: World Health Organization

1. INTRODUÇÃO

1.1. Contextualização dos estudos

Embora seja ferramenta útil e largamente difundida, a nutrição parenteral (NP) é uma estratégia terapêutica com várias possibilidades de complicações, dentre estas, as alterações metabólicas e sepse que são potencialmente letais.

Hoje, a equipe multiprofissional de terapia nutricional (EMTN) do Hospital de Clínicas (HC) da Universidade Estadual de Campinas (Unicamp) faz acompanhamento sistematizado de pacientes sob NP através de fichas pré-estabelecidas (Anexo 1). Os registros coletados de pacientes adultos e pediátricos hospitalizados (2010 a 2013) foram organizados em um banco de dados, fonte de nossa pesquisa.

Hoje no Brasil, na graduação em Nutrição, é dada ênfase à avaliação nutricional, ao cálculo de necessidades energéticas e às numerosas facetas da Nutrição, mas a NP, incluindo os distúrbios metabólicos acabam por serem deixados em segundo plano, o que deixa uma lacuna na formação do nutricionista.

Por isso, o presente trabalho nasceu de uma preocupação pessoal, visto que o nutricionista desempenha papel fundamental no acompanhamento de pacientes em NP e nas equipes multidisciplinares em NPD. Não há no Brasil hoje, dados sobre a população em tratamento nutricional através da NPD e também há falta de centros de referência estruturados para o atendimento destes pacientes.

Para aprimorar meu conhecimento e quiçá, auxiliar na implantação e sistematização de um Centro de Referência em Nutrição Parenteral Domiciliar (NPD) no Brasil, contatei pesquisadores de um centro de referência na UHN - University Health Network - Universidade de Toronto, onde a NPD é reconhecida por sua excelência, daí o trabalho

canadense. Sendo assim, a experiência vivida no HC da Unicamp e no *Toronto General Hospital* no Canadá foi uma oportunidade inestimável e muito importante para minha formação pessoal e profissional.

Este trabalho evidencia que apesar de a NP ser uma via especializada da nutrição amplamente utilizada, ainda é uma ferramenta com grandes riscos de complicações. Este método tem sido aperfeiçoado ao passar dos anos, com a utilização de novos materiais de acesso venoso, novas composições de soluções e também evoluído com novos estudos direcionando o tratamento das doenças. No entanto, ainda há uma grande trajetória de aperfeiçoamento necessário para seu entendimento.

1.2. Nutrição Parenteral

A nutrição parenteral (NP) é uma combinação de nutrientes para uso intravenoso composta por aminoácidos cristalinos, glicose, emulsões de lipídios, eletrólitos, minerais, vitaminas e água estéril. As formulações podem ser 2 em 1 (com glicose e aminoácidos como macro-nutrientes) ou 3 em 1 (além dos aminoácidos e glicose também a presença de lipídios) (1).

Nos fins de 1960 Dudrick, Vars e Rhoads observaram que o estado nutricional era fator importante para a sobrevida de pacientes em pós-operatório que necessitavam de jejum (2). Surgiram as primeiras formulações parenterais, as quais eram obtidas a partir de hidrolisados de proteínas e cuja fonte principal era a caseína, além da presença de fibrinas e dextrose. Estes tipos de substratos não eram adequados, podendo ocasionar complicações como as relacionadas ao excesso de alumínio na solução podendo

ocasionar toxicidade hepática. Hoje, há mais de cinco décadas de experiência, o avanço tecnológico foi tamanho que é possível o uso da NP como terapia domiciliar.

A NP é vital para recém-nascidos, crianças e adultos que não podem obter suas necessidades nutricionais pela ingestão oral ou enteral devido às várias causas de falência intestinal (1, 4-6).

A falência intestinal ocorre se o trato gastrointestinal for incapaz de ingerir, digerir e absorver os macro-nutrientes e/ou água ou eletrólitos em quantidades suficientes para manter a saúde e no caso de crianças também o crescimento (1). Embora a terapia de suporte nutricional não possa reverter totalmente a resposta metabólica ao estresse, lesão, cirurgia ou inflamação, a falta de nutrientes durante a fase de falência intestinal irá resultar em deficiências nutricionais e na desnutrição, que podem afetar o desfecho clínico (7).

A NP é indicada para pacientes que estão em risco de se tornarem desnutridos ou que têm ingestão inadequada oral ou enteral. Isso ocorre principalmente quando há mal funcionamento do intestino ou este está inacessível. Doença de Crohn, colite ulcerativa, síndrome do intestino curto, intestino obstruído, alto débito intestinal ou fístula enterocutânea e outras situações que impeçam a nutrição oral ou enteral, como a digestão e/ou absorção de nutrientes prejudicada, vômitos persistentes ou diarreia, são também indicação de NP (8). Pacientes com desnutrição grave em período pré-operatório também podem se beneficiar da NP, propiciando melhor condição cicatricial (9).

1.3. Vias de Administração

A escolha da via de acesso da NP deve levar em consideração alguns fatores, como tempo previsto de uso, condição vascular, estado de coagulação, necessidade nutricional atual, ambiente onde será infundida a NP (domiciliar ou hospitalar) e doenças associadas (8).

A NP por via periférica (NPp) é ofertada por veias com baixo fluxo sanguíneo, assim, suas soluções devem ser de baixa osmolaridade (até 850 mOsm/L)(10) e portanto, fornecem menor aporte protéico-calórico em relação às soluções infundidas por acesso venoso central. Deste modo, a utilização desta ocorrerá se o suporte nutricional parenteral for de até sete dias, caso contrário, se for mantida por mais tempo, poderá aumentar o risco de desnutrição devido à sua baixa concentração nutricional (7).

A NP de acesso central (NPc) é administrada em uma veia de grande diâmetro e alto fluxo sanguíneo, normalmente a veia cava superior, acessada pela veia jugular ou subclávia (10). Eventualmente o acesso se dá pela veia cava inferior pela punção da veia femural. Quando administrada através de cateter venoso central (CVC), a NP pode atingir todas as necessidades nutricionais devido à tolerância para soluções hiper osmolares. Opta-se por esta via quando é necessário administrar soluções de grande osmolaridade (acima de 850 mOsm/L) (10) e por tempo prolongado (superior a sete dias) (4, 8, 11).

1.4. A escolha do Cateter

Sempre que possível, deve ser utilizada uma via exclusiva para a NP ou em caso de cateter multi-lúmen, o lúmen distal deve o ser designado para uso exclusivo desta (5).

Para a escolha do cateter venoso central (CVC), considera-se o tempo de utilização previsto para o NP. Os de curta permanência são chamados de CVC- *intracath* (por punção percutânea colocados em veia central e não tunelizados). Esta última terminologia popularizou-se devido ao fato de ter sido a primeira marca registrada destes no Brasil. Quando a utilização for acima de 1 mês, os cateteres podem ser:

- Broviac–Hickmann® (tunelizado), semi-implantado;

- Port-a-Cath® (tunelizado), totalmente implantado;

- Cateter Central de Inserção Periférica (não tunelizado) (PICC);

O cateter central semi-implantado, de Broviac–Hickmann, é indicado para NP de longa permanência, principalmente para uso domiciliar. A inserção é realizada por ato cirúrgico. Os cateteres são confeccionados em silicona, podendo ter luz única, dupla ou tripla. É dividido em dois segmentos: venoso e subcutâneo.

O cateter totalmente implantado (Port-a-Cath) é frequentemente indicado para quimioterapia. Consta de duas porções: cateter de silicona e câmara (geralmente de aço inoxidável). Por ser totalmente implantável, proporcionando maior conforto, sendo assim melhor aceito pelos pacientes e, quando não está em uso, não necessita de curativos locais(1). Porém para infusões contínuas e diárias por longo tempo, acaba por ser de menor durabilidade. Por isso, cada vez vem sendo menos utilizado para NP.

O PICC é introduzido por via percutânea, perifericamente, até a veia cava superior, com menor risco de acidentes ao ser introduzido e de contaminação durante a sua permanência (1). Este normalmente é introduzido por punção de veia em membros superiores embora

possa também ser locado por outras veias periféricas como a jugular externa, por exemplo. É a via de escolha de acesso venoso em pediatria e em neonatologia, sendo também uma opção para a NPD em qualquer idade. A inserção e a troca de curativos devem ser realizadas por enfermeiro treinado (7).

A utilização do PICC tem sido objeto de discussão em países como os Estados Unidos da América (EUA) e Canadá. Os dispositivos de acesso venoso são de importância crucial para um número crescente de pacientes em uma variedade de estados de doença e situações clínicas (12). No entanto, os riscos - principalmente, infecções da corrente sanguínea e trombose - são preocupações comuns atualmente (13, 14), além de alta taxa de morbimortalidade e alto custo (15).

Algumas hipóteses, incluindo menor densidade bacteriana na pele ao longo do braço, temperaturas mais baixas nas extremidades, e a relativa facilidade de cuidados locais em comparação com o pescoço ou virilha, foram aventadas para apoiar o ponto de vista de que o uso do PICC oferece proteção em comparação aos outros dispositivos com relação a complicações infecciosas. No entanto, os dados publicados, mostram-se controversos (12, 15-17).

Em 2006, uma revisão de estudos feitos em pacientes cirúrgicos mostrou que comparando o uso de PICC e CVC, os números de complicações infecciosas eram similares, 40% dos PICC's foram removidos antes de completar a terapia e os episódios trombóticos foram mais frequentes e precoces nos pacientes que usaram PICC (17).

Em 2013, meta-análise de 23 estudos e 57.250 pacientes, o uso de PICC em pacientes hospitalizados foi associado com taxas de infecção similares aos relacionados a outros CVCs (16). Assim questiona-se se o uso de PICC é verdadeiramente mais "seguro" do

que o uso de outros CVCs no que diz respeito às complicações infecciosas. No entanto, um estudo prospectivo, avaliando as variáveis relacionadas à infecção sanguínea associadas à CVC em adultos internados em oito unidades de terapia intensiva (UTI) durante dois anos, mostrou menor risco de infecção de cateter em pacientes que receberam NP por PICC (12). Maki e colaboradores avaliaram o risco de infecção sanguínea associada ao tipo de dispositivo de acesso central. Neste trabalho as taxas de infecção de corrente sanguínea associadas ao uso de PICC foram menores do que os relatados com dispositivos tradicionais, não tunelizados (15). Estudos recentes relataram que a infecção da corrente sanguínea relacionada ao uso do PICC parece associar-se com o tempo de permanência hospitalar, UTI e número de lúmens do dispositivo (18, 19).

Algumas vantagens podem ter contribuído para o aumento do uso do PICC comparado ao CVC. De fato, a inserção é mais fácil e segura e pode ser feita à beira do leito por enfermeiro treinado usando o recurso do ultrassom, diminuindo o risco de mau posicionamento. Além disso, não há neste tipo de punção risco de hemotórax e pneumotórax que são potencialmente letais. Fornecendo um acesso venoso durável, o PICC também facilita a transição do hospital para atendimento domiciliar (18), aumentando a qualidade de vida (20).

Ao considerar o uso de CVC não tunelizado no ambiente doméstico, o PICC é considerado uma opção para administrar a nutrição para pacientes que necessitam de uma via menos invasiva para obtê-la, além de reduzir o tempo de internação, acelerando a transição dos pacientes do ambiente hospitalar para atendimento domiciliar (18).

1.5. Complicações da NP

As complicações associadas à NP podem ser categorizadas em mecânicas, infecciosas e metabólicas (4), sendo as duas últimas mais comumente encontradas e são motivo de preocupação devido à gravidade (1, 4, 10).

Dentre as numerosas complicações metabólicas, os distúrbios de minerais intracelulares "hipos" (fósforo, magnésio e potássio) merecem atenção especial. Os riscos de hipofosfatemia, hipomagnesemia e hipocalemia são comumente relacionados à realimentação, desnutrição prévia e inflamação sistêmica (21-23).

Os distúrbios "hipos" são presentes na Síndrome da Realimentação (SR). Apesar de muito estudada, não há consenso sobre a definição desta, mas alguns conceitos são bem aceitos. Ela representa um grupo de sintomas e sinais clínicos comumente observados em pacientes com desnutrição grave, anorexia nervosa, câncer, síndromes disabsortivas, alcoolismo, período pós-cirurgia e diabetes mellitus crônico descontrolado (24). Complicações da SR podem incluir insuficiência cardíaca, insuficiência respiratória, alterações metabólicas e morte (25). Os sintomas da SR ocorrem devido ao desequilíbrio mineral resultante da suplementação nutricional via oral, enteral ou parenteral após um período de adaptação à fome prolongada ou desnutrição, portanto, a depleção nutricional é um denominador comum em pacientes com SR. Durante o jejum ou estado catabólico há perda dos minerais intracelulares fósforo, potássio e magnésio para o compartimento extracelular (26). Os estoques de glicogênio são gastos, enquanto as proteínas são conservadas, as gorduras serão então, fonte predominante de energia (24). Com a realimentação (reintrodução principalmente de carboidratos) pela alimentação via oral (enteral ou NP principalmente) há uma mudança repentina para a glicose como fonte

predominante de energia, levando a liberação de insulina e consequentemente à rápida entrada de glicose e dos minerais intracelulares para dentro das células (21, 24, 26). Sendo assim, hipofosfatemia, hipomagnesemia e hipocalemia são achados comuns relacionados com a SR, assim como anormalidades no metabolismo da glicose, hipovitaminose (principalmente de tiamina) e deficiência de elementos-traço (24). É necessário ressaltar que a liberação de insulina ocorre em todas as situações de resposta inflamatória sistêmica devido à descarga maciça de hormônios contra reguladores que ocasionam hiperglicemia e posterior liberação de insulina (25). Este fato é comum em UTI Ped.

Assim, ao administrar NP, recomenda-se a introdução gradual de nutrientes. O ditado "iniciar baixo, e ir devagar" serve como uma boa orientação (30). Em pacientes pediátricos e adultos, a ingestão ou infusão de calorias deve ser aumentada de 10% a 25% ao dia ou ao longo de 4 a 7 dias até que a meta de calorias seja atingida (27). A proteína não é restrita durante o suporte nutricional visto que pacientes internados que recebem NP são, amiúde, hipercatabólicos. Vários estudos mostram que a alta ingestão de proteína poupa a massa muscular magra e ajuda na sua restauração (28).

Na prática clínica, a hipofosfatemia, hipomagnesemia e hipocalemia são distúrbios que podem ocorrer em uma resposta normal à introdução de energia e nutrientes e não estar necessariamente relacionados com a SR, não manifestando quaisquer sintomas (29, 30). No entanto, mesmo sem um consenso na literatura, esses distúrbios são claramente evidentes (21, 23, 29, 31-33). Estudar este delicado equilíbrio é de importância crucial, devido à gravidade das suas repercussões se não monitorados, inclusive podendo resultar em óbito se não tratados a tempo (30).

Os distúrbios de minerais continuam sendo um importante problema para pacientes pediátricos e adultos. O reconhecimento dos pacientes em risco; fornecimento adequado de minerais, vitaminas e elementos-traço; cautelosa e gradual progressão de energia e monitoramento laboratorial diário são os caminhos mais eficazes e recomendados para prevenir ou tratar (24, 29, 30).

1.6. Nutrição Parenteral Cíclica

A NP cíclica (NPc) é a NP de escolha para NPD. Nesta, há uma pausa entre o fim da NP e o começo da NP seguinte. De modo geral, não deve ser utilizada se o paciente não está apto a receber nenhum aporte oral ou enteral principalmente em crianças pequenas para que não haja hipoglicemia no horário de pausa da mesma. Devido à maior reserva de glicogênio esta pausa pode ser possível em adultos e crianças maiores mesmo em situações de jejum.

Como a NP não é infundida durante a totalidade das 24 horas, evita-se a constante hiperinsulinemia e deposição de lipídios no fígado diminuindo a possibilidade de lipogênese devido às mudanças na relação insulina e glucagon provocada pela alternância entre períodos de jejum e de alimentação diminuindo o risco de doença hepática. Ela também pode ser considerada mais fisiológica pelo fato de ter um período sem infusão contínua de macronutrientes melhorando o apetite (7).

1.7. Nutrição Parenteral Domiciliar (NPD)

Cuidados recebidos em ambiente domiciliar oferecem aos pacientes a possibilidade e a capacidade de receber tratamento complexo tais como a NPD em um ambiente

confortável, com o apoio de membros da família e a supervisão de profissionais qualificados. De fato, os grandes benefícios da NPD estão associados ao menor custo (34), melhor sobrevida e qualidade de vida (20).

No domicílio dá-se continuidade ao atendimento já iniciado no hospital. Ressaltando-se que os distúrbios dos minerais devem ser corrigidos e estabilizados no ambiente hospitalar antes de cogitar-se a NPD. Se a opção for administração de NP cíclica é fundamental que o paciente já tenha passado pelo período de transição de NP contínua para cíclica no ambiente hospitalar (7).

Para o adequado manejo da NP, é fundamental que haja uma equipe multiprofissional para seguimento do paciente. Os profissionais necessários são ao menos: nutricionista, enfermeiro, farmacêutico e médico. Caberá ao nutricionista o monitoramento do estado nutricional e seguimento nutricional. Do enfermeiro espera-se o fornecimento de informações sobre o estado clínico e de hidratação, assim como a repercussão da doença, as condições do cateter e a instalação da NPD. Ao farmacêutico atribui-se a função de avaliar compatibilidades fluídicas e de minerais na solução parenteral e as interações entre as drogas e os nutrientes. O médico é responsável pelo cálculo da NP e pelo cumprimento das metas estabelecidas, assim, é fundamental que tenha conhecimento das alterações metabólicas e da fisiopatologia básica da nutrição e renutrição. História completa, exame físico e prescrições são atribuições do médico. Com atenção criteriosa da equipe multiprofissional de atenção ao paciente, obtém-se bons resultados e evitam-se complicações (35).

As complicações da NPD são as mesmas observadas em NP hospitalar. Porém, as complicações metabólicas são menos frequentes, pois o período de maior risco para isso

(primeira semana de NP) já foi superado. Dessa forma em NPD, as complicações mais frequentes relacionam-se às lesões hepáticas e a sepse. A sepse é a complicação mais temida (5).

O Brasil não possui dados publicados sobre a população sob NPD. Nos EUA, o gasto estimado de 652 milhões de dólares por ano (2010), beneficiando aproximadamente 33.000 pacientes sob NPD (36). O registro de pacientes sob NPD dos EUA, o "SUSTAIN", possui atualmente 1251 pacientes participantes (37). O Canadá possui hoje 510 pacientes adultos cadastrados.

1.7.1. Nutrição Parenteral Domiciliar (NPD) – Experiência Canadense

Desde 2006, é estabelecido e validado no Canadá o HPN Registry, com o objetivo de avaliar dados demográficos de pacientes que recebem NPD, bem como determinar os fatores que afetam a sobrevivência e complicações (39). O registro é alimentado via web, reunindo dados de pacientes de centros de excelência em NPD que participam, voluntariamente, da coleta e inserção de dados.

O HPN Registry foi especialmente projetado para coletar informações como: dados demográficos, anatomia gastrointestinal, indicações para NPD, avaliação nutricional (peso, altura, índice de massa corporal [IMC], necessidades estimadas de energia e proteína, prescrição total, acesso vascular, qualidade de vida (escala de desempenho de Karnofsky), exames laboratoriais, medicações, investigações hepáticas, densidade mineral óssea, número de hospitalizações e sobrevida (38). Todos os pacientes devem assinar o termo de consentimento livre e esclarecido antes de seus dados serem inseridos no registro (Anexo 2).

Desde o ínício, seus pesquisadores têm publicado dados sobre esta população (3, 38-41). Estudo preliminar avaliando 150 (37,9% homens e 62,1% mulheres), a média (±SD) de idade foi de 53,0±14 anos e a duração de NPD foi de 70,1 ± 78,1 meses. A média do IMC antes do início da NPD foi de 19,8±5,0 kg/m^2. A indicação principal para NPD foi síndrome do intestino curto (60%), seguido de doença de Crohn (51,1%), e por isquemia mesentérica (23,9%). Em relação às complicações, 62,7% dos pacientes foram internados ao menos uma vez, com 44% das internações relacionadas à NP. Além disso, 28,6% dos pacientes apresentaram pelo menos uma infecção de cateter (duplo lúmen mais do que único lúmen; P=0,025) e 50% tinham pelo menos uma troca cateter. Enzimas hepáticas anormais foram documentadas em 27,4% dos pacientes e doença metabólica óssea em 60% (3). A média de pontuação de Karnofsky foi de 63 (Anexo 2).

Estudo de corte transversal em 2012 avaliou 189 pacientes participantes do registro canadense (39). O objetivo foi avaliar a prática de suplementação de vitamina K e a relação com a densidade mineral óssea. Os pacientes suplementados com vitamina K (43%) tiveram melhor densidade mineral óssea no quadril em comparação com nenhuma suplementação, sugerindo um importante papel da vitamina K na preservação da densidade mineral óssea.

Em 2013, com o mesmo registro, fez-se um estudo objetivando-se avaliar a suplementação de elementos traços em cinco centros de referência em NPD no Canadá. Neste, a suplementação diária média de zinco, manganês, cobre e selênio excederam as atuais recomendações (4, 42). Alertou-se acerca da necessidade da suplementação de elementos traço através da NPD nos programas canadenses ser revista e ajustada para evitar potencial toxicidade (40). Também estudou-se o efeito da suplementação de

manganês (Mn) em uma amostra de pacientes sob NPD que o receberam, como parte de um suplemento contendo elementos-traço (41). A média da suplementação diária de Mn foi de 7,28±0,97 mmol/d excedendo o preconizado pela Sociedade Americana de Nutrição Parenteral e Enteral (ASPEN) (4) de 1,09-1,82 mmol/d. O nível médio de Mn total no sangue foi de 1,38±0,29 vezes o limite superior do normal (upper limit of normal (ULN), e 8 de 14 pacientes tinham níveis de Mn no sangue acima do UL. Na ressonância magnética, 81% dos pacientes apresentavam sinais que se presume serem depósitos de Mn em seus gânglios basais. Várias queixas neuropsiquiátricas foram relatadas, incluindo depressão (66%), falta de concentração (42%), distúrbios de memória (17%) e instabilidade de marcha (8%). Todos sinais e sintomas são compatíveis com toxidade pelo Mn.

Nos *guidelines* E.S.P.E.N.(6) e A.S.P.E.N.(4) enfatiza-se avaliar o ambiente doméstico e educar os pacientes em NPD a fim de reduzir o risco de complicações. No Canadá, a NPD é gerida por um equipe multiprofissional especializada, lotada no *Toronto General Hospital* – UHN (University Health Network) que supervisiona e acompanha todos os aspectos de cuidados médicos e de nutrição, incluindo a formação e educação do paciente.

Uma iniciativa importante para acompanhar os pacientes que moram em áreas distantes da UHN – University Health Network em Toronto-Ontário-Canadá, foi a implementação do programa TeleHealth (43), com o objetivo de fornecer telemedicina regional, monitorando e propiciando a oportunidade de discutir alterações no cuidado e no tratamento de pacientes que moram em áreas remotas e que são ou estão incapazes de viajar para Toronto, devido ao custo, distância ou condição climática. Desde 2002, foram

atendidos mais de 3200 pacientes por ano e há mais de 1.400 sites TeleHealth em Ontário e estes estão inseridos em boa parte de hospitais, centros de saúde comunitários e consultório de médicos da família.

Cada sessão é de aproximadamente 30 minutos. Uma enfermeira de um hospital próximo ao paciente pertencente ao programa solicita uma consulta pelo TeleHealth. O formulário de pedido de consulta *on-line* inclui informações de contato, diagnóstico e dados de avaliação física (por exemplo, peso e sinais vitais) para ser incluída antes da sessão agendada.

O TeleHealth videoconferência funciona com um aparelho de televisão com um dispositivo de controle remoto que liga o equipamento, regula o volume e a imagem e manobram as câmeras remotas e locais. Os equipamentos são conectados via IP (provedor de internet) por conexão de banda larga. Todos os *sites* são equipados de forma semelhante. Esta iniciativa ajuda a equipe de NPD locada em Toronto a identificar complicações (infecção de cateter, problemas com o acesso venoso, falta de aderência, etc...), dificuldades e necessidade de modificação no tratamento.

1.8. O papel da Equipe Multidisciplinar de Terapia Nutricional (EMTN)

As complicações relacionadas à NP podem ser minimizadas com monitorização cuidadosa e supervisionada por uma EMTN. No Brasil há legislação específica que regula a atuação da EMTN (Portaria MS/SNVS nº 272, de 8 abril de 1998) com, ao menos, os seguintes profissionais: enfermeiro, farmacêutico, médico e o nutricionista. Desenvolvimento de protocolos, programas educacionais e assegurar o cumprimento das normas de boa prática e conduta são tarefas da EMTN.

No Hospital de Clínicas da Unicamp, a NP é calculada diariamente pela EMTN. Todos os dados dos pacientes são anotados em fichas pré-estabelecidas (Anexo 1) de acordo com os recentes *guidelines* (1, 4), como diagnóstico, motivos para NP, peso, altura, exames laboratoriais e prescrição da NP.

O corpo clínico de atendimento de pacientes sob NPD no Canadá é formado por médicos, enfermeiro, farmacêutico e nutricionista. Os dados são registrados em formulário específico (Anexo 2).

2. OBJETIVOS

2.1. Geral

Investigar as complicações metabólicas mais frequentes em pacientes pediátricos hospitalizados admitidos para receber NP em um hospital terciário no Brasil. Investigar as complicações infecciosas e mudanças na prática clínica no tratamento de pacientes adultos sob NPD no Canadá.

Para tanto, o presente trabalho é dividido em 2 capítulos com os seguintes objetivos específicos.

2.2. Específicos

1- *Hypophosphatemia, hypomagnesemia and hypokalemia in pediatric patients admitted to receive exclusive parenteral nutrition***.**

O objetivo foi estudar em uma coorte histórica de pacientes pediátricos admitidos para receber NP exclusiva, a prevalência de hipofosfatemia, hipocalemia e hipomagnesemia e investigar a relação entre desnutrição, infusão de caloria e proteína com os distúrbios.

2- *Practice and outcomes based on the Canadian home parenteral nutrition registry: a comparison between two time periods*.

O objetivo deste estudo foi avaliar se houve mudanças na prática clínica e indicadores em NPD na última década no Canadá nos centros participantes do HPN Registry.

3. MÉTODO GERAL

Obedeceram-se às recomendações para pesquisa biomédica envolvendo seres humanos propostas pela Resolução n° 196 de 10 de outubro de 1996, do Conselho de Saúde.

Os protocolos de pesquisa foram aprovados pelo Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da Unicamp, Campinas, SP e estão definidos em cada capítulo do estudo (Apendice 1).

O estudo foi dividido em 2 capítulos:

Capítulo 1. *Hypophosphatemia, hypomagnesemia and hypokalemia in pediatric patients admitted to receive exclusive parenteral nutrition***.**

Trata-se de um estudo tipo coorte histórica de pacientes pediátricos hospitalizados no HC da Unicamp no período de janeiro de 2008 a janeiro de 2013 que receberam NP exclusiva e individualizada. Utilizou-se ficha padronizada do serviço para coleta de dados (Anexo 1).

Capítulo 2. *Practice and outcomes based on the Canadian home parenteral nutrition registry: a comparison between two time periods.*

Estudo retrospectivo, multicêntrico, feito através da análise de dados de 369 pacientes inseridos prospectivamente via web no registro canadense – HPN Registry. Os dados de dois períodos foram comparados: 2005–2008 e 2011–2014. Seis centros especializados em NPD participaram: Toronto (Toronto General Hospital, St. Michael's Hospital), Hamilton (Hamilton Health Sciences), Edmonton (Capital Health/University of Alberta),

Calgary (Foothills Medical Centre), Vancouver (British Columbia Home Parenteral Nutrition Program). Para obtenção dos dados, utilizou-se ficha de coleta de dados (Anexo 2).

4. CAPÍTULO 1. Hypophosphatemia, hypomagnesemia, and hypokalemia in parenteral nutrition pediatric patients.

Background: Hypophosphatemia, hypomagnesemia, and hypokalemia occur in patients on parenteral nutrition (PN), mainly when the body's stores are depleted due to fasting or inflammation. In spite of these disorders are potentially fatal outcome, there are few studies reporting the incidence in pediatric population admitted to receive PN. Methods: This study aims to evaluate in a historical cohort of pediatric patients, the prevalence of hypophosphatemia, hypokalemia and hypomagnesaemia until 48th hours before beginning PN infusion (P1), from 1st–4th day (P2); from 5th–7th day (P3) of PN infusion and, investigate if malnutrition, calories, and proteins infusion were correlated to these disorders. Results: Malnutrition was present 32.8% of 119 patients, 66.4% were in pediatric intensive care unit (PICU), 13.5% died. P1 was the period of highest prevalence of mineral disorders 54 (58.1%), P2 had 35 (37.6%) new events, and P3 four (4.3%). Hypokalemia events were related to malnutrition OR 2.79 (95% CI 1.09-7.14) p=0.045. In the first seven days, infused calories were below the amount recommended by current guidelines in up to 84.9% of patients and protein infused was adequate in up to 75.7%. Protein infused above recommendation at first four days was related to hypomagnesaemia OR: 5.66 (95% CI 1.24 – 25.79) p=0.033. Conclusion: Hypophosphatemia, hypokalemia and hypomagnesemia were frequent in hospitalized pediatric patients before and during the first four days of PN infusion. Patients with malnutrition had more chances to have hypokalemia and those that received high protein infusion had more chances to develop hypomagnesemia.

Key words: Parenteral Nutrition, Child, Hypophosphatemia, Hypomagnesemia, Hypokalemia

Introduction:

Parenteral nutrition (PN) is associated with numerous metabolic complications such as mineral disorders hypophosphatemia, hypokalemia and hypomagnesemia (1). Infusing PN solution can stimulate these disorders, as well as, insulin metabolism is strongly activated with displacement of predominantly these intracellular minerals (phosphorus, magnesium and potassium) into the cell. To avoid these altered levels there are several strategies, which include close monitoring before and during PN infusion, adequate replacement of minerals and progressive increase of calories (1-3) but, once established, individualization of PN prescription seems to be an important step to management (1).

Usually, hypophosphatemia, hypomagnesemia and hypokalemia have been reported individually or in case series (4-7), most of times related to refeeding syndrome and malnutrition (4, 8). Frequently, the patients admitted to receive PN are most of times catabolic, hyperglycemic, with reserves of macro and micronutrients substrates depleted, but not necessarily achieved some degree of malnutrition. The main aim of this study was to investigate the prevalence of hypophosphatemia, hypokalemia and hypomagnesemia in a historical cohort of pediatric patients prior to PN infusion and, during the first seven days of PN treatment. Another aim was to investigate if malnutrition and, calorie and protein infusion are correlated to these disorders.

Methods

A historical cohort study was conducted with patients younger than 19 years old who were admitted to a tertiary hospital in Campinas, Brazil from January, 2008 until January, 2013. It were selected all those admitted to receive exclusive individualized PN for at least 24 hours, or until to begin receiving enteral or oral nutrition. The study was approved by the institutional ethics committee (#1304/2011).

All patients who had incomplete laboratory evaluations, and those with chronic or acute renal insufficiency were excluded. Those were fed with oral and enteral nutrition concomitantly with PN, were also excluded. The patient's research records were completed during treatment and filed after hospital discharge. These records were prepared in order to monitor anthropometry and laboratory results, and PN prescription, and are based on normative recommended in the literature (1).

Patients were classified into surgical groups: gastrointestinal (GI)/ liver surgery, cardiac surgery, thoracic surgery, otolaryngology surgery; or into clinical groups: GI/liver diseases, respiratory diseases, sepsis, neurologic, trauma, others (malnutrition lacking sufficient nutrition by enteral or oral administration).

Nutritional status: each patient underwent nutritional assessment prior to starting nutritional support, including current body weight. Nutritional status was defined by Z-scores, which were calculated by the anthropometric weight/age (W/A) index for all subjects. Z-score were calculated using the programs WHO Anthro (7) for children younger than five years and WHO Anthro PLUS (8) for children aged five years and older. Nutritional status was classified according to the World Health Organization (WHO) classification (9,10). Malnutrition was defined when W/A Z-scores$\leq$-2.

PN routine: Nutritional support multidisciplinary team (NSMT) is composed by physician, dietitian, nurse, and pharmaceutical. For all pediatric patients, before the start of infusion, mineral measurements (sodium, potassium, ionic and total calcium, chloride, magnesium, phosphorus), along with levels of triglycerides, cholesterol, HDL cholesterol, alanine aminotransferase, gamma-glutamyl transferase, albumin, pre-albumin, urea, creatinine and glucose were made. In patients with severely depleted mineral levels, i.e. Na ≤125 mEq/L, K ≤2.5 mEq/L, Pi ≤1.5 mg/dL, Ca (i) ≤1.0 mmol/L or Mg ≤1.0 mEq/L, levels were individually corrected separately before the start of the PN treatment, infusing the specific mineral at the highest level, according to the recommended and in respect to the compatibility (1, 9).

The NSMT calculates the daily PN based on patient weight and guided by Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR) (1). The volume restrictions suggested by the patient's physician were respected.

Laboratory monitoring: It was performed in three periods: (P1) until 48 hours before beginning PN infusion; (P2) 1st–4th day of PN infusion; (P3) 5th–7th day of PN infusion. The classification P1–P2 refers to patients who developed a mineral disorder in P1, which remained during P2. The values of phosphorus, potassium and magnesium used for the PN infusion were those recommended by current guidelines, namely phosphorus: 7-10 mmol/1000 Kcal/day, potassium: 1-3 mEq/Kg/day and magnesium: 0.2-0.4 mEq/Kg/day (1).

Hypophosphatemia, hypokalemia, and hypomagnesemia were defined by levels below the laboratory reference values (10-12) (Table 2). The definition of severe disturbances was defined as Pi ≤1.5 mmol/L for hypophosphatemia (13) , K ≤2.5 mmol/L for hypokalemia (14) and Mg ≤1 mEq/L for hypomagnesemia (15). The first hypophosphatemia, hypokalemia or hypomagnesemia observed at P1, P2, and P3 was considered as an event. Clinical manifestations of severe hypophosphatemia, hypokalemia or hypomagnesemia were monitored (16) (Table1). Albumin levels (≤3.5 g/dL) were also assessed.

The amount of phosphorus in mmol/Kcal (17) was determined by calculating the mean quantity of phosphorus from 1st–4th day divided by the mean number of calories infused. The amount of Mg in mEq/Kg and K in mEq/Kg was determined by calculating the mean quantity of Mg or K from 1st–4th day divided by the patients' average weight.

The amount of the infused solution containing protein (g/Kg/day) and calories (Kcal/Kg/day) was either classified as adequate, below or above the recommended values from the literature (18) and was evaluated during the same periods of laboratory monitoring, i.e. P1, P2, and P3. The energy and protein infusions were classified considering the full 100% target from 1st–7th. Considering the progression of macronutrients during the initial days of TPN, the classification of the last day of each period was considered.

Statistical analysis: To compare categorical variables between groups, we assessed risk factors using the chi-square test, crude odds-ratio (OR) and the Fisher exact test (the Fisher exact test was used if the value for each cell <5). Confidence intervals for proportions were calculated using the Bayesian calculation with central confidence

intervals. A bicaudal p-value of 0.05 or less was considered statistically significant. All statistical operations were performed using SPSS version 15.0 (SPSS, Chicago, IL).

Results

A total of 140 patients were selected from January 2008 to December 2013. Out of these, 19 patients were excluded due to lack of laboratory data and two were excluded with acute renal failure. The excluded patients did not differ from the remaining patients in their basic demography and outcomes (data not shown).

A total of 119 patients, 60 (50.4%) were male, mean age of 71.6±70.8 months received PN for 7.3±4.5 days; 67 (56.4%) patients had undergone surgical treatment, 79 (66.4%) were in PICU and 16 (13.4%) died during the hospitalization period. Malnutrition was present in 39 (32.8%) patients (Table 3). Depleted albumin levels (≤3.5 g/dL) were found in 99 (83.2%) patients.

Mineral disorders were most prevalent before beginning PN infusion, and during the first 4 days of PN. The period of highest prevalence of mineral disorder was P1, followed by P2, and P3. Analyzing prior and during the PN infusion, 93/119 (78.5%) of the patients had any mineral disorders (Table 4). Some patients, 2/115 (1.7%) had hypophosphatemia at P1 and this disorder remained at P2, 9/110 (8.2%) had hypomagnesemia during both periods, P1 and P2.

Hypokalemia events were correlated to malnutrition. Hypophosphatemia and hypomagnesemia were not correlated to malnutrition (Table 5).

There were 14 events of severe mineral depletion before the start of PN infusion (P1). Nine of these cases had K ≤2.5 mEq/L, two cases had Pi ≤1.5 mg/dL, and three cases had

Mg ≤1.0 mEq/L. There were three events of severe hypokalemia during P2. These events were not correlated with malnutrition, OR= 0.39 (95% CI 0.01 – 40.77) p=1. There were no events of severe hypomagnesemia or hypophosphatemia at P2. No clinical manifestations related to severe depletion were observed and none of the patients required further action beyond setting the PN, such as dialysis.

The mean weight was 23 kg. Concentration of phosphorus provided by the solutions from 1st–4th day was mean 8.33 mMol/1000 kcal, potassium 1.41 mEq/kg, and magnesium 0.29 mEq/kg.

During the 7 days, were infused mean of 821 kcal and 35 kcal/g of amino acids. Infused calories were below the amount recommended by current guidelines in up to 84.9% of patients, and there was a tendency of adaptation in caloric infusion up to day 7. In fact there was a decrease in the number of patients classified as receiving calories below the recommended amount from 1st–4th day ($p<0.001$), and from 5th–7th day ($p<0.001$) (Figure 1).

The average amount of protein infused was 23 g/day or 1.43 g/kg/day. Infused protein was adequate in up to 75.7% of patients, and there was an improvement in protein infusion, thus reducing the number of patients classified as having protein levels below those recommended from 1st–4th day ($p<0.001$), and from 5th–7th day ($p<0.001$) (Figure 2). Infused protein above the recommended levels was related to hypomagnesemia (Table 6).

Discussion

Mineral disorders prior and during PN therapy are events that should be promptly monitored to avoid their occurrence and to prevent the severity of metabolic complications. This study shows that hypophosphatemia, hypokalemia and hypomagnesemia events were frequent before, and especially at first four days of PN treatment. The patients with malnutrition had more chances of develop hypokalemia, and those receiving protein infused above recommendation at first four days had five times more chances to develop hypomagnesemia.

Hypophosphatemia, hypokalemia and hypomagnesemia were present before beginning PN infusion in 58.1% of patients, highlighting the need for previous monitoring prior to starting PN infusion and the requirement for prescribing individualized formula for these patients.

The initial few days of PN treatment is known as the greatest period of risk of developing mineral disorders (16). In our study, the first 4 days of exclusive PN, 35 new events of hypophosphatemia, hypomagnesemia and hypokalemia were triggered. However, the individualization appeared to be sufficient to normalize mineral levels in the blood during the main phase of mineral disorders triggered by PN infusion and, avoided the occurrence of severe events. Indeed, a concern during the initial days of PN is the possibility of mineral disturbances stimulated by PN composition. In fact, with the reintroduction of carbohydrates, there is a sudden shift back to the use of glucose as the predominant fuel source, creating a high demand for the production of phosphorylated intermediates of glycolysis, with inhibition of fat metabolism (8). The massive insulin liberation, stimulate the cellular uptake of glucose, potassium, phosphate and magnesium, which lowers the

serum concentration of these minerals in the plasma, leading to a dangerous levels (18). In this scenario, refeeding a malnourished patient by PN may be an extra concern, due to their limited mineral reserves. Our malnourished patients had twice as much chance of developing hypokalemia compared with eutrophic patients.

Standards of care to avoid mineral disturbances can include a gradual caloric increase, such as a 10% to 25% increment each day until achieving the caloric goal in the pediatric patients (19), or gradual increase of calories with the aim of reaching the ultimate energy requirements within 3 to 7 days of initiating PN (7, 18, 20). It is, therefore, a common practice to begin PN with fewer calories than recommended by the literature and to slowly increase calorie intake. This practice was undertaken by our team, and we observed that the supply of calories in the first days of PN was lower than the goal recommended by recent pediatric guidelines (1). Some factors could be contributed to slow progression of PN energy supply, including fluid restriction and cautious decision-making in the early phases of stress. Our study population is mainly composed of PICU patients with a large prevalence of hypoalbuminemia, which is common in severely distressed patients. The mortality rate (13.5%) corroborates this fact.

Although the full energy recommendations were not achieved during the first week, infusion of amino acids reached the recommended. High protein prescription is recommended during the initial days of intensive care, especially for hypercatabolic patients, where stimulating protein synthesis in tissues with high turnover is necessary for potentially reducing catabolism (3), and should be combined with a sufficient amount of energy to avoid proteolysis (21). The European Society of Paediatric Gastroenterology,

Hepatology and Nutrition suggest 30-40 Kcal/g of amino acids (1). Our patients received PN formulation according this recommendation.

The high protein intake was correlated to hypomagnesemia in our study. We hypothesized that a high protein infusion stimulates the gluconeogenesis pathway and tissue synthesis: magnesium is involved in hundreds of enzymatic reactions and is an important co-factor for many biological processes, such as playing a central role in a large number of reactions of cell metabolism, including the synthesis of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) (16).

One of the limitations of our study was that nutritional status wasn't evaluated by history of recent weight loss, as a historical cohort was being analyzed. The weight/age index shows us the current nutritional status but is not an indicator of recent weight loss. Usually, the risk of mineral disturbances is directly correlated with the degree of weight loss, and patients suffering from severe malnutrition, particularly where weight loss exceeds 10% during a 2-month period or lengthy fasting are higher risk population(18). Out of all the patients, 99 (83.2%) had depleted albumin levels, featuring kwashiorkor malnutrition, but albumin, which has a long half-life (14-20 days), is not indicative of the immediate nutrition status and was not useful in diagnosing recent nutritional depletion. Moreover albumin level can also be changed due to alterations in the organic compartments due to the inflammatory state, so this is a good marker of severity.

Although data collection was retrospective, the present study was based on a pre-established standardized form, completed daily by doctors specialized in PN, Therefore we believe that the present study was helpful for integration into the literature and clinical practice.

Conclusion

Hypophosphatemia, hypokalemia and hypomagnesemia were frequent in hospitalized pediatric patients before and during the initial four days of exclusive PN infusion. Hypomagnesemia was the most important metabolic disorder in our population and it was more prevalent in patients who received a greater amount of protein.

Regular corrections interventions associated with suitable individualization, based on current guidelines, seems to be the key on the controlling of mineral disorders before and, during the first week of PN.

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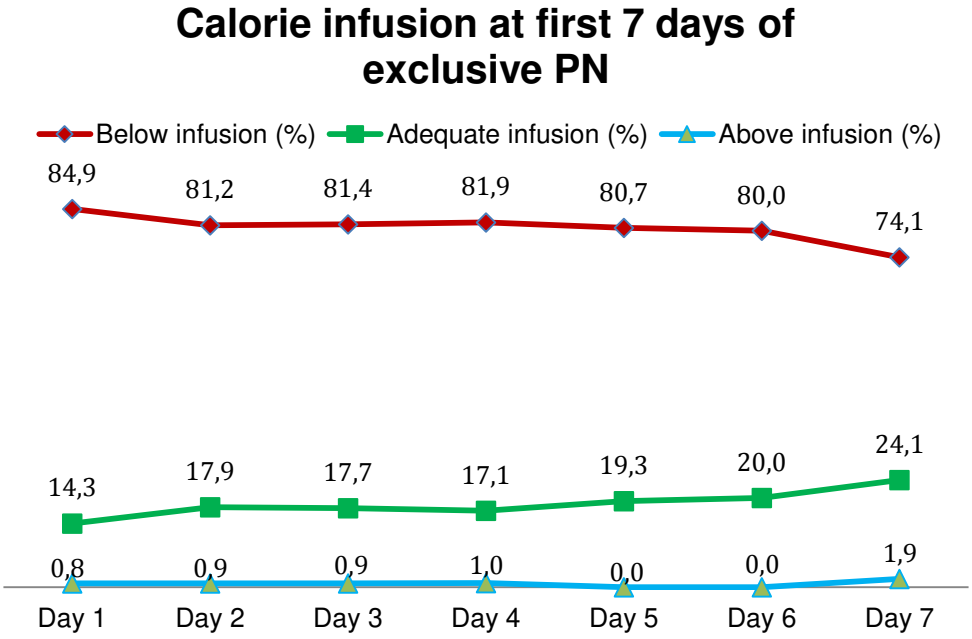

Figure 1. Calorie infusion (Kcal/Kg/day) in the first 7 days of infusion of exclusive PN classified according to Canada et al., 2009. Adequate calorie intake in 0-6 months patients: 85–105; 6–12 months: 80-100; 1-7 years: 75-90; 7-12 years: 50-75; 12-18 years: 30-50 Kcal/Kg/day. There was a decreasing of patients receiving calories below recommendation from 1st–4th day ($p<0.001$), and from 4th–7th day ($p<0.001$).

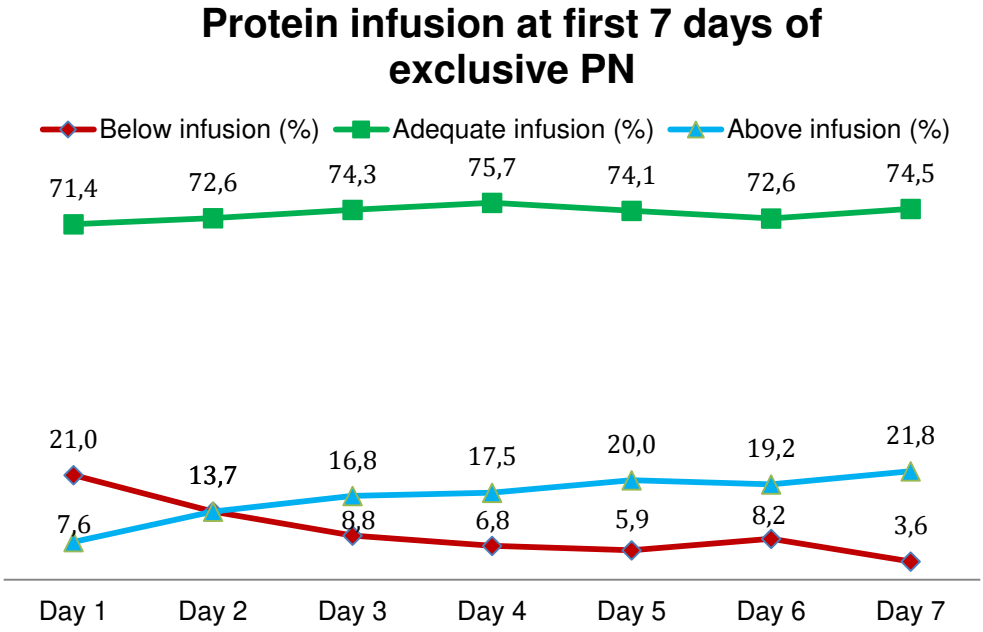

Figure 2. Protein infusion (g/Kg/day) in the first 7 days of infusion of pediatric exclusive parenteral nutrition classified according to Koletzko et al., 2005. Adequate protein intake in newborn term patients: 1.5–3.2 months-3 years: 1-2.5; 3-18 years: 1-2 g/Kg/day. There was an improvement in protein infusion, reducing the number of patients receiving protein below recommendation from 1st–4th day ($p<0.001$), and from 4th–7th day ($p<0.001$).

Table 1. Clinical consequences of severe hypophosphatemia, hypomagnesemia, and hypokalemia.

Hypophosphatemia	Hypokalemia	Hipomagnesemia
Respiratory failure	Rhabdomyolysis	Weakness
Paresthesias	Electrocardiograph changes	Tremor
Weakness	Cardiac arrhythmias	Electrocardiograph changes
Lethargy	Weakness	Cardiac arrhythmias
Somnolence	Paralysis	Tetany
Disorientation	Muscle necrosis	Convulsions
Areflexic paralysis		Seizures
Seizures		Coma
Coma		

Adapted by Crook MA, 2001.

Table 2. Laboratory reference values of phosphorus, potassium, and magnesium.

Phosphorus mg/dL		
Age	**Male**	**Female**
1 – 12 m	3.5 – 6.6	3.7 – 6.5
1 -3 years	3.1– 6.0	3.4– 6.0
4 - 6 years	3.3 – 5.6	3.2 – 5.5
7 – 9 years	3.0 – 5.4	3.1 – 5.5
10 – 12 years	3.2 – 5.7	3.3 – 5.3
13 – 15 years	2.9 – 5.1	2.8 – 4.8
16 – 18 years	2.7 – 4.9	2.5 – 4.8
Magnesium mEq/L		
5 m – 6 years	1.4 – 1.8	
12 – 20 years	1.4 – 1.8	
Potassium mEq/L		
1 – 12 m	3.6 – 5.8	
>1 year	3.1 – 5.1	

From Soldin SJ, Brugnara C, Wong EC. Pediatric Reference Intervals Fifth Edition. Washington, DC USA: AACC Press; 2005 to phosphorus reference values. From Keller H (ed.). Klinisch-chemische Labordiagnostik für die Praxis, 2a ed. Stuttgart/New York: Georg Thieme Verlag, 1991:222 to potassium reference values. From Wu, AHB. Tietz - Clinical Guide to laboratory tests, WB Saunders Co., 4a. ed., 2006: 706-709 to magnesium reference values.

Table 3. Clinical data concerning 119 pediatric patients admitted to receiving individualized exclusive PN.

Clinical data	Values
Male, n (%)	60 (50.4)
Age (months)	71.6±70.8
Total parenteral nutrition period (days)	7.3 ±4.5
Current weight (kg)	21.3±18.3
Malnutrition, n (%)	39 (32.8)
Thinness, n (%)	14 (11.8)
Severe thinness, n (%)	25 (21)
Diagnosis on admission	
Clinical (%)	52 (43.6)
GI/liver diseases (%)	23 (19.3)
Respiratory (%)	11 (9.2)
Sepsis (%)	7 (5.9)
Neurologic (%)	6 (5)
Trauma (%)	2 (1.7)
Others (%)	3 (2.5)
Surgical (%)	67 (56.4)
GI surgery (%)	48 (40.3)
Cardiac surgery (%)	12 (10.1)
Thoracic surgery (%)	2 (1.7)
Trauma surgery (%)	4 (3.4)
Otolaryngology surgery (%)	1 (0.8)
Pediatric intensive care unit n (%)	79 (66.4)
Death n (%)	16 (13.4)

Values are mean ± SD (standard deviation).

Table 4. Prevalence of hypophosphatemia, hypomagnesaemia and hypokalemia in pediatric patients during the first seven days of pediatric individualized exclusive PN.

Variable	P1*		P2*		P3*	
	N	n (%)	N	n (%)	N	n (%)
Hypophosphatemia	119	13 (37.9)	110	14 (48.3)	112	2 (6.9)
Hypomagnesaemia	119	29 (48.8)	110	11 (26.8)	112	1 (2.5)
Hypokalemia	119	12 (52.1)	110	10 (43.5)	112	1 (4.4)
Total		54 (58.1)		35 (37.6)		4 (4.3)

*Patients who started the disorder in the specified period. (P1) until 48th hours before beginning PN infusion; (P2) 1st–4th day of PN infusion; (P3) 5th–7th day of PN infusion. Data are expressed as n (%).

Table 5. Relationship between hypophosphatemia, hypomagnesemia, and hypokalemia events with malnutrition at first seven days of exclusive PN in pediatric patients.

Variable		Malnutrition*		OR	95% IC	p-value
		Yes	No			
Hypophosphatemia	Yes	11	18	1.41	0.58 – 3.4	0.493
	No	26	60	1.00		
Hypomagnesemia	Yes	16	25	1.56	0.69 – 3.54	0.299
	No	20	49	1.00		
Hypokalemia	Yes	12	11	2.79	1.09 – 7.14	0.045*
	No	25	64	1.00		

*Nutritional status was defined by Z-scores was calculated for anthropometric weight/age index for all subjects and classified according to classification of the World Health Organization (WHO). Malnutrition (Z-scores≤-2) was present 32.8% of patients: 11.8% had severe thinness (Z-scores≤-3) and, 21% thinness (Z-scores≤-2). Data is expressed as odds ratio (OR) and 95% confidence interval. $\chi 2$ test was used to test the differences between the two groups and * indicates significantly different between the two groups ($p < 0.05$).

Table 6. Relationship between hypophosphatemia, hypomagnesemia, and hypokalemia events with calorie and protein infusion of exclusive PN.

		Variable	Yes	No	OR	95% IC	p
Hypophosphatemia	$1^{st} – 4^{th}$ day	Calorie below*	12	80	0.67	0.12 – 3.5	0.643
		Calorie above*	-	-			
		Calorie adequate*	2	19	1.00		
		Protein below∞	1	8	0.62	0.05 – 7.03	0.643
		Protein above∞	10	76	0.65	0.16 – 2.67	0.690
		Protein adequate∞	3	15	1.00		
	5^{th} - 7^{th} day	Calorie below	2	65	-	-	1.000
		Calorie above	0	1	-	-	1.000
		Calorie adequate	0	17	1.00		
		Protein below	1	13	4.53	0.26 – 77.38	0.344
		Protein above	0	17	-	-	1.000
		Protein adequate	1	59	1.00		
Hypomagnesemia	$1^{st} – 4^{th}$ day	Calorie below*	8	82	0.55	0.13 – 2.30	0.416
		Calorie above*	-	-			
		Calorie adequate*	3	17	1.00		
		Protein below∞	1	8	1.64	0.17 – 15.43	0.517
		Protein above∞	4	12	4.38	1.07 – 17.65	0.049*
		Protein adequate∞	6	79	1,00		
	5^{th} - 7^{th} day	Calorie below	1	63	-	-	1.000
		Calorie above	0	1	-	-	1.000
		Calorie adequate	0	16	1.00		
		Protein below	0	3	-	-	1.000
		Protein above	0	16	-	-	1.000
		Protein adequate	1	57	1.00		
Hypokalemia	$1^{st} – 4^{th}$ day	Calorie below*	12	80	0.67	0.12 – 3.5	0.643
		Calorie above*	-	-			
		Calorie adequate*	2	19	1.00		
		Protein below∞	1	8	0.62	0.05 – 7.03	1.000
		Protein above∞	10	56	0.65	0.16 – 2.67	0.690
		Protein adequate∞	3	15			
	5^{th} - 7^{th} day	Calorie below	2	65	-	-	1.000
		Calorie above	0	1	-	-	1.000
		Calorie adequate	0	17	1.00		

	Protein below	1	13	4.53	0.26 – 77.38	0.344
	Protein above	0	17	-	-	1.000
	Protein adequate	1	59	1.00		

Calories infusion (Kcal/Kg/day) from 1st–4th day and from 5th–7th day of exclusive parenteral nutrition classified according to Canada et al., 2009. Protein infusion (g/Kg/day) was classified according to Koletzko et al., 2005. Data is expressed as odds ratio (OR) and 95% confidence interval. $\chi 2$ test was used to test the differences between the two groups. * Indicates significantly different between the two groups ($p < 0.05$).

5. CAPÍTULO 2 Changes in home parenteral nutrition practice assessed by the Canadian registry: a comparison between two time periods

Abstract

Background: Since 2005, the Canadian Home Parenteral Nutrition (HPN) Registry has collected data on patients' demography, outcomes, and HPN clinical practice; at annual meetings, Canadian HPN programs review and discuss results. *Aim:* To evaluate changes over time in patients' demography, outcomes and HPN clinical practice using the registry data. *Methods*: This is a retrospective study evaluating 369 patients who were prospectively entered in the registry either in 2005–2008 (n=182) or in 2011–2014 (n=187) from 6 HPN programs in Canada. Changes in patient demography, indications for HPN, HPN regimen, nutritional assessment, vascular access, and number of line sepsis per 1000 catheter days were evaluated. *Results*: In 2011–2014 compared with 2005–2008: indications for HPN changed significantly with an increased proportion of patients with cancer (37.9% versus 16.7%) and decreased short bowel syndrome (32% versus 65.5%); line sepsis rate decreased from 1.58 to 0.97 per 1,000 catheter days; tunnelled catheters decreased as the most frequently chosen vascular access method from 64.3% to 38.0% and the proportion of peripherally inserted central catheters (PICC) increased from 21.6% to 52.9%. In addition, there was a reduction in number, and days of hospitalizations related to HPN, and favourable changes in the prescription of energy, proteins, and trace elements were noted. Conclusion: The Canadian HPN Registry is useful in tracking trends in demography, outcomes and clinical practice. Results suggest a shift in patient demography and line access with improvement in line sepsis, hospitalizations and HPN prescriptions.

Keywords: home parenteral nutrition, clinical practice, clinical outcomes, indications, line sepsis

Introduction

Home parenteral nutrition (HPN) is a lifesaving therapy for outpatients who cannot meet their nutritional requirements through oral or enteral intake because of various causes of intestinal failure. However this form of nutrition support is associated with complications and frequent hospitalizations (1-3). Indications and complications may also fluctuate over time due to changes in patients' demography and practice. We could find only two studies looking at changes over time. One (4) collected data retrospectively over a five-year period from patients serviced by one HPN provider in the United States. This included data from 72 university and non-university HPN programs. The authors reported that diagnoses related to malnutrition of any causes, malabsorption, intestinal obstruction, and pancreatic disease were the main indications for HPN, and that this did not change over time. However, during the observation period, the average time on HPN therapy increased overall from 98 days/year in 1997 to 120 days/year in 2001, whereas the incidence of suspected catheter infections decreased from 0.84 to 0.44 cases per 1,000 catheter days. Weaning and death were the two most frequent reasons to discontinue HPN with changes from 50% to 58% and from 17% to 22% respectively over the time period. In Spain, a retrospective study of patients receiving HPN between 1986 and 2012 compared the first 13 years of observation with the last 13 years. The authors reported a significant increase in the use of HPN for cancer (+45.1%), Crohn's disease (+5.5%), and radiation enteritis (+6.6%) ($p=0.004$) (5). Overall complication rate ($p=0.01$) and catheter-related complication rate ($p<0.001$) decreased during the last 13 years of the

period studied. The total mean complication rate was 3.58/1,000 HPN days and this was consistently associated with HPN duration ($p<0.001$). Liver disease incidence (8.8%) was also related to HPN length ($p<0.05$). Overall survival rate was 72% at 1 year and 42% at 5 years after HPN initiation and varied across the underlying conditions ($p<0.05$).

Since 2005, the Canadian HPN Registry has been collecting information on demography, gastrointestinal anatomy, indications for HPN, nutrition assessment, HPN regimen, vascular access, quality of life, laboratory investigations, medication, liver investigations, bone density, hospitalizations, and survival of HPN patients in Canada. This registry has been validated (6) and data are entered about every 2 years to monitor clinical parameters and outcomes as well as HPN practice across HPN programs in Canada. Several studies were published using the patients cohort from the HPN Registry (7, 6, 8, 9, 10) and results are discussed at yearly HPN workshops to reflect upon and to optimize practice as it relates to the PN prescription and the management of complications related to intestinal failure and its treatment. For example, the micronutrient prescription was found to not comply with recent guidelines. Particularly, manganese dose was found to be too high in several HPN centers and this was associated with manganese deposits in basal ganglia based on magnetic resonance imaging (10). Another study showed that patients who were not prescribed vitamin K supplements were more at risk of developing osteoporosis (8).

The main goal of the present study was to evaluate if there have been changes in HPN clinical practice and outcomes over the last decade in Canada in multiple HPN centers participating in the Canadian HPN Registry.

Methods

This is a retrospective study evaluating changes in practice and clinical outcomes of patients receiving HPN in Canada. Study patients were prospectively entered in the web-based HPN Registry over a period of 10 years and data were extracted from two separate time periods: 2005–2008 and 2011–2014. A total of 510 patients were entered into the registry from 2005–2014, and data from 369 patients belonging to these two time periods were used. Six specialized programs entered baseline data during this time: Toronto (Toronto General Hospital, St. Michael's Hospital), Hamilton (Hamilton Health Sciences), Edmonton (Capital Health/University of Alberta), Calgary (Foothills Medical Centre), Vancouver (British Columbia Home Parenteral Nutrition Program).

All data were assessed by a standard questionnaire filled in by the HPN nurse or clinician and then entered into the online Registry. In order to ensure that the two patient's samples from the two time periods were independent from each other (different patients), only patient's first data entry was considered for this study. Time on HPN per year was calculated from the start of parenteral nutrition (PN) support to the end date of PN or if PN has not ended, to the date of data extraction. All participants gave their informed written consent.

Changes over the two time periods were evaluated for: patient demography: age, sex, time on HPN; indications for HPN; HPN regimen: energy per day kcal/kg, energy prescribed compared to estimated requirement (%), protein per day g/kg, protein prescribed compared to estimated requirement (%), vitamins and minerals, days on HPN per week and hours on HPN per day; nutritional assessment: BMI at start of HPN, BMI at data extraction, additional dietary intake and method of delivery. In addition, over the

year preceding data entry, number of hospitalizations including those related to PN, days of hospitalization including those related to PN, number of line sepsis per 1,000 catheter days, vascular access: type of vascular access, type of insertion, and number of lumens were also compared.

Statistical Analysis

The distribution of continuous variables was assessed using graphical methods, and the median (q1, q3) was calculated for many variables because of skewed distributions. Categorical variables were characterized using counts and percentages. The data between the 2 periods (2005-2008 and 2011-2014) were compared using Mann Whitney test for continuous variables and Fisher's exact test for categorical variables. Rates of line infections were calculated per 1,000 catheter days for each period and were compared using z-test for log rate ratio statistic. The analyses were performed using SPSS version 16 (SPSS, Inc, an IBM Company, Chicago, IL) and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). A two-sided p-value of 0.05 or less was considered statistically significant.

Results

A total of 369 baseline entries from six different sites were available for the two time periods. 182 patients entered the HPN registry in 2005–2008, and 187 in 2011–2014.

The median age of the patients increased significantly from 2005–2008 to 2011–2014 (Table 1). The distribution of genders was similar in both periods with more females than males among HPN patients. Short bowel syndrome was the most frequent diagnosis

(65%) in 2005-2008, whereas in the subsequent period, tumor/cancer (37.9%) was the most frequent indication to HPN treatment, followed by surgical complications (Table 1). The time on HPN was significantly lower in the second period (Table 2) likely because patients were entered at an earlier stage of HPN support compared with the first period, which was when the registry was created and all HPN patients were entered for the first time. The number of hospitalizations related to PN and days of hospitalization related to PN over the year preceding the registry entry were lower in the second time period (Table 2) versus the first.

Line sepsis rates decreased significantly when comparing the two periods. In the 2005-2008 and 2011-2014 period, the rates of line sepsis were 1.58 (n=179) and 0.97 (n=159) per 1000 catheter days respectively, with rate ratio of period 2 to 1 of 0.61(p=0.030). In the period 2005-2008, tunnelled catheters were the most frequently chosen vascular access method (64.3%) but this decreased in 2011-2014 (38.0%). On the other hand, proportion of peripherally inserted central catheters (PICC) increased over time (21.6% to 52.9%). Radiology was used for the majority of line insertions in both periods, and the proportion increased over time, whereas surgical insertion decreased. Other modes of insertion, for example, PICC inserted at bedside were only used in the second period (Table 3).

The average reported PN micronutrient supplementation across the six HPN centers was compared with published American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) guidelines (Table 4). In both periods, zinc, manganese and copper supplementation exceeded the published recommendations, whereas chromium supplementation corresponded with the guidelines. Selenium provision exceeded the

A.S.P.E.N. guidelines in 2005-2008, and in 2011-2014 periods with more than 25% of patients receiving more than recommended. There are no specific guidelines for iodine provision, although the daily requirements in adult patients receiving parenteral nutrition are estimated to be between 0.55 and 1.18 μmol (11). Supplementation of zinc, manganese, selenium, chromium and iodide in HPN decreased significantly from 2005-2008 to 2011-2014. In contrast, provision of copper by HPN increased significantly when comparing the two periods (Table 4).

The median BMI was higher in the second period, at the time of data entry (Table 4), and patients were prescribed significantly more energy and protein per day. Compared to patients' requirements, energy and protein prescriptions were higher in the 2011-2014 period, and HPN was given over more days per week (Table 5).

Discussion

The HPN Registry was created and used to define patient demography and outcomes as well as to assess practice across Canada. This study shows that patient demography has changed significantly over the past decade with more cancer and less short bowel syndrome in the recent period, and that there has been a significant change in the type of vascular access. In addition, a reduction in hospitalizations and line sepsis rates over the year prior to data entry was noted along with favourable changes in the prescription of energy, proteins, vitamins and trace elements. These results suggest that the HPN Registry is useful for tracking trends in patient demography, outcomes and practice and that perhaps it plays a role in improving care when used for clinical studies (7, 6, 8, 9, 10) and for yearly meetings among HPN programs to review results and discuss practice.

The patient demography significantly changed with more cancer as an indication for HPN and less short bowel syndrome. The reduction in short bowel syndrome may reflect better treatments for Crohn's disease with reduction in bowel resections (12). With oncology cases increasing and more advanced treatments, this segment of the patient population may require more HPN. Our results are similar to HPN programs in other countries. Oncology patients represented the largest percentage of HPN patients in studies from Spain (49.5%) (5), Switzerland (57.4%) (13), and the United States (42%) (14). The increasing number of cancer patients in the HPN programs might contribute to the more frequent use of PICC lines in some centers where chemotherapy might be delivered using this route. According to the recent literature (15,16), PICCs can be safely used in cancer patients receiving chemotherapy and/or HPN, with a long catheter life span, and a low probability of catheter removal because of complication, low incidence of thrombosis, mechanical complications, and line sepsis.

We observed a decrease in line sepsis from the 2005-2008 to the 2011-2014 period. Episodes of line sepsis are common complications in patients receiving HPN and are associated with significant morbidity and mortality (17). They are associated with several factors such as quality of training and patient's compliance following the aseptic protocol, HPN duration, underlying disease, number of central catheter lumen, insertion site, type of catheter, clinical practice (18) and socioeconomic environment (17,18). Although it is difficult to determine which specific factor(s) may have played a role in the reduction of line sepsis, it is important to note that yearly HPN program meetings may identify practice issue(s) that need to be improved. For example, during the first time period, one HPN program had a significantly higher rate of line sepsis compared with

other programs (data not shown). This was examined, and the program identified that the use of a positive pressure port was the cause of increased line sepsis, which was subsequently also reported by another group (19).

The major causes of line sepsis are migration of organisms of the skin along the line, poor aseptic technique when inserting, contaminated infusion, and difficulties of line care maintained by patients. The guidelines from E.S.P.E.N. and A.S.P.E.N. recommend that the home environment is assessed before any training, and they state that educating patients on HPN is essential in order to reduce the risk of complications (2,3). In Canada, HPN is managed by dedicated and specialized health care team that closely supervise and follow all aspects of medical care and nutrition including training and patient education. An important initiative to follow patients in remote areas was the implementation of a Telehealth videoconference program (20) at the University Health Network in Toronto, Ontario, Canada, with the goal of providing regional and provincial telemedicine and monitoring. This initiative helped to promptly identify and treat medical problems, including line infection and catheter complications.

Our results also showed a shift in the type of line insertion from tunnelled to peripherally inserted central catheters (PICC). HPN patients usually receive tunnelled catheters and PICC lines because they need to receive nutritional therapy over a long period of time. The literature indicates that PICCs are only preferred if the estimated duration of HPN is at least 3–4 months or limited to 12–18 months (1). We can observe that there is a transition from the use of tunnelled catheters to PICC lines in Canada, and this may also explain the significant increase in the use of radiology and line insertion at bedside shown by our data. The tunnelling of the catheter reduces the risk of infection but has been

reported to be associated with complications such as pneumothorax and accidental arterial puncture. The HPN teams may choose PICCs as alternative to the conventional tunnelled catheter because insertion is easy and safe due to their placement into peripheral veins of the arm, and because the central location of catheter tip is still suitable for all osmolality and pH solutions. This choice may be also due to lower costs compared to conventional central lines or ports (21). We also observed an increase of ultrasonography demand in our population compared with past years. The use of ultrasonography-guide insertion is important to minimize the risk of pneumothorax (22).

The increased use of PICC lines in Canada is in contrast to the E.S.P.E.N. guidelines that do not recommend PICCs for HPN. The reason is that patients with short bowel may need a high volume of HPN with high osmolality of infusion, exceeding the capacity of the line. PICC access also has the disadvantage of being "less cost effective" because of the difficulty in inserting and maintaining the catheter (21), and the possibility that the catheter has to be removed before completion of HPN therapy (23). A recent study (24), demonstrated that PICCs are appropriate for use in HPN for at least 3–4 months, with complication rates comparable to those reported for tunnelled central catheters. Another prospective study (25) comparing the rates of complications associated with tunnelled catheters (Broviac) and PICC in HPN patients found that overall, complications were similar in both the PICC and the Broviac groups (26/71 vs. 91/133) and that the PICC catheter was associated with a decrease in catheter infection (1.87 vs. 1.05 per 1,000 catheter-days; $p = 0.01$).

Patients who had their first entry in 2011-2014 were on HPN for a shorter duration compared with those entered in the 2005-2008 period. They also had less hospital days,

including those related to HPN, over the year prior to data entry. Time on HPN might have influenced our results. Many patients who were entered into the registry in the first period were already on HPN for several years while in the second period, patients were approached for the registry within 2 years of HPN start. Therefore, some of the differences observed between the two periods may be due to differences in HPN duration as well as differences in patient demography.

Adequate trace element supplementation is important for patients on long-term PN, especially in patients with severe malabsorption such as those with short bowel syndrome, high-output fistulas, ostomy, or significant diarrhea that may require higher supplementation. Other conditions such as the presence of organ failure (e.g. liver disease) may also affect requirements and serum trace element concentrations. In addition, intestinal absorption has a significant role in the homeostasis of trace element physiologic levels, and HPN supplementation bypasses this important regulatory feedback mechanism and makes the patient more susceptible to toxicity. Our results showed some improvement in the trace element prescription when compared to guidelines. Abdalian et al., evaluated trace element prescription practice across Canada in adults HPN patients entered in the Canadian HPN Registry between 2005 and 2007 (9), and found that the average nationwide daily HPN supplementation of zinc, selenium, manganese, cooper, and iodide exceeded A.S.P.E.N. recommendations. Only the average nationwide daily chromium met the guidelines. In addition, the trace element prescription was not determined by the underlying medical condition (e.g. severe malabsorption) or oral dietary intakes. The authors suggested that PN trace-elements supplementation in Canadians HPN programs needed to be reviewed and adjusted according to the most

current guidelines to improve the safety and efficacy of PN therapy. This, along with findings of manganese deposition in basal ganglia by medical resonance imaging due to over-supplementation [10] was presented and discussed at the yearly HPN program meeting and subsequently, HPN programs revised their trace element prescription. As a result, we observed that zinc, manganese, selenium, chromium and iodide supplementation in HPN decreased significantly in the 2011-2014 period compared with 2005-2008. These improvements may be the results of these studies (9,10). However, the amount of copper has increased, still exceeding the guidelines in both the 2005-2008 and the 2011-2014 periods. Reasons for this are not clear. Copper toxicity is rare and may cause liver cirrhosis (26). On the other hand, copper deficiency produces hypochromic, microcytic anemia and neutropenia (27,28).

In our study, patients had higher BMI and received more energy and proteins per day in the second period, with an increase from 21.8 kcal/kg to 25 kcal/kg. The prescriptions in both periods were in accordance with guidelines from E.S.P.E.N. and the Australasian Society for Parenteral and Enteral Nutrition (AuSPEN) that suggest 20–35 kcal of total energy per kilogram per day for stable HPN patients. Canadians patients also received more protein per day (1.3 g/kg) in the 2011-2014 period, which is according to E.S.P.E.N. and AuSPEN (0.8–1.4 g/kg). For ambulatory cancer patients E.S.P.E.N. guidelines of parenteral nutrition in oncology suggest 25-30 kcal/kg/day, protein supply recommendations range between a minimum of 1 g/kg/d and a target of 1.2–2 g/kg/day. This approach of our programs in protein and calories prescription might be due to the increased number of the cancer patients receiving HPN.

Conclusion:

In the last decade, HPN in Canada has evolved with several changes related to patient demography, routes for central venous catheter and HPN prescriptions as well as improvements in line sepsis rates, hospitalizations and HPN trace elements. These changes may reflect new standards of care but they also demonstrate the usefulness of a patient registry with concomitant studies and meetings to review patient population, outcomes, and clinical practice.

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Tables

1. Demography and indication for HPN in patients entering the registry in 2005-2008 and 2011-2014.

	2005-2008		2011-2014		p-value
	N	median (p25; p75)	N	median (p25; p75)	
Age (years)	182	52 (42, 62)	187	57 (46.5, 63.5)	0.047
		n (%)		n (%)	
Gender	182				
Female		107 (58.8%)	187	114 (61%)	
Male		75 (41.2%)	187	73 (39%)	
Indication for HPN*					
Short Bowel Syndrome	168	110 (65.5%)	169	54 (32%)	<0.001
Mucosal Dysfunction	168	15 (8.9%)	169	4 (2.4%)	0.010
Motility Disorder	168	29 (17.3%)	169	17 (10.1%)	0.058
Tumor/Cancer	168	28 (16.7%)	169	64 (37.9%)	<0.001
Surgical Complication	168	28 (16.7%)	169	51 (30.0 %)	0.005
Pancreatic disorders	168	1 (0.6%)	169	2 (1.2%)	1.000

HPN, Home Parenteral Nutrition. Variables were compared using Mann–Whitney U test or Fisher's exact Test. *More than one category could be selected per patient.

2. Time on HPN and hospitalizations over the preceding year in patients entering the registry in 2005-2008 and 2011-2014.

	2005-2008		2011-2014		p-value
	N	median (p25; p75)	N	median (p25; p75)	
Time on HPN (years)	169	2.31 (0.99;5.8)	176	0.30 (0.17;0.9)	<0.001
Number of hospitalizations/year	146	0 (0;2)	160	1 (0;2)	0.843
Number of hospitalizations related to PN	118	0 (0;1)	146	0 (0;0)	0.006
Days of hospitalization/year	115	2 (0;22)	148	8 (0;36)	0.215
Days of hospitalization/year related to PN	136	0 (0;2)	143	0 (0;0)	<0.001

PN, Parenteral Nutrition. HPN, Home Parenteral Nutrition. Time on HPN was calculated from start of PN support to end date of PN or if PN has not ended to the date of baseline data extraction. Values are median (25^{th} percentile; 75^{th} percentile). Variables were compared using Mann–Whitney U test.

3. Vascular access in HPN patients entering the registry in 2005-2008 and 2011-2014.

		2005-2008		2011-2014	p-value*
Type of vascular access		n (%)		n (%)	
Implanted Catheter	171	24 (14.0%)	187	17 (9.1%)	0.183
Tunneled Catheter	171	110 (64.3%)	187	71 (38.0%)	<0.001
PICC	171	37 (21.6%)	187	99 (52.9%)	<0.001
Type of insertion					
Radiology	162	96 (59.3%)	178	155 (87.1%)	<0.001
Surgical	162	66 (40.7%)	178	9 (5.0%)	<0.001
Other	162	0 (0.0%)	178	14 (7.9%)	<0.001
Number of lumens					
1	154	55 (35.7%)	180	73 (40.6%)	0.369
2	154	98 (63.6%)	180	106 (58.9%)	0.431
3	154	1 (0.6%)	180	1 (0.6%)	0.719

HPN, Home Parenteral Nutrition. Data were compared using Fisher's Test.

4. Daily trace element supplementation across all Canadians HPN programs in comparison to A.S.P.E.N Guidelines [3] and vitamins supplementation in patients entering the registry in 2005-2008 and 2011-2014.

	A.S.P.E.N Guidelines	2005-2008		2011-2014		p-value
Trace elements		N	median (p25; p75)	N	median (p25; p75)	
Zinc, µmol	38.75 – 76.50	174	91.80 (76.5;153.0)	185	76.50 (76.50;125.60)	0.002
Manganese, µmol	1.09 – 1.82	174	9.10 (5.42;9.12)	185	7.80 (0.32;9.10)	<0.001
Selenium, µmol	0.25 – 0.76	174	0.76 (0.75;1.50)	185	0.76 (0.75;1.01)	0.049
Chromium, µmol	0.19 – 0.29	174	0.19 (0.14;0.27)	185	0.19 (0.09;0.19)	<0.001
Copper, µmol	4.73 – 7.88	174	11.20 (4.50;15.74)	185	15.74 (6.30;15.75)	<0.001
Iodine, µmol		174	0.59 (0.42;0.72)	185	0.59 (0.29;0.59)	<0.001
Vitamins		N	n (%)	N	n (%)	
Vitamin K		184	76 (41.5)	185	61 (33)	0.106
Vitamin B12		183	161 (88.0)	185	160 (86.5)	0.755

A.S.P.E.N., American Society for Parenteral and Enteral Nutrition. HPN, Home Parenteral Nutrition. The data are expressed by median (percentiles 25; percentiles 75). Mann–Whitney U test or Fisher's exact test was used to compare variables, as appropriate.

5. Body mass index and HPN prescription in patients entering the registry in 2005-2008 and 2011-2014.

	2005-2008		2011-2014		p-value
	n	median (p25; p75)	n	median (p25; p75)	
BMI [β] Kg/m²	172	20.3 (18;23)	178	20.7 (18.5;25)	0.043
Days on HPN/week	166	7 (5;7)	185	7 (7;7)	<0.001
Hours on HPN/day	161	12 (12;14)	181	12 (12;13)	0.670
Energy per day kcal/kg	162	21.8 (15;26.9	178	25 (18.6;30.6)	0.019
% of energy requirement*	159	77.5 (49.8;95.4)	174	86.7 (67.7;98)	0.006
Protein per day g/Kg	154	1.1 (0.78;1.3)	175	1.3 (1.0;1.6)	<0.001
% of protein requirement*	39	95.4 (67.2;109.8)	171	100 (84.5;111.6)	<0.001
Additional dietary intake	N	n (%)	N	n (%)	
Oral	190	131 (68.8%)	188	143 (76.1%)	0.135
Enteral	190	3 (1.6%)	188	4 (2.1%)	0.723
Method of delivery					

3-in-1	184	157 (91.8)	185	175 (96.6)	0.065
2-in-1	184	14 (8.2)	185	6 (3.3)	0.064

NA, Not Available. HPN, Home Parenteral Nutrition. [α]BMI at start of HPN treatment. [β]BMI at data extraction. * % of prescribed compared to estimated requirement. Values are given in % of patients or median (25^{th} percentile; 75th percentile). Variables were compared using Mann–Whitney U test or Fisher's Exact Test as appropriate.

6. CONCLUSÃO GERAL

As complicações metabólicas hipofosfatemia, hipomagnesemia e hipocalemia foram frequentes antes do início e na primeira semana de infusão de NP. A individualização da NP foi necessária para prevenir novos casos e corrigir os já estabelecidos. A individualização seguindo as recomendações dos *guidelines* vigentes mostrou-se eficaz para gerenciar estes distúrbios.

Embora a desnutrição seja fator conhecidamente importante relacionado a estes distúrbios, o único mineral relacionado à desnutrição foi o potássio.

A progressão gradativa de energia não evitou que acontecessem os distúrbios metabólicos, mas associado à individualização, pode ter evitado distúrbios metabólicos graves durante a infusão da NP.

A ingestão protéica acima da recomendação parece estar relacionada à maior risco de hipomagnesemia.

Em relação à NPD no Canadá, uma importante constatação é a mudança no perfil demográfico. De fato, houve aumento de pacientes diagnosticados com câncer e diminuição de SIC, influenciando a prescrição de energia e proteína. A prescrição de elementos-traço diminuiu, mas ainda prescreve-se acima das recomendações atuais.

Apesar do uso do PICC não ser indicado para pacientes em NPD pelos *guidelines* vigentes, o uso deste aumentou significantemente, mostrando-se ser a mais frequente escolha de acesso vascular no segundo período. Assim, o uso do PICC para NPD parece ser uma estratégia estabelecida.

A incidência de sepse, comparando dados da última década diminuiu, assim como o número de internações e as internações relacionadas à NPD.

As mudanças na prática clínica e nos indicadores no Canadá na última década foram significativos. Mais estudos serão necessários para preconizar novas recomendações na prescrição de elementos-traço assim como avaliar os riscos na prática do uso de PICC em NPD.

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8. APÊNDICES

APÊNDICE 1. Termo de Consentimento Livre e Esclarecido (TCLE)

FACULDADE DE CIÊNCIAS MÉDICAS
COMITÊ DE ÉTICA EM PESQUISA

www.fcm.unicamp.br/fcm/pesquisa

CEP, 20/12/11
(Grupo III)

PARECER CEP: N° 1304/2011 (Este n° deve ser citado nas correspondências referente a este projeto).
CAAE: 1210.0.146.000-11

I - IDENTIFICAÇÃO:

PROJETO: **"DISTÚRBIOS DOS MINERAIS EM PACIENTES SOB NUTRIÇÃO PARENTERAL EM UM HOSPITAL TERCIÁRIO E PREVALÊNCIA DA SÍNDROME DO ROUBO CELULAR".**
PESQUISADOR RESPONSÁVEL: Taís Daiene Russo Hortencio
INSTITUIÇÃO: Hospital de Clínicas/UNICAMP
APRESENTAÇÃO AO CEP: 12/12/2011
APRESENTAR RELATÓRIO EM: 20/12/12 (O formulário encontra-se no *site* acima).

II – OBJETIVOS.

Avaliar e relacionar os distúrbios dos minerais com a mortalidade e a prevalência da síndrome do roubo celular.

III – SUMÁRIO.

Trata-se de projeto retrospectivo onde os pesquisadores analisarão fichas de pacientes (adultos e crianças, ao redor de 1.200) que foram hospitalizados no HC da UNICAMP no período de janeiro de 2008 a agosto de 2011 e que tenham recebido NP durante a hospitalização (fichas de acompanhamento de NP da Equipe Multiprofissional de Terapia Nutricional do HC). Os dados bioquímicos descritos na monitorização laboratorial da NP serão relacionados com o sexo, tipo de diagnóstico, indicação, início e término da NP, antropometria e com a quantidade da infusão infundida. Os pesquisadores acreditam que a elucidação de como os distúrbios de minerais influem no prognóstico e mortalidade de pacientes sob NP poderá contribuir para futuro aperfeiçoamento em estratégias terapêuticas. Por se tratar de estudo retrospectivo de análise de dados já gerados, os pesquisadores solicitam dispensa do Termo de Consentimento Livre e Esclarecido.

IV - COMENTÁRIOS DOS RELATORES.

Projeto muito bem elaborado, com todos os critérios adequadamente preenchidos.

V - PARECER DO CEP.

O Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP, após acatar os pareceres dos membros-relatores previamente designados para o presente caso e atendendo todos os dispositivos das Resoluções 196/96 e complementares, resolve aprovar sem

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restrições o Protocolo de Pesquisa, a dispensa do Termo do Consentimento Livre e Esclarecido, bem como todos os anexos incluídos na pesquisa supracitada.

O conteúdo e as conclusões aqui apresentados são de responsabilidade exclusiva do CEP/FCM/UNICAMP e não representam a opinião da Universidade Estadual de Campinas nem a comprometem.

VI - INFORMAÇÕES COMPLEMENTARES.

O sujeito da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (Res. CNS 196/96 – Item IV.1.f) e deve receber uma cópia do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado (Item IV.2.d).

Pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado e descontinuar o estudo somente após análise das razões da descontinuidade pelo CEP que o aprovou (Res. CNS Item III.1.z), exceto quando perceber risco ou dano não previsto ao sujeito participante ou quando constatar a superioridade do regime oferecido a um dos grupos de pesquisa (Item V.3.).

O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo (Res. CNS Item V.4.). É papel do pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.

Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Em caso de projeto do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma junto com o parecer aprovatório do CEP, para serem juntadas ao protocolo inicial (Res. 251/97, Item III.2.e).

Relatórios parciais e final devem ser apresentados ao CEP, de acordo com os prazos estabelecidos na Resolução CNS-MS 196/96.

VII – DATA DA REUNIÃO.

Homologado na XII Reunião Ordinária do CEP/FCM, em 20 de dezembro de 2011.

Prof. Dr. Carlos Eduardo Steiner
PRESIDENTE do COMITÊ DE ÉTICA EM PESQUISA
FCM / UNICAMP

ANEXO 1. Ficha de avaliação e seguimento de NP do HC da Unicamp - Brasil

HOSPITAL DE CLÍNICAS – UNICAMP
EQUIPE MULTIPROFISSIONAL DE TERAPIA NUTRICIONAL (EMTN)

Ficha de avaliação e Seguimento – NUTRICÃO PARENTERAL

Nome: _____ HC: _____ PM:_____

Enfermaria: _____Especialidade:_____Leito 1 (data):_____ Leito 2 (data/enfermaria):_____

Leito 3 (data/enfermaria):_____Idade: ___ Sexo: (M) (F)

Diagnósticos: _____ Data de internação ___/___/___

Data de nascimento___/___/___

Antecedentes: _____

Diagnóstico Nutricional: _____

Necessidades Nutricionais: (GEB: _____ FA: _____ FI: _____) _____ Kcal Protéicas:_____ g Hídricas : _____ ml

Indicação NP (prescritor): _____

Indicação NP (EMTN): _____

Início da TN: ____/____/____ Término da TN: ___/___/___ (Alta) (Óbito) (Transf. P/) _____ em ___/___/_____

Avaliação nutricional inicial:

Estatura (cm):	PA/aferido (kg):	PA/referido/estimado(kg):	Peso ajustado (kg):	PI (kg):	PU (kg):	Compleição:	% perda de peso
IMC (kg/m²):	CB (cm):	PCT (mm):	CMB (cm):	PCB (mm):	Punho (cm):	Altura do Joelho:	

TN/Data															
VO prescrito															
VO recebido															
NE prescrito															
NE recebido															
NP tipo															
Kcal total															
Evolução															
TN/Data															
VO prescrito															
VO recebido															
NE prescrito															
NE recebido															
NP tipo															
Kcal total															
Evolução															

NOME: _____HC: _____

Data														
Na / K	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Ca(t) / Ca(i)	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Pi/Mg	/	/	/	/	/	/	/	/	/	/	/	/	/	/
U/Cr														
Proteína T														
Albumina														
Pré-albumina														
PCR														
Hb / Ht	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Leucócitos														
Linfócitos														
Plaquetas														
ALT / AST	/	/	/	/	/	/	/	/	/	/	/	/	/	/
FA / γGT	/	/	/	/	/	/	/	/	/	/	/	/	/	/
COL. TOTAL														
HDL														
TGL														
Glicemia</>	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Bili (T/D)	/	/	/	/	/	/	/	/	/	/	/	/	/	/

RNI / R	/	/	/	/	/	/	/	/	/	/	/	/	/	/
AMI/LIP	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Cl/Bic	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Lactato														

ANEXO 2. Ficha de coleta de dados de pacientes sob NPD - *Toronto General Hospital* – Canadá.

HTPN PATIENT REGISTRY FORM 2014

Informed consent signed? □ Yes □ No

HTPN Registry Patient code: _____
(3 code letters for the center followed by any 5 numbers, e.g. TGH00001)

HTPN CENTER (Full name): _____

Code: _____ Province: _____

Date of data extraction: _____ (mm/dd/yyyy)
(Enter this value for all forms on the website)
NOTE: *If patient expired or is weaned off TPN, use the day of death or the last visit to the TPN clinic, respectively, as date of data extraction!*

Type of record (please check):

□ Baseline Follow up: □ 2 year □ 4 yr □ 6 yr □ 8 yr □ 10 yr □___ yr

PATIENT BASIC

This is □ an adult record □ a pediatric record
Has this patient been seen previously in your clinic? □ Yes □ No
Gender: □ F □ M Date of birth: _____ (mmm/yyyy)
Age: _____
Occupation: _____
Highest level of education attained (if known): _____

Please note:

- *Suggested document source: clinic or hospital charts over the past 12 months*
- *If patient expired or is weaned off TPN, use the day of death or the last visit to the TPN clinic, respectively, as date of data extraction! When previous 12 months are asked in the form, use the 12 months before death/weaning.*
- *Pages 1-2 are permanent patient information. If there are changes from one year to the next, only write the change, e.g. change in anatomy due to additional surgery).*
- *For the entire form, write "NA" if data is not available.*

ANATOMY *(Website: click ANATOMY)*

What type of record is this? □ Baseline □ Follow-Up _____years

Is the anatomy known? □ Yes □ No

If baseline, enter information below.
If follow-up, has there been any change in GI anatomy since last entry? □ Yes □ No
If yes, enter information below. **If no**, go to the last question on this page: Other medical diagnosis

Does the entire small bowel remain? □ Yes □ No

If no, is the length of the small bowel known? □ Yes □ No

If yes, what is the total length of small bowel? cm: _____
If known, describe the small bowel remaining:
_____

Does the full colon remain? □ Yes □ No

Only part of the colon remains? □ Yes □ No

If yes, describe: _____

Only rectum remains? □ Yes □ No

Remaining colon? □ Yes □ No

Is the gastrointestinal tract in continuity (re-anastomosed)? □ Yes □ No

Is there an ostomy bag? □ Yes □ No
If yes, what type (Gastromy Venting Tube, Duodenostomy, Jejunostomy, Ileostomy, Colostomy, Other: Specify)? _____
Describe other GI surgery (e.g. whipple, cholecystectomy, etc.):
_____

Other medical diagnosis:
_____
_____

NUTRITION ASSESSMENT *(Website: click NUTRITION)*
What type of record is this? □ Baseline □ Follow-Up: _____ years

Anthropometry

Actual Body Weight (ABW): _____ kg Height_____ cm BMI: _____kg/m^2

Weight at start of TPN: _____kg BMI at start of TPN: _____ kg/m^2
*(If patient had an interruption in TPN, please enter here weight at **re-start** of TPN)*

Estimated Nutrient Requirement

Current Total Estimated Energy Requirement (TEER)(kcal/day) calculated by Harris-Benedict (HB)

HB Male: [66.5 + 13.7 W (kg) + 5.0 H (cm) – 6.7 A (y)]: _____ kcal/d

HB Female: [655 + 9.5 W (kg) + 1.8 H (cm) – 4.7 A (y)]: _____ kcal/d

Multiply HB by Stress factor (1.0 if sedentary – 2.5 if physically active)
Stress factor used: _____

TEER = HB x Stress factor: _____ kcal/day (Enter this value in website)

Protein Requirements (g/kg): _____

Nutrient Intake

TPN:
Energy (kcal/day): _____ (If TPN < 7 days/week, indicate average per day)
Protein (g/day): _____ (If TPN < 7 days/week, indicate average per day)

Oral (Estimate only. If applicable, include nutritional supplements):
Energy (kcal/d)_____Protein (g/d): _____

Specify Oral Diet Type (low oxalate, short gut, post-gastrectomy, lactose restricted, modified fibre, DAT, anti-dumping, other) _____

Enteral Diet (if applicable):
Energy (kcal/day): _____ (If < 7 days/week, indicate average per day)
Protein (g/day): _____ (If < 7 days/week, what is average per day)

Name of enteral product: _____
Specify tube site: □ Gastrostomy □ Gastrojejunostomy □ Jejunostomy
□ Other (specify): _____

Alcohol (g/week): _____ (e.g. 1 glass wine; 1 beer; or 2 oz. liquor = 10 g)
or: □ Alcohol intake unknown

Smoking (# cigarette/day): _____ or: □ unknown

BONE MINERAL DENSITY *(Website: click BONE MINERAL DENSITY)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

If baseline, enter information below.

If follow-up, did this patient have a bone mineral density performed since last data entry?
□ Yes □ No

If yes, enter information below. **If no,** go to Bone Fractures

Date of BMD: _____ (mm/dd/yyyy)

Spine: BMD (g/cm^2): _____ T-score: _____ Z-score: _____

Femoral neck: BMD (g/cm^2): _____ T-score: _____ Z-score: _____

Total hip: BMD (g/cm^2): _____ T-score: _____ Z-score: _____

Bone Fractures

Risk of fracture:
Average_____ Minimal Increase: _____ Moderate Increase: _____ High Risk: _____

Has the patient had bone fractures? □ Yes □ No

If yes, number of fractures over past 12 months or since last record: _____

Type of fracture: _____

- See medication section to record bone medications

QUALITY OF LIFE *(Website: click QUALITY OF LIFE)*

Date of home TPN start? _____ (mm/dd/yyyy)

What type of record is this? □ Baseline □ Follow-Up: _____ years

Is patient alive? □ Yes □ No

If no, date of death? _____ (mm/dd/yyyy)

Is patient still on Home TPN? □ Yes □ No

If no, when was TPN stopped? _____ (mm/dd/yyyy)

Determine the Karnofsky Performance Scale at:

- Present time:_____
- Start of Home TPN (if available or estimated retrospectively): _____

<u>Karnofsky Performance Scale:</u>

100 - Normal, no complaints, no evidence of disease
90 - Able to carry normal activity, minor signs/symptoms
80 - Normal activity with effort, some signs/symptoms
70 - Cares for self, unable to carry normal activity/active work
60 - Requires occasional assistance, able to care for most needs
50 - Requires considerable assistance, frequent medical care
40 - Disabled, requires special care and assistance
30 - Severely disabled, hospitalization indicated, death not imminent
20 - Hospitalization necessary, very sick, active supportive treatment
10 - Moribund, fatal processes progressing rapidly
0 - Dead

HOSPITALIZATION *(Website: click HOSPITALIZATION)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

Is the number of hospitalizations available over past 12 months? □ Yes □ No

If yes, number of hospitalizations over past 12 months: _____

Total number of days in hospital over past 12 months: _____

How many of those hospitalizations are due to TPN-related complications? _____

How many of those total days in hospital are due to TPN-related complications? _____

HTPN REGIMEN *(Website: click HTPN REGIMEN)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

Is this patient still on Home TPN? □ Yes □ No

When did Home TPN regimen start? _____ (mm/dd/yyyy)

When did Home TPN regimen end? (if applicable)_____ (mm/dd/yyyy)

Has there been an interruption in HTPN since last entry? □ Yes □ No

If yes, how many months? _____

Has there been any change (macronutrients, micronutrients, volume, calories, days per week) in HTPN regimen since the last entry? □ Yes □ No

Reasons HTPN regimen ended:

□ Weaned

□ Deceased

If death:

- Is it TPN-related? □ Yes □ No

If yes, cause(s) of TPN-related death:

□ Sepsis □ Thrombosis/embolus □ Liver failure

□ Other (specify)_____

- Is it non-TPN related death? □ Yes □ No

If yes, cause(s) of non-TPN related death:

□ Underlying disease □ Cardiovascular □ Cancer □ Other (specify): _____

□ Intestinal transplantation

□ TPN-related complications Specify_____

□ Non-TPN related complications Specify_____

□ Other Specify_____

Current HTPN Regimen Details

Please note: If patient expired or off TPN, record the last available TPN prescription

Is the TPN bags/month known? □ Yes □ No

Number of bags per month: _____

TPN regimen cycled? □ Yes □ No

Is the TPN hours of infusion/day known? □ Yes □ No

Number of hours of infusion/day: _____

Number of days/week on TPN: _____

□ 3-in-1 system □ 2-in-1 system □ Hydration only

NOTE: For the following please describe the quantity of the following macro and micronutrients as daily averages over a one-week period. For example: multiply nutrient infused per day, by the number of days per week the patient receives HTPN, then divide that value per 7, to obtain the daily average.TPN daily average:

Amino acid content (g/day): _____ Dextrose (g/day): _____

Lipids (mL/day): _____

Name of lipid: _____ Concentration □ 10% □ 20% □ 30%

Total calories from TPN (amino acid + dextrose + lipids) (kcal/day): _____*

(*Note: dextrose - 3.4 kcal/g; protein - 4 kcal/g, lipid 20% - 2 kcal/mL)

Total volume (mL/day): _____

Additional IV fluids (average over 7 days) (mL):

Describe additional IV fluids _____

Additives:

Multi-12 - □ Yes □ No Vitamin K - □ Yes □ No

Other TPN vitamins: _____

Heparin (units): _____

Other medication(s) added to TPN bag: _____□ None

Trace elements/electrolytes converted to umol/day and mmol/day, respectively?

□ Yes □ No

Trace elements contents (umol/day) *daily average*:

Zinc: _____ Manganese: _____

Selenium: _____ Chromium: _____

Copper: _____ Iodide: _____

Iron: _____

Electrolytes contents (mmol/day) *daily average*:

Na: _____ Cl: _____

K: _____ Ca: _____

Phosphate: _____ Acetate: _____

Mg: _____ Other (specify): _____

INDICATIONS FOR HTPN *(Website: click INDICATIONS FOR HTPN)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

If baseline, enter information below.

If follow-up, has the indications for HTPN changed since last entry? □ Yes □ No
If yes, enter information below. **If no**, proceed to the next page.

1. Short bowel syndrome: - □ Yes □ No **If yes, choose the cause(s):**
   - □ Volvulus
   - □ Crohn's disease
   - □ Mesenteric infarction due to
     - □ venous thrombosis or
     - □ arterial thrombosis/embolus
   - □ Surgical complication
   - □ Other(specify): _____
   - □ Trauma
   - □ Necrotizing Enterocolitis
   - □ Intestinal atresia
   - □ Gastrochesis

2. Mucosal defects: □ Yes □ No **If yes, choose the cause(s):**
   - □ Secretory diarrhoea due to (diagnosis): _____
   - □ Celiac disease
   - □ Autoimmune enteritis
   - □ Microvillus inclusion
   - □ Radiation Enteritis
   - □ Other(specify): _____

3. Motility disorder: □ Yes □ No **If yes, choose the cause(s):**
   - □ Pseudo-obstruction (□ Primary □ Secondary)
   - □ Aganglionosis / Hirschprung's Disease
   - □ Visceral neuropathy
   - □ Other(specify): _____
   - Cause of pseudo-obstruction: _____
   - □ Visceral myopathy
   - □ Neuronal Intestinal Dysplasia

4. Tumour/cancer: □ Yes □ No **If yes, choose diagnosis:**
   - □ Desmoids
   - □ Gardner's syndrome
   - □ Familial Polyposis
   - □ Other cancer(specify location): _____
   - □ Carcinoid
   - □ Ovarian
   - □ GI tract (specify location):_____

5. Surgical complications: □ Yes □ No **If yes, define:**
   - □ Enterocutaneous fistula
   - □ Other (specify)_____
   - □ Obstruction
   - □

6. Pancreatic Disorders: □ Yes □ No Cause: _____

7. Other (specify): _____

VASCULAR ACCESS *(Website: click VASCULAR ACCESS)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

If baseline, enter information below.

If follow-up, has there been any change in vascular access since last entry?
□ Yes □ No **If yes,** enter information below**. If no,** proceed to LINE SEPSIS section below**.**

Type of catheter:

□ PICC
□ Tunnelled Catheter (e.g. Hickman): _____
□ Implanted Catheter (e.g. PortaCath): _____
□ Other (specify): _____

Number of lumens: _____

Inserted □ surgically □ radiologically □ Other (specify): _____ □ unknown

Date of insertion: _____ (mm/dd/yyyy)

Line Sepsis

NOTE: *If patient expired or off TPN, look at the 12 months prior to death/weaning, i.e. 12 months from the extraction date, which might not be the actual day you are filling out this form (see also first page).*

Is the number of line sepsis over last 12 months available: □ Yes □ No

If yes, number of documented line sepsis over past 12 months (positive line blood culture + fever): _____

Number of changes in vascular access over past 12 months: _____ unknown: _____

Reason for line change:

How many times has the line been changed for each of the following reasons over the past 12 months?

- Sepsis: _____

- Break: _____
- Occlusion: _____

LABORATORY RESULTS (W*ebsite: click LABORATORY RESULTS)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

NOTE: Record recent blood work while patient has been stable over 2 months and not hospitalized. The lab results should be from the same period of time every year unless unstable clinically. Write "NA" if not available. Please enter in specified units.

Date of Lab Results: _____ (mm/dd/yyyy)

Hb (g/L): _____
WBC (x 10^9/L): _____
Platelets (x 10^9/L): _____

MCV (fL): _____
Neutrophils (x 10^9/L): _____

Na (mmol/L): _____
K (mmol/L): _____
Mg (mmol/L): _____
Phosphate (mmol/L): _____
Creatinine (umol/L): _____
ALP(U/L): _____
AST(U/L): _____
Total protein (g/L): _____
INR: _____
PT(s):_____
PTT(s):_____

Cl (mmol/L): _____
Bicarbonate (carbon dioxide)(mmol/L): __
Ca (mmol/L): _____
BUN (urea) (mmol/L): _____
Random Glucose(mmol/L): _____
TBILI(umol/L): _____
ALT(U/L): _____
Albumin (g/L): _____
Pre-albumin (if available)(g/L): _____

Cholesterol (mmol/L): _____
Ferritin (ug/L): _____
Iron Sat: _____
RBC Folate (nmol/L): _____
PTH (pmol/L): _____

Triglycerides (mmol/L): _____
Iron (umol/L): _____
Transferrin (g/L): _____
Vit B12 (pmol/L): _____
25-OH vit D (nmol/L): _____

Plasma trace elements:
Zinc (umol/L): _____
Chromium (umol/L): _____
Copper (umol/L): _____

Selenium (umol/L): _____
Manganese (nmol/L): _____

24-H Urine:

Total Oxalates(umol/d): _____ Total Citrate(mmol/d): _____
Total Calcium(umol/d): _____ Total Creatinine(mmol/d): _____
Total urine volume(mL): _____

LIVER COMPLICATIONS (W*ebsite: click LIVER COMPLICATION)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

If baseline, enter information below.

If follow-up, has there been any change in liver condition since last entry?
□ Yes □ No **If yes,** enter information below. **If no,** proceed to CURRENT THERAPY FOR LIVER DISEASE

Liver disease? □ Yes □ No

In the physicians judgement, is the liver disease TPN-related? □ Yes □ No

- If TPN-related, diagnosis of liver disease (specify):
  _____
- If non-TPN related, diagnosis of liver disease:
  □ Viral Hepatitis: □ Hepatitis A □ Hepatitis B □ Hepatitis C
  □ Autoimmune □ Hemachromatosis □ Alcohol-induced □ Metastasis

Liver biopsy? □ Yes □ No
If yes, date of biopsy: _____ (mm/dd/yyyy)
Results: □ TPN cholestasis □ Steatosis □ Fibrosis □ Cirrhosis

Other diagnosis (specify): _____

Abdominal Ultrasound/Computed Tomography? □ Yes □ No □ US □ CT
If yes, date of ultrasound/CT: _____ (mm/dd/yyyy)
Results: □ steatosis □ cirrhosis □ gallstones □ common bile duct stones
□ cholecystectomy □ fibrosis □ other (specify):
_____

Other causes of liver disease excluded? □ Yes □ No

CURRENT THERAPY FOR LIVER DISEASE

Has there been change in TPN Regimen for liver disease? □ Yes □ No
If yes, what was the action taken:
Reduce dextrose in TPN? □ Yes □ No

Reduce lipids in TPN? □ Yes □ No
Reduce TPN days/week? □ Yes □ No
Discontinue TPN? □ Yes □ No

Changes to Enteral: □ Yes □ No
Changes to Oral: □ Yes □ No
Define changes: _____

See medication section to record liver medications.

MEDICATIONS (*Website: click MEDICATIONS)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

Type/name of current oral and IV medications:
Immuno suppressors (specify):_____
Motility agents (specify):_____
Antidepressors (specify): _____
Narcotics (specify): _____
Antidiarrheal medication (specify): _____
Sedatives (specify): _____
Anticoagulation medication (specify): _____
Reason (specify):_____
Insulin medication (specify): _____
□ Subcutaneous □ in TPN □ subcutaneous + TPN
Inhibitor of acid secretion: H2 Antagonist □ Oral □ IV
PPI □ Oral □ IV
Other (specify) _____

Liver Medications:
URSO: □ Yes □ No Dosage: _____
Antibiotics: □ Yes □ No Specify antibiotic: _____
Carnitine: □ Yes □ No
Choline: □ Yes □ No
Other (specify):_____

Bone Medications:
Oral calcium: □ Yes □ No Dosage (g/day): _____
Oral vitamin D: □ Yes □ No Dosage (IU/day): _____
Oral bisphosphonate: □ Yes □ No Name of oral bisphosphonate: _____

IV bisphosphonate: □ Yes □ No Name of IV bisphosphonate:_____
Frequency of infusion: _____

Other medications:

_____

_____

_____

ADDITIONAL DIAGNOSIS (*Website: click Additional Diagnosis)*

What type of record is this? □ Baseline □ Follow-Up: _____ years

Date of last assessment: _____ (mm/dd/yyyy)

Other medical diagnosis

Seizures: □ Yes □ No

Stroke: □ Yes □ No

Heart disease: □ Yes □ No

Artificial heart valve: □ Yes □ No

Organ transplant: □ Yes □ No

High blood pressure: □ Yes □ No

Blood disorder: □ Yes □ No

Liver disease: □ Yes □ No

Diabetes: □ Yes □ No

Pacemaker: □ Yes □ No

Kidney disease: □ Yes □ No

Arthritis/Joint: □ Yes □ No

Other: □ Yes □ No