Journal of the Canadian Association of Gastroenterology, 2019, 2(4), 178–185
doi: 10.1093/jcag/gwy045
Original Article
Advance Access publication 10 August 2018

OXFORD

Original Article

Anxiety, Depression and Quality of Life Improve After One Month and Three Months of Home Parenteral Nutrition: A Pilot Study in a Canadian Population

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Abstract

Background: Patients receiving home parenteral nutrition (HPN) have a reduced quality of life (QoL), but it is unknown if this is associated with psychiatric comorbidities such as anxiety or depression.
Aim: The aim of this study was to assess anxiety, depression and QoL in patients transitioning from hospital to HPN.
Methods: We conducted a prospective study in adult patients receiving parenteral nutrition (PN) during transition from hospital to home. We assessed anxiety and depression (Hospital Anxiety and Depression Scale; HADS), health-related quality of life (HRQoL; SF-36) and health status (EQ-5D) before discharge and again later at one and three months after HPN was started.
Results: Of the 29 patients, 15 had an underlying malignancy. At baseline, 93% of patients with malignancy had anxiety or depression (HADS A and/or HADS D >7) or both, while of the patients without malignancy, 60% had anxiety, and 40% had depression. Questionnaires were completed by 21 patients at one month and by 15 at three months. Anxiety and depression scores decreased significantly after one month of HPN (mean difference [MD] anxiety: 4.3; 95% CI, 1.2–7.5, $P = 0.004$; MD depression: 4.0; 95% CI, 1.5–6.5, $P = 0.001$), and the decrease persisted at three months (MD anxiety: 35; 95% CI, 0.35–6.6, $P = 0.02$; MD depression: 2.5; 95% CI, 0.06–5.0, $P = 0.04$). Overall, patients reported an improvement in HRQoL (SF-36) after one month of HPN, and this improvement was maintained at three months in those patients who survived.
Conclusion: Home parenteral nutrition is associated with improvements in anxiety, depression and HRQoL at one month and three months after discharge from hospital. The improvements in Qol, anxiety and depression seem greater in patients with underlying malignancy.

Keywords: *Home PN, Malignancy, Parenteral nutrition, Quality of life*

Parenteral nutrition (PN) has been used to provide nutritional support for patients with intestinal failure for more than four decades (1). The concept of providing PN in the patient's home rather than in hospital was first suggested in the 1970s (2). Since then, advances in medical knowledge and technology, combined with improved community support networks, have

Nonstandard abbreviations:

HHS-HPN Program,	Hamilton Health Sciences Home Parenteral Nutrition Program

Clinical Relevancy Statement

Although the nutritional benefits of HPN are well documented, there are concerns that the physical and social limitations imposed by HPN may reduce recipients' quality of life (QoL). Despite increasing interest in the role of anxiety and depression on QoL in chronic disease, the effect of HPN on anxiety and depression is unknown. In this pilot study, a high proportion of patients reported increased anxiety and depression before starting HPN, with significant improvements in anxiety, depression and quality of life after one month of HPN. These findings are clinically relevant because the effects of anxiety and depression on QoL may be independent of the effects of malnutrition. Improvements in anxiety and depression may result from improved nutrition, but they may also be affected greatly by the manner in which the HPN is managed. Our study has extended the current literature in demonstrating improvements in anxiety, depression and QoL during longitudinal follow-up of PN-dependent patients transferred from hospital to home, but further studies are needed to determine the roles of adequate nutritional delivery and patient-centred management strategies in reducing anxiety and depression and improving quality of life for HPN patients.

greatly facilitated the provision of home PN (HPN). Although beneficial effects are associated to HPN, there are concerns that associated physical and social limitations may impair recipients' Health-related quality of life (HRQoL) (3, 4). HRQoL has been defined as the specific impact of an illness or medical treatment on a patient's QoL (5).

Numerous studies of HPN and QoL suggest that HPN patients have a lower HRQoL than the general population (6–10). Some studies have shown HPN may be beneficial in patients with a diagnosis of cancer (11–13), while others have reported that the diagnosis or the duration of HPN support has little effect on QoL (14). Home parenteral nutrition (HPN) is a complex, expensive, burdensome intervention, and a better understanding of how this affects anxiety, depression and HRQoL is important to optimize outcomes. Therapies that improve well-being, decrease depression and increase adherence to treatment are encouraged in cancer patients (15). However, it is important to understand that both HPN and the underlying disease may affect QoL, anxiety and depression independently.

To date, there are few studies evaluating HRQoL during the transition from hospital to home setting, and the potential impact of HPN on psychiatric comorbidities has not been fully investigated. In this pilot study, we prospectively assessed the effects of transitioning from hospital to home PN on anxiety, depression and HRQoL in patients with and without underlying malignancy.

METHODS

Study Design and Patient Recruitment

We conducted a single-center, longitudinal assessment of HRQoL in a group of adult patients accepted to the HPN program between 1999 and 2003 and followed them throughout their transition from hospital to home. The Hamilton Health Sciences HPN Program (HHS-HPN) accepts patients from a catchment area that has a population of about 1.5 million. All patients were referred from an inpatient ward in a regional hospital; PN prescription regimens were stabilized before discharge, and patient education, including HPN training, was provided during the hospital stay. Patients were accepted in the HHS-HPN program if they 1) had received HPN training in hospital prior to discharge; 2) were expected to receive HPN after discharge; or 3) were expected to be under the care of the HHS-HPN Program after discharge in collaboration with regional community care access centres (CCA, LIHN) and associated nursing/medical supply companies. The inpatient nurses assisted the patients with TPN on a daily basis and provided education HPN-related procedures with the intent that the patients would be independent after discharge. Patients meeting the criteria for the home PN program were invited to participate in the study. In those who agreed to participate, the investigators (SMK, SG, MR, AC) administered the questionnaires in-hospital immediately before discharge and then again one and three months after discharge. Participants were asked to attend scheduled outpatient visits at one and three months after discharge. Demographics and medical history were collected from all patients at baseline. Underlying conditions leading to HPN that were related to malignancy included gastrointestinal, gynecological and lymphoma and those not related to malignancy included things such as short bowel syndrome, inflammatory bowel disease and dysmotility. The use of anxiolytics and antidepressants was allowed during the study period, but patient data were analyzed only if the treatment regimen remained stable. The principal investigators (DA, JKM) monitored the study. The protocol was approved by the Hamilton Health Sciences (HHS) Research Ethics Board, and all participants signed an informed consent.

Home Parenteral Nutrition

Home parenteral nutrition formulae were prescribed by a registered dietitian with physician approval and were calculated to meet the individuals' macro- and micronutrient needs. Oral intake was allowed as tolerated. Home parenteral nutrition was administered overnight in the majority of cases.

Anxiety and Depression

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS), a validated and extensively used self-reported questionnaire designed for the outpatient setting. The questionnaire consists of 14 items: seven for

anxiety and seven for depression. The items are rated on a zero to three integer scale to give individual anxiety and depression scores, each with a maximum value of 21. A score >7 for each subscale is suggestive of anxiety or depression. Higher scores reflect increasing severity of distress (16, 17)

Health-Related Quality of Life

Health-related quality of life was assessed using the SF-36, a validated 36-item, self-administered questionnaire that uses a four-week recall period and is very sensitive to change in both general and disease-specific populations (18). The SF-36 consists of two domains: physical (PCS) and mental (MCS), with eight subdomains: physical functioning (PF), role limitations due to physical health (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE) and general mental health (MH).

Quality of Life and Health Status

Health status was assessed using the EQ-5D, a standardized measure developed by the EuroQol Group (19); this is one of the most commonly used generic health status measurement tools with good validity and reliability in various health conditions. It consists of two sections—the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D descriptive system is comprised of the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels from 'no problem' to 'extreme problems'. The EQ-5D health states can be reported as individual scores by level or they can be converted to a single summary index (19). The questionnaire has an additional simple question which records the respondent's self-rated health on a vertical visual analogue scale (VAS), with endpoints labelled 'the best health you can imagine (score 100)' and 'the worst health you can imagine (score 0)'.

Statistical Analysis

The statistical analyses were carried out using IBM SPSS (IBM SPSS Statistics Version 22, Chicago, IL, USA). Missing values accounting for less than 10% of total values were replaced with a mean, with over 10% with multiple imputations. Comparison of continuous variables was performed using ANOVA with Bonferroni correction and paired *t*-test. Chi-squared tests or Fisher exact tests were used to compare categorical variables. Subgroup analysis was performed to evaluate outcomes in patients with and without malignancy. A P value less than 0.05 was considered statistically significant.

RESULTS

Sample Population

Twenty-nine patients participated in the study; the most common primary diagnoses (Table 1) were malignancy (52%) and inflammatory bowel disease (28%), and the most common indications for PN were fistula (31%), malnutrition or malabsorption (31%) and intestinal obstruction (28%). Medication doses for patients taking antidepressants (6%) or anxiolytics (2%) remained stable during the study. At one month, 21 patients completed the questionnaires; eight were deceased due to end-stage cancer. At the end of the study period (three months), 18 patients completed the questionnaires and continued to receive HPN; in total, 11 were deceased. Results are presented for those who completed questionnaires at each time point.

Table 1. Characteristics of study population

Study population n (%)	
Total Number	29 (100)
Females	25 (86)
Mean age: years (range)	47.5 (19–70)
Primary diagnosis	
Dysmotility	3 (10)
IBD	8 (28)
Malignancy	15 (52)
Gastrointestinal	7 (47)
Gynecological	7 (47)
Leukemia	1 (6)
SBS	2 (7)
Other	1 (3)
Psychiatric medication	
Antidepressants	6 (20)
Anxiolytics	2 (7)
Indication for HPN	
Fistula	9 (31)
Malnutrition/malabsorption	9 (31)
Intestinal obstruction	8 (28)
Dysmotility	1 (3)
Other	2 (7)
Status of patients at 3-month time point	
HPN therapy completed	15 (52)
HPN therapy ongoing	three (10)
HPN stopped (deceased)	11 (38)

IBD: inflammatory bowel disease, GI: gastrointestinal, SBS: short bowel syndrome, HPN: home parenteral nutrition

Anxiety and Depression

At baseline before discharge from hospital, 20 of 29 patients (70.0%) had depression (HADS-D >7) and 22 (75.9%) had anxiety (HADS-A >7) (Figure 1, Appendix). Both anxiety and depression scores decreased significantly after one month of HPN therapy (mean differences: anxiety 2.7; 95% CI, 0.3–5.1; $P = 0.02$; depression 2.6; 95% CI, 0.57–4.5], $P = 0.007$), but this decrease was not sustained after three months of follow-up (Table 3, Figure 2).

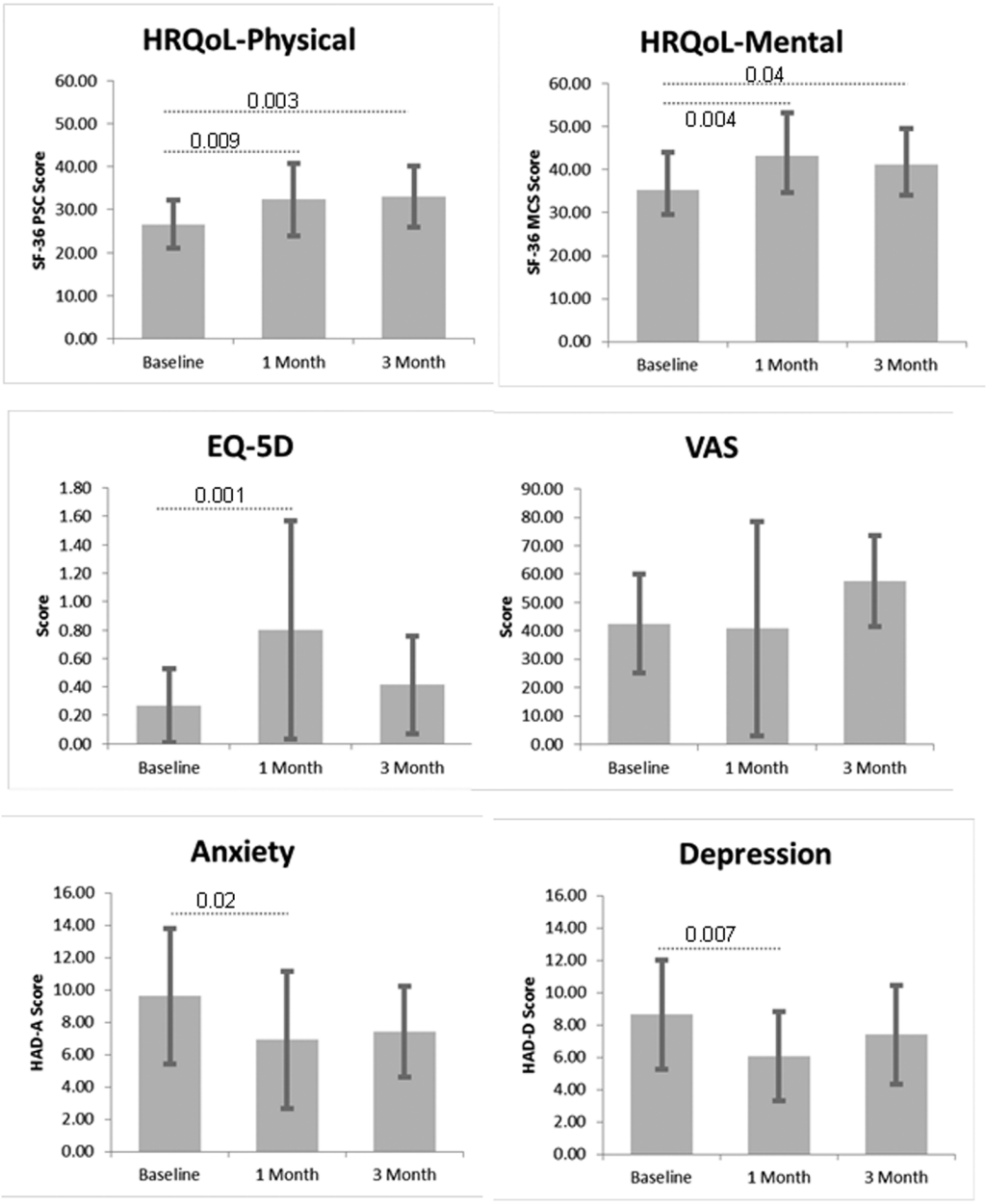

Figure 1. Mean scores of health status, anxiety and depression and HRQoL at baseline (n = 29), one month (n = 21) and three (n = 17) months after HPN was initiated.

Decreases in depression scores after one month (r = 0.42; P = 0.02) and anxiety scores after three months (r = 0.52; P = 0.003) were correlated with improvement in perceived health status.

In subgroup analysis, a greater proportion of patients with underlying malignancy had depression compared with those without (14 of 15 versus six of 14; P = 0.005). Anxiety levels at baseline were similar in patients with and without malignancy. After one month of HPN, anxiety and depression decreased significantly only in those patients with a diagnosis of malignancy (anxiety F: 6.72, P = 0.003; depression F: 8.29, P = 0.001; Table 4 and Figure 2), and the effect was sustained at three months of HPN in survivors who had a diagnosis of malignancy.

Health-Related Quality of Life

Heath-related quality of life (SF-36) mental health scores (MCS) and physical health scores (PCS) scores improved significantly after one month, and the effect persisted after three months of HPN therapy (Table 2). At one month, there was improvement in physical functioning, bodily pain, vitality, social functioning and mental health scores. The increment in HRQoL scores persisted at three months (Table 2). The individual domains of the physical role, general health and the emotional role remained unchanged.

There was a significant increase in the overall health status scores measured by EQ-5D at one month (–0.5; 95% CI, –0.08–0.01; $P < 0.001$), but the effect was not sustained at three months (Table 3). The health perception (VAS) remained unchanged after one month and three months of HPN (Figure 1).

Patients with and without malignancy reported improved HRQoL (SF-36) overall during HPN. However, the subgroup with underlying malignancy had an improvement in MCS (F: 4.24; $P = 0.021$), while the subgroup without underlying malignancy had an improvement in PCS (F: 6.83; $P = 0.003$) (Table 4).

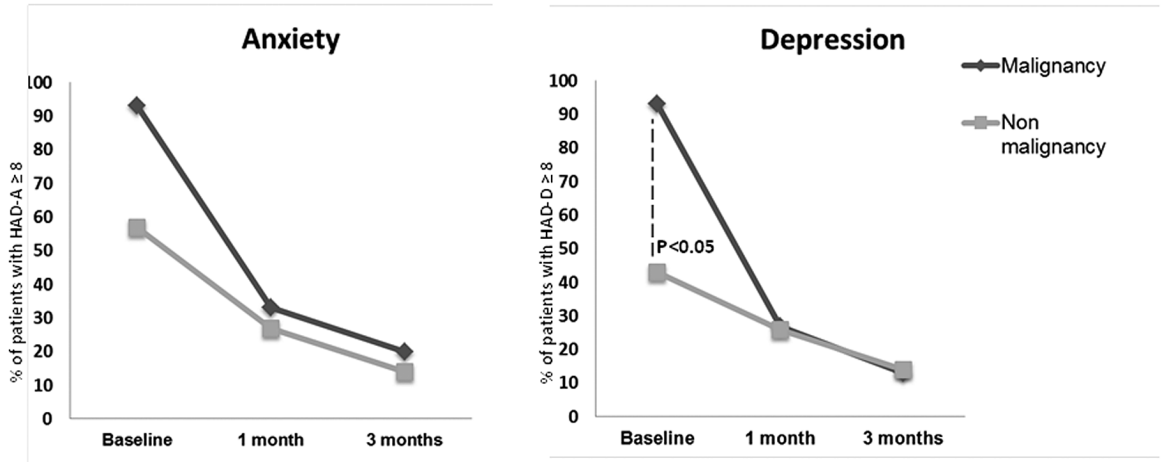

Figure 2. Percentage of patients with anxiety and depression subgrouped according to the presence of underlying malignancy at baseline (n = 29), one month (n = 21) and three months (n = 17) after HPN was initiated.

Table 2. Mean score differences for HRQoL measures

Measure	Baseline n = 29	Month 1 n = 21		Month 3 n = 18	
	Baseline (SD)	AΔMean (95% CI)	*P*	AΔMean (95% CI)	*P*
SF–36 PCS	26.6 (5.7)	–5.8 (– 8.5,–3.1)	0.009	–6.5 (–4.1,8.8)	0.003
SF–36 MCS	35.3 (8.8)	–7.9 (–12.0,–3.9)	0.004	–6.0 (–11.8,–0.22)	0.039
PF	22.4 (18.0)	–19.6 (–36.3,–3.0)	0.01	–22.6 (–39.2,–5.9)	0.004
RP	27.9 (12.6)	–7.7 (–27.2,11.7)	0.168	–4.1 (–23,6,15.2)	0.607
BP	22.0 (21.3)	–25.3 (–42.5,–8.0)	0.002	–30.6 (–47.8,–13.6)	<0.001
GH	30.3 (22.3)	–6.3 (–205,7.9)	0.84	–13.1 (–18.2,–8.0)	.149
VT	19.1 (15.4)	–14.7 (–27.9,–1.5)	0.02	–12.7 (–26.0,0.4)	0.06
SF	16.6 (15.4)	–25.5 (–41.6,–8.6)	0.001	–29.2 (–45.7,–12.7)	<0.001
RE	19.9 (37.0)	–21.35 (–51.1,8.4)	0.25	–14.4 (–44.20,15.3)	0.72
MH	50.3 (19.2)	–15.5 (–29.1,–1.9)	0.02	–14.6 (–28.2,–1.01)	0.03

[A]ΔMean = Baseline – Month; PF: Physical Functioning; RP: Role functioning Physical; BP: Bodily Pain; GH: General Health; VT: Vitality; SF: Social role Functioning; MH: Mental Health SF-36 PCS: Physical dimension; SF-36 MCS: Mental dimension.

Table 3. Mean score differences for health status, anxiety and depression

Measure	Baseline (n = 29)	Month 1(n = 21)		Month 3(n = 18)	
	Baseline (SD)	[A]ΔMean (95% CI)	*P*	[A]ΔMean (95% CI)	*P*
EQ-5D	0.27 (0.3)	–0.5 (–0.8, –0.1)	0.001	–0.13 (–0.4,0.02)	0.09
VAS	42.5 (17.4)	–4.5 (–12.9,22.0)	0.771	–15.1 (–32.4,2.3)	0.11
HADS-Anxiety	9.6 (4.2)	2.7 (0.3,5.1)	0.02	2.2 (–0.3,4.6)	0.09
HADS-Depression	8.7 (3.4)	2.6 (0.57,4.5)	0.007	1.2 (–0.7,3.1)	0.38

AΔMean = Baseline – Month; EQ-5D: EuroQoL five Dimensions; VAS: Visual Analogue Scale; HADS: Hospital Anxiety and Depression Scale.

Table 4. Mean score differences for HRQoL, health status, anxiety and depression by subgroup with and without malignancy

Measure	Baseline	Month one (n = 21)		Month three (n = 18)	
	Baseline (SD)	[A]ΔMean (95% CI)	*P*	[A]ΔMean (95% CI)	*P*
Malignancy					
SF-36 PCS	26.9 (6.5)	−4.5 (−12.9,22.0)	0.771	−15.1 (−32.4,2.3)	0.17
SF-36 MCS	34.8 (10.0)	−9.9 (−18.7, −1.0)	0.02	−7.4 (−16.2,1.4)	0.12
EQ5D	0.23 (0.2)	−0.78 (−1.2, −0.3)	<0.001	−0.21 (−0.6,0.2)	0.74
VAS	43.5 (19.6)	15.5 (−8.5,39.6)		−14.9 (−39.0,9.1)	0.38
HADS-Anxiety	11.0 (3.8)	4.3 (1.2,7.5)	0.34	3.5 (0.35,6.6)	0.02
HADS-Depression	10.3 (3.0)	4.0 (1.5,6.5)	0.004	2.5 (0.06,5.0)	0.04
Non-malignancy					
SF-36 PCS	26.2 (4.7)	−7.7 (−13.5, −1.9)	0.006	−7.2 (−13.0, −1.4)	0.01
SF-36 MCS	35.7 (7.7)	−5.8 (−13.8,2.1)	0.22	−4.5 (−12.5,3.5)	0.50
EQ5D	0.31 (0.3)	−0.2 (−0.7,0.3)	0.83	−0.05 (−0.57,0.4)	0.99
VAS	41.4 (15.3)	−7.2 (−33.4,18.9)	0.99	−15.3 (−41.4,10.8)	0.45
HADS-Anxiety	8.1 (4.2)	0.9 (−2.9,4.8)	0.99	0.8 (−3.0,4.7)	0.99
HADS-Depression	6.8 (2.8)	1.0 (−1.9,4.0)	0.99	−0. (−3.1,2.8)	0.99

[A]ΔMean = Baseline – Month; SF-36 PCS Short form 36 items physical domain; SF-36 MCS Short form 36 items mental domain; EQ-5D EuroQoL five Dimensions; VAS visual analogue scale; HADS Hospital Anxiety and Depression Scale.

An improvement in perceived general health scores was limited to those patients with malignancy during one month of HPN (EQ5D F: 10.38, $P > 0.001$; VAS F 5.01, $P = 0.01$) but not in those with a nonmalignant diagnosis (Table 4).

DISCUSSION

The results of this study indicate that the transfer of PN treatment from a hospital to home setting is associated with improved patient outcomes including decreases in anxiety and depression and an increase in overall quality of life.

Anxiety and depression are common among patients with chronic illness and especially with malignancy (14). Patients who suffer from advanced forms of cancer usually experience high levels of anxiety and pain (20). The great majority of patients receiving HPN involved in our study reported some degree of anxiety and depression, and this was especially evident in those with a diagnosis of malignancy. The prevalence of anxiety and depression in our population was over three times that reported by others (21) in patients with benign conditions. After one month of HPN, anxiety and depression decreased significantly; however, the improvement in anxiety and depression appeared to be limited to patients with underlying malignancy. Few patients were taking psychiatric medication at baseline, and their doses remained stable through the study period, suggesting that the improvement in both psychiatric conditions during HPN administration was independent of pharmacological psychotropic therapy. Although the reasons for improvement in anxiety and depression in patients with malignancy receiving TPN at home are unknown, it is possible that improvement in nutritional status through TPN may contribute to this. It is also possible that a greater acceptance of the diagnosis at the later stage in the grief cycle may influence the results.

Quality of life improved significantly after one month, and the effect persisted over the three months of HPN therapy. These improvements during HPN appeared to reflect improvements in physical functioning, bodily pain, vitality, social functioning and mental health, as assessed by the SF-36; there were no changes in the physical role, general health or the emotional role. The effect of HPN on quality of life was previously assessed by others (18), and the results have been controversial, probably due to differences in study design, study population and the instruments used to assess outcomes.

In this study, over half of the HPN patients had an underlying malignancy; this was not a common practice at the time of the study. However, data from the Canadian HPN registry (22) indicate a significant increase in the proportion of HPN patients who had an underlying malignancy in recent years. In many HPN programs, the proportion of patients with an underlying malignancy is now greater than the proportion of patients with short bowel syndrome or Crohn's disease. When a subgroup analysis was performed with respect to the underlying diagnosis, we found that patients with and without malignancy responded differently to HPN. Our results are in accordance with a previous study (8) which reported that patients with malignant disease benefited more from HPN therapy, in terms of QoL, than those with benign disease. It has been reported that up to 80% of patients with malignant disease will fail to meet

their nutrition requirements (23) and that nutritional support through HPN may have a positive effect on QoL (24).

The aim of this pilot study was to determine whether discharge from hospital on HPN was associated with a change in patients' anxiety, depression and quality of life. It was not designed to recruit sufficient patient numbers to allow a multivariate analysis of the many factors potentially associated with differences in these outcomes, and as a result, no detailed data were recorded with regard to the severity and progression of the underlying conditions, the patients' nutritional status, nutrient delivery, home care intensity or comorbidities such as pain and analgesic use. The baseline questionnaires were completed before the patients were discharged when their parenteral nutrition prescriptions had been stabilized, so for the most part, nutrition delivery remained stable over the next three months. If anything, there was less direct medical attention after discharge. Further prospective studies will be required to explore this and to clarify whether the improvement in psychological status and quality of life are related to improved nutrition, greater medical attention or other factors. Moreover, it has been suggested that the presence of psychiatric comorbidity in patients with malignancy could affect response to therapy. Home parenteral nutrition may have additional therapeutic benefits in this population (15). In fact, patients with malignancy improved preferentially in the mental component, while patients without malignancy improved in the physical component of the HRQoL instrument. Our results are discrepant with others reporting a beneficial effect of HPN, particularly in the physical component (12). However, the apparent contradiction may be explained by the fact that the previous study only included patients with gastrointestinal cancer.

One of the main concerns related to the assessment of QoL in this context is that it is very difficult to determine whether the effects on QoL are direct results of HPN itself or are consequences of the underlying disease and its natural history. The increased burden of disease may be enough to cause an initial observation of high depression scores among patients with malignancy. Patients with a benign disease may view the move from hospital to home and initiation of HPN as a further step towards regaining health, while patients with malignant disease view HPN as a beneficial intervention that allows a much better QoL during their last few weeks or months of life. Unfortunately, none of these questions can be assessed by an randomized control trial (RCT) of HPN versus no HPN due to ethical concerns (25), and also, the absence of HPN in eligible patients would have major effects related to caloric deprivation and malnutrition. Future prospective studies may be able to identify and elucidate additional factors associated with decreased QoL in HPN related to the underlying disease such as length of bowel, surgeries, infections and life expectancy compared with other contributing factors such as reduced mobility, impaired sleep, loss of independence, loss of job prospects, effects on caregivers, ancillary therapies and concomitant conditions.

We acknowledge some limitations of our study, including its observational design, the lack of control group and the long delay from patient recruitment to publication. Observational studies cannot infer causality from relationships among subgroups, and additional controlled studies would be needed in order to identify cause-effect relationships. We should also consider a potential limitation related to response shift with repeated measures of HRQoL. It has been proposed that the response shift phenomenon has an impact on self-report measures, and this may subsequently affect measurement of true treatment effects (26). Another limitation relates to the small sample size. The current study was designed as a pilot study, and its findings should be confirmed in a larger population. Finally, this study followed patients for only a relatively short period of time, so the long-term effects of HPN on anxiety, depression and quality of life remain unclear. Therefore, it would be important to evaluate these outcomes in larger groups of patients, with and without underlying malignancy, in short-term and long-term studies; it is important to recognize that cancer patients may significantly derive benefit from HPN, but it will be difficult to study the long-term effects of HPN in end-stage cancer.

In conclusion, anxiety, depression and HRQoL improved in PN-dependent patients discharged from hospital to home under the supervision of the HPN program. This beneficial effect of HPN is more evident in those with underlying malignancy, suggesting that improved nutrition delivery may confer some benefit at the end of life. Our results showed that HPN is not necessarily too troublesome or burdensome to be offered to patients with a primary diagnosis of cancer; and HPN was not associated with greater anxiety or depression or a worse quality of life. This study has also provided valuable information which should be used to advocate for and support HPN patients and their families with regards to the decision of home-based therapy. We believe the current pilot study should be extended in a larger population and hope it will stimulate research into interactions between HPN and other therapies in patients with and without underlying diagnoses of malignancy.

SUPPLEMENTARY DATA

Supplementary data are available at *Journal of the Canadian Association of Gastroenterology* online.

ACKNOWLEDGEMENTS

The authors wish to thank their community partners who, as an integral part of the HHS-HPN team, provided collaborative support: Hamilton-Wentworth CCAC, Halton CCAC, Niagara CCAC, Calea Ltd., and Marchese Pharmacy.

Author contributions

SG, AC, SH, JKM and DA contributed to the design of the research; SM, MR, SG and AC contributed to the acquisition; and MIPS,

MR and MT contributed to the analysis of the data; MIPS, SG, MT, SH, JKM and DA contributed to the interpretation of the data; and MIPS and SM drafted the manuscript. All authors critically revised the manuscript, agreed to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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