NUTRITION SUPPORT FOR BONE MARROW TRANSPLANT PATIENTS

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This review should be cited as: Murray SM, Pindoria S. Nutrition support for bone marrow transplant patients (Cochrane Review). In: *The Cochrane Library,* Issue 4, 2004. Oxford: Update Software.

A substantive amendment to this systematic review was last made on 23 February 2002. Cochrane reviews are regularly checked and updated if necessary.

ABSTRACT

Background: Bone marrow transplantation involves the administration of toxic chemotherapy and infusion of marrow cells. After treatment, patients can develop a poor appetite, mucositis and gastrointestinal failure, leading to malnutrition. To prevent this, parenteral nutrition (PN) support is the first choice but is associated with an increased risk of infection. Enteral nutrition (EN) is an alternative, as is the addition of substrates e.g. glutamine to enteral and parenteral solutions. However, the relative effectiveness of these treatments is not clear.

Objective: To determine the efficacy of EN or PN support for patients receiving a bone marrow transplant.

Search strategy: Trials were identified by searching the Cochrane Library (Issue 4, 2000), MEDLINE (1966-2000), EMBASE (1988-2000) and CINAHL (1982-2000). Reference lists of identified trials and conference proceedings were searched for relevant reports. Date of the most recent search: 2000.

Selection criteria: RCTs that compared one form of nutrition support with another, or control, for bone marrow transplant patients were included.

Data collection and analysis: Thirty five reports were identified, 11 were excluded. Two reviewers extracted data from 24 studies; 16 were allocated to four interventions: oral glutamine versus placebo; PN and glutamine versus standard PN; PN versus IV hydration; PN versus EN. Eight studies were other interventions. Data were collected on participants' characteristics; adverse effects; neutropaenia; % change in body weight; graft versus host disease; and survival. Trialists were contacted for unreported data.

Main results: Two studies (82 subjects) found that glutamine mouthwash reduced days of neutropaenia (6.82 days, 95% CI (1.67-11.98) p=0.009) compared with placebo. Three studies (103 subjects) showed that patients receiving PN with glutamine had a reduced hospital stay, 6.62 d (95% CI 3.47, 9.77, P=0.00004) compared with patients receiving standard PN. Two studies (73 subjects) indicated that patients receiving PN plus glutamine had a reduced incidence of positive blood cultures (OR 0.23, 95% CI 0.08-0.65, p=0.006) compared to those receiving standard PN. One study, (25 subjects) showed patients receiving PN had a higher incidence of line infections (odds ratio 21.23, 95% CI 4.15,108.73, P=0.0002) compared to those receiving standard IV fluids. There were no evaluable data to compare PN with EN.

Reviewers' conclusions: Lack of evaluable data means that the relative effectiveness of EN versus PN cannot be evaluated. Further studies and missing data from completed trials need to be retrieved. Studies comparing PN with glutamine versus standard PN suggest that patients leave hospital earlier, and experience a reduced incidence of positive blood cultures, than those receiving standard PN. Patients with gastrointestinal failure should consider PN with the addition of glutamine if enteral feeding is not possible.

BACKGROUND

Patients receiving bone marrow transplantation (BMT) for malignant and non malignant diseases are prone to varying degrees of gastrointestinal failure. The main symptoms are prolonged vomiting, diarrhoea and at worst but rarely, intestinal obstruction. The cause of gastrointestinal failure is unclear but BMT patients in addition to receiving chemotherapy, which is toxic to the gut and destroys the host's marrow cells, receive either donor marrow cells (allogeneic) or their own marrow cells (autologous). The receipt of marrow increases the potential complication of graft versus host disease and infection which can magnify the difficulties in the nutritional management of these patients. Many patients experience a significant reduction in appetite and therefore calorie intake within a few days of admission to hospital which is frequently associated with a significant decrease in body weight. Consequently optimum delivery of nutrition support often becomes essential early on in the course of treatment for a BMT.

Traditionally, parenteral nutrition (PN), which is the administration of intravenous nutrition given to bypass the alimentary canal when it is not functioning adequately, has been given as the first option of nutrition support to BMT patients (Weisdorf 1984; Herrmann 1993). This is in preference to enteral nutrition (EN) which is the delivery of oral or tube feeding via any route connected to the gastrointestinal tract. The reasons for this are probably because routine insertion of long lines has enabled PN to be delivered relatively effortlessly and also because there was a belief that enteral feeding is an unacceptable form of 'force feeding' (Rickard 1980) and may not be well tolerated. The advantages of either of these types of nutrition support in BMT

patients are not clear but PN is associated with more complications e.g. increased line infections and reduction in gut mucosal integrity (Kudsk 1994) which may lead to longer hospitalisation. There are some reports from prospective studies, on the successes of enteral feeding in these types of patients (Papadopoulou 1997). Several authors would now argue that enteral feeding should always be considered as the first option of nutrition support for these patients (Mercadante 1998, Iestra 1999). However, there have been few attempts from prospective randomised controlled trials to prove the benefits of enteral or parenteral nutrition support for BMT patients.

Two authors Lipman 1991b and Klein 1994 have previously, independently, reviewed the efficacy of nutrition support in cancer patients. Both authors examined controlled trials of various forms of nutrition support in a variety of patients receiving therapy for cancer and BMT. They reported that nutrition support did not appear to consistently improve nutritional parameters and was not clinically effective in improving other important outcomes for cancer patients. However, there was some evidence from two randomised controlled trials (Szeluga 1987 and Weisdorf 1987) that BMT patients, survival rate improved when given PN but infection rates and costs were higher for those receiving PN compared to those receiving EN.

Both reviews have been assessed by reviewers from the Centre for Reviews and Dissemination, York, UK, (reviews on Cochrane Library). They commented that, whilst the conclusions of these reviews may reflect the benefits of nutrition support for patients receiving treatment for cancer, they were unable to determine the completeness of the reviews because they did not satisfy the methodological criteria that has been proposed for scientific overviews.

Since then, and in the last decade, there has been increasing interest in the addition of glutamine to both enteral and parenteral solutions. Glutamine is considered to be a non-essential amino acid which may become an essential amino acid for the catabolic sick patient. It may also have an affect on preventing gut atrophy and also enhance immune function (Sax 1992), both of which are potentially debilitating problems for BMT patients. As a result there have been an increasing number of controlled and uncontrolled trials reporting the benefits of glutamine in BMT patients.

Since the treatment for BMT patients differs significantly from cancer patients because of the receipt of marrow cells, this review (unlike Lipman 1991b and Klein 1994) has focused specifically on BMT patients. The aim was to assess the effectiveness of any type of feeding regime that has been compared in patients receiving BMT.

OBJECTIVES

To determine the efficacy of any form of enteral or parenteral nutrition support given to patients receiving bone marrow transplantation. Efficacy will be considered in terms of time in hospital, complications, change in nutritional status e.g. change in body weight, and survival.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Any randomised (strict format of patient allocation to experimental group e.g. centralised randomisation) or quasi randomised (e.g. alternate patient admissions) controlled trial.

Types of participants

Patients of all ages receiving any type of bone marrow transplant.

Types of intervention

Randomised controlled trials comparing one type or mode of nutrition support (enteral or parenteral) with another or with an intravenous solution of glucose/saline. Where enteral nutrition (EN) is the delivery of any substance of nutritional value in solid or liquid form (and can include usual food intake) that passes any part of the digestive tract, regardless of the method of delivery e.g. orally or via a tube (e.g. nasogastric, gastrostomy, jejunostomy). Parenteral nutrition (PN) is the administration of nutritional liquids containing a minimum of glucose and amino acids which is administered through the central or peripheral venous system and therefore bypasses the gastrointestinal tract.

Types of outcome measures

Defined outcome measures considered most important are listed below.

PRIMARY OUTCOMES

- Hospital duration e.g. mean duration admission to discharge or from day 0 to discharge home
- Mucositis - mean number of days patient groups had some degree of mucositis from start to end of study
- GVHD - number of patients who developed > grade 2 graft versus host disease (GVHD)
- Nutritional status -difference in mean % change in body weight from start to end of study between the trial groups

- Duration of nutritional intervention/time to resume adequate oral intake
- Neutropaenia mean number of days to achieve normal neutrophil level after day of BMT, day 0
- Line infection - number of patients who developed line infections from start to the end of the study
- Number with positive blood cultures
- Survival to 100 day - actual numbers who have completed study surviving to the 100th day post-BMT
- Survival beyond 100 days - actual numbers who have completed study surviving beyond day 100 or two year survival

SECONDARY OUTCOMES

- Vomiting - mean number of days patients had >/= than 3 vomits/day from start to end of study
- Diarrhoea - mean number of days patients had >/= 3 bowel motions /day from start to end of study
- Veno Occlusive Disease - number of patients who developed veno occlusive disease (VOD) actual number /per group
- Liver function disturbances - number of patients who had an abnormal bilirubin level from the start of study to end of study
- Hepatomegaly - number of patients who developed hepatomegaly from start to end of study
- Albumin - mean change in albumin from start to end of study between the trial groups
- Pre-Albumin - mean change in pre-albumin from start to end of study between the trial groups
- Engraftment - mean duration for each group to achieve engraftment, post-BMT (from day 0)

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

See: Cochrane Pain, Palliative Care and Supportive Care Group search strategy

A search strategy (with no randomised controlled trial (RCT) filter) was designed for identifying trials from the following databases: the Cochrane Library (Issue 1,2000), MEDLINE (1966-2000), Embase (1988-2000) and CINAHL (1982-2000).

Hand searching included nutrition and bone marrow transplant conference proceedings, reference lists of papers found through electronic searching, and consultation with experts.

The following search strategy was used:

#1 explode "Nutrition"/ all subheadings

#2 explode "Nutrition-Assessment"/ all subheadings

#3 explode "Feeding-Methods"/ all subheadings

#4 "Intubation,-Gastrointestinal"/ all subheadings

#5 "Gastrostomy"/ all subheadings

#6 "Eating"/ all subheadings

#7 explode "Foods,-Specialized"/ all subheadings

#8 explode "Food"/ all subheadings

#9 explode "Feeding-Behavior"/ all subheadings

#10 explode "Appetite"/ all subheadings

#11 "Jejunostomy"/ all subheadings

#12 "Glutamine"/ all subheadings

#13 glutamin*

#14 nutrition*

#15 food*

#16 feed*

#17 nasogastr*

#18 nasojejun*

#19 nasoduoden*

#20 gastrostom*

#21 gastrojejunostom*

#22 naso near duoden*

#23 naso near1 gastr*

#24 jejun*

#25 bolus*

#26 intub*

#27 appetite*

#28 parenteral*

#29 calor*

#30 intake*

#31 sip*

#32 oral*

#33 diet*

#34 intraven*

#35 enteral*

#36 tube*

#37 supplement*

#38 fortif*

#39 formula*

#40 eat*

#41 hydrolysate*

#42 novel* substrate*

#43 elemental

#44 PN in TI,TO,CM,AB

#45 EN in TI,TO,CM,AB

#46 TPN in TI,TO,CM,AB

#47 NG in TI,TO,CM,AB

#48 PEG in TI,TO,CM,AB

#49 "Bone-Marrow-Transplantation"/ all subheadings

#50 bone marrow near transplan*

#51 Peripheral blast stem cell transplan*

#52 BMT*

#53 MATCH* SIB* DON*

#54 MATCH* UNREL* DON*

#56 PBSCT*

#57 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 # or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #5 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48

#58 #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56

#59 #57 and #58

METHODS OF THE REVIEW

STUDY SELECTION

Studies identified by the computerised search were scanned by the lead reviewer and all apparently relevant studies were retrieved. These were assessed independently by the lead reviewer (SM) and co-reviewer (SP) for inclusion or exclusion in the review according to the pre-specified inclusion criteria. A data extraction form was designed and used

to record data on participants, interventions and outcomes as described in the 'Criteria for considering studies for this review' section above. Differences between reviewers' extracted results were resolved by discussion.

CORRESPONDENCE WITH AUTHORS

Many of the authors of included studies either did not report all of the desired outcomes of interest or presented them in a format unsuitable for meta-analysis. Where it was possible to locate the authors of the main studies, a standard letter requesting further information was sent.

STATISTICAL METHODS

Outcomes measured as continuous data (time in hospital, change in nutritional status) were analysed using means and mean differences with their corresponding standard deviations and standard errors, and reported with 95% confidence intervals. Dichotomous data were analysed using odds ratios and reported with 95% confidence intervals. Where meta-analyses were possible, summary estimates of measures of relevant outcomes with 95%confidence intervals were reported using a fixed effect model.

Statistical heterogeneity was tested using a Chi square test. Where the p value was less than or equal to 0.05 this indicated significant heterogeneity, and If this is the case a random effects model will be used to derive a summary statistic with 95% confidence intervals.

It was planned to investigate clinical heterogeneity by performing analyses on the following sub-groups: adults versus children (0 -18 years); disease type; transplant type. However, insufficient data were available.

Similarly, there were insufficient data to

- assess the effect of the type of allocation concealment
- assess the effect of loss to follow-up
- calculate a 'number needed to treat'

DESCRIPTION OF STUDIES

Thirty-five potential randomised controlled trials were identified. One was located through hand searching. Twenty four trials fulfilled all the inclusion criteria. Eleven studies were excluded. Sixteen of the included studies were grouped into four main comparison groups. The details of trials in each group are listed below.

- Oral glutamine versus placebo:

Four trials (Anderson 1998; Coghlin Dickson 2000; Jebb 1995; Schloerb 1999) compared oral glutamine versus placebo and included 343 patients. In one trial by Schloerb 1999, patients failing to take the oral supplement were given either PN with glutamine or standard PN according to which group the patients were originally randomised. Despite this, the results of this study were allocated to this group because the original allocation was to oral glutamine or placebo.

- Parenteral nutrition with glutamine versus standard parenteral nutrition:

There were seven publications of trials comparing PN with glutamine versus standard PN. Four of these were duplicate reports of one original study by Ziegler 1992. They were MacBurney 1994, Scheltinga 1991, Ziegler 1998, Young 1993. Only data from studies by Ziegler 1992, Brown 1998, Schloerb 1993 were used (totalling 108 patients).

- Standard parenteral nutrition versus intravenous hydration:

Two trials involving a total of 166 patients were identified (Lough 1990; Weisdorf 1987).

- Parenteral nutrition versus enteral nutrition:

One full report and two abstracts (Cope 1997; Szeluga 1987; Young 1997), including a total of 144 patients, were identified.

The other eight trials (Aldamiz 1996; Charuhas 1997; Jimenez 1999; Lenssen 1987; Lenssen 1998; Malhotra 1996; Mulder 1989; Muscaritoli 1998) compared a miscellany of nutritional interventions, and could not be allocated to the above groups.

METHODOLOGICAL QUALITY

Three aspects of study methodology were addressed:

- allocation concealment (Mulrow 1997)
- blinding (although this was not considered to be a real threat to biasing the results since the main outcomes were considered to be objective measures)
- loss to follow up

The details of these can be viewed in Additional tables: Table 01

RESULTS

The results of the four main groups of comparisons of nutrition support are listed below.

- Oral glutamine versus oral placebo:

  For a number of the main outcomes adequate data were provided by Jebb 1995 and Schloerb 1999 only.

  The use of an oral placebo mouth wash,resulted in a significant reduction in days to achieve a normal neutrophil level (6.82 days, 95% CI (1.67-11.98) p=0.009) compared to an oral glutamine mouth wash.

The results for hospital duration, change in body weight, duration of nutritional intervention, numbers with positive blood cultures and survival at 100 days were not significant.

- PN and glutamine versus standard PN:

Data were provided by either two or all three authors on all the main outcomes of interest except line infections. One of the most significant outcomes was that, for patients receiving glutamine enriched PN, hospital duration was reduced by 6.62 days (weighted mean difference) with 95% CI -9.77--3.47, p=0.00004. The odds of these patients developing positive blood cultures were less compared to those on standard PN. The odds ratio was 0.23 with a 95% CI 0.08-0.65, p=0.006.

There was no significant difference in treatment affect for either PN and glutamine or standard PN for severity of mucositis, change in body weight, duration parenteral nutrition required, incidence of > grade 2 GVHD, duration of neutropaenia and survival at 100 days.

- PN versus IV hydration

Although Lough 1990 and Weisdorf 1987considered a number of similar outcomes, the majority of outcomes presented by Weisdorf 1987 were expressed in a format unsuitable for meta-analysis. However, Lough 1990 provided data on a number of outcomes of interest, some showing significant differences between the PN and IV hydration group. His data showed that the odds of having a line infection when given PN compared to IV hydration were 21.23 than for patients receiving IV hydration (95% CI 4.15-108.73, p=0.0002). Also, the mean percentage change in albumin for the IV hydration group showed surprisingly significant increases in albumin concentrations compared to the PN group. The mean difference was -5.93 (95% CI (-9.90 - -1.96), p=0.003). Data on percentage change in body weight indicated that PN was more beneficial than IV hydration for preventing weight loss. The weighted mean difference for percentage change in weight was 2.76 (95% CI 1.26-4.26, p=0.0003). There was no significant difference in survival at 200 days post BMT. Lough 1990 showed that the odds of surviving this long post BMT were 2.10 (95%CI 0.48-9.18, p=0.3) favouring PN over IV hydration (29 patients).

- PN versus EN

Whilst the authors for these three studies reported on a number of outcomes of interest, none of the data could be utilised. Data provided by Szeluga 1987 on change in body weight indicated that patients receiving parenteral nutrition were more likely to gain weight with this form of nutrition support. However, the crossover of patients from one group to another during the study provided uncertainty on the clarity of the data presented in the paper. Young 1997 presented similar data as median and ranges, which could not be utilised but also favoured parenteral nutrition for maintaining body weight, although the results were not significant. All three authors (Cope 1997, Szeluga 1987 and Young 1997) reported measuring hospital duration but the data were inadequate for analysis.

Cope 1997and Young 1997 both suggested that length of hospitalisation was significantly shorter in the enteral feeding group, whilst Szeluga 1987 implied that there was no significant difference between either group.

Since all the other included studies could not be grouped and had low power, no comprehensive assessment of the results could be made. If future randomised controlled trials of studies of these interventions are performed, it may then be possible to group some of the outcomes.

DISCUSSION

This review had wider inclusion criteria than those on nutrition support and cancer by Lipman 1991band Klein 1994, but included only BMT patients. The identification of 24 randomised controlled trials suggests an increasing interest in identifying the best mode of nutrition support for BMT patients. Furthermore, seven separate trials assessed the benefits of glutamine given either orally or parenterally, highlighting a surge of interest in the benefits of glutamine for BMT patients.

For oral glutamine v oral placebo trials, data from two out of four studies only could be used. This reduced the pooled sample size significantly. Most of the results were inconclusive for the outcomes of interest. One of the authors of a trial with no usable data (Coghlin Dickson 2000) concluded that the benefits of oral glutamine were inconclusive and that further trials are required. Since the studies of Coghlin Dickson 2000 and Anderson 1998 included 251 patients, it would be beneficial if the missing data from these studies could be retrieved to increase the pooled sample size and improve the reliability of detecting a true affect of the intervention, before further studies are performed.

For the PN and glutamine versus standard PN trials, the reduced incidence of positive blood cultures and hospital duration provided significant results favouring PN and glutamine. These results are probably the most interesting, and reinforce the theory that glutamine does have a protective affect on the prevention of clinical infections which subsequently influences length of hospital stay. However, in all three of these studies there were varying doses of glutamine administered daily, with no reported adverse affects, and so the appropriate dose required could not be estimated from these studies.

The results of the studies on parenteral nutrition versus intravenous hydration remain unclear because of insufficient data. However, the study by Lough 1990 highlights the higher incidence of line infections associated with parenteral nutrition compared to the intravenous hydration group, and reminds us that parenteral nutrition should be administered with caution when there is evidence of poor tolerance of enteral feed and prolonged gastrointestinal failure.

It is disappointing that the results from the parenteral nutrition versus enteral nutrition trials are inconclusive because of inadequate data, since enteral nutrition is potentially easier and safer to administer. Whilst there is a suggestion from the results that PN is more effective than EN in maintaining body weight. The authors of these studies hint that enteral nutrition when compared to PN may have an affect on reducing hospital duration which could have important benefits to patients as well as cost saving advantages, suggesting the need for a large randomised controlled trial to compare parenteral nutrition versus enteral nutrition.

- The benefits of oral glutamine mouth washes compared to oral placebo remain unclear and further studies or the provision of complete data from the studies already performed are required.
- The benefits of glutamine in PN compared to standard PN are more evident. There appears to be significant reduction of positive blood cultures and hospital duration suggesting that glutamine may specifically benefit patients receiving a BMT.
- Caution in the routine use of PN is still required because of the increased risk of line infection.
- The benefits of enteral nutrition in preference to PN are still not clear, reflecting an urgent need for a prospective RCT in this area.

REVIEWERS' CONCLUSIONS

Implications for practice

Routine use of parenteral nutrition and glutamine for bone marrow patients predicted to have prolonged gastrointestinal failure, should be considered.

Implications for research

Another trial of oral glutamine v placebo is required if it not possible to retrieve data from existing studies. Since glutamine in parenteral nutrition shows some benefits, a multi-centred, four arm RCT comparing parenteral nutrition to enteral feed with and without added glutamine should also be considered.

ACKNOWLEDGEMENTS

Systematic Reviews Training Unit at the Institute of Child Health, London for providing Susan Murray with funding to undertake training in systematic reviews. Professor PR Schloerb and Dr CH Poynton kindly provided unpublished data for this review.

POTENTIAL CONFLICT OF INTEREST

None known

TABLES

Characteristics of included studies

Study	Aldamiz 1996
Methods	Randomised controlled trialMethod of randomisation is not clear.
Participants	24 recruitedBMT type 6 Allogeneic and 18 Autologous BMT patients.Disease type not specifiedAge mean(+/-SD) years:Continuous PN = 37(+/-9.3)Cyclical PN = 35.4(+/- 11.1)
Interventions	12 Continuous PN 12 Cyclical PNStart criteria: Day +1 after BMTStop criteria: not clear.
Outcomes	Hospital durationChange in body weightGraft versus host diseaseDuration of PNDuration neutropaenia
Notes	There were no losses to follow up.
Allocation concealment	B
Study	**Anderson 1998**
Methods	Randomised controlled trial.Method of randomisation is truly random (computer generated random number list.)
Participants	195 recruitedBMT type: 106 Allogeneic/87 AutologousDisease type: Haem malignancy 106Haem disorders 8Solid tumour 62Inherited disorders 17Age (yrs) - mean (range)Oral Glutamine = 29 (1-62)Oral Placebo = 27 (1-62)
Interventions	Randomisation:98 -Oral mouth rinse glutamine or 1g/m2, x4/day.95 - Oral mouth rinse glycine 1g/m2, x4/dayStart criteria: 7 days before BMTStop criteria: 28 days after BMT
Outcomes	MucositisGraft versus host diseaseSurvival at day 28 and day 100.
Notes	Follow up:195 recruited, 2 withdrew98 - Glutamine group (2 did not participate)95 - Control
Allocation concealment	A
Study	**Brown 1998**
Methods	Randomised controlled trialMethod of randomisation is truly random
Participants	34 recruitedBMT type: 7 Allogeneic/ 27 AutologousDisease type: 34 Haem malignancyAge- years, median (range) Glutamine = 41(19-62)Control = 32 (16-55)
Interventions	Randomisation:18 PN + Glutamine (50g glutamine/day)16 to Standard PN (no glutamine)Start criteria: day -7 before BMTStop criteria: on day discharge.
Outcomes	Change in body weightGraft versus host diseaseSurvival
Notes	Follow up :34 recruited, 8 withdrew.18- Glutamine group (four withdrew)16- Control group (four withdrew)
Allocation concealment	A
Study	**Charuhas 1997**
Methods	Randomised controlled trialMethod of randomisation is not clear.
Participants	265 BMT (Out patients) recruitedBMT type: 212 Allogeneic/ 53 AutologousDisease type: 241 Haem malignancy,2 Haem disorders12 solid tumour3 Inherited disordersAge (range) years:PN group = 2.7 - 64.2yrsIV hydration = 2.1 - 63.1 yrs.
Interventions	Randomisation:128 PN 130 IV HydrationStart crtieria: at discharge Stop criteria: oral intake >85% energy requirements, for 3 consecutive days.
Outcomes	Hospital readmissionTime to resume oral intakeChange in body weightGVHDSurvival to day 150 (post BMT)
Notes	
Allocation concealment	B
Study	**Coghlin Dickson 2000**
Methods	Randomised controlled trialMethod of randomisation is not clear.
Participants	58 recruitedBMT type: 24 Allogeneic/ 34 Autologous Disease type: 59 Haem malignancyAge (range) years:Glutamine group:17-58 yrsControl: 21-59 yrs
Interventions	Randomisation:29 Oral Glutamine (10g x 3 doses/day).29 Placebo (Sucrose, 10g x 3/day).
Outcomes	Hospital durationMucositisDuration of PNEngraftmentSurvival at 2 years
Notes	There were no losses to follow up.
Allocation concealment	B
Study	**Cope 1997**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	63 recruitedBMT type: not specified Disease type: not specifiedAge - not specified

Interventions	Randomisation:23 EN40 PNStart/Stop criteria:not stated.
Outcomes	Hospital durationMucositisChange in nutritional status
Notes	Loss to follow up is not clear.
Allocation concealment	B
Study	**Jebb 1995**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	24 recruitedBMT type: 24 AutologousDisease type: 24 Haem malignancyAge range not specified.
Interventions	Randomisation:12 Oral mouth rinse glutamine, 4g x 4/d.12 Oral mouth rinse polycal, 4g x 4/d. Start criteria: day +1 after BMT until Stop criteria: mucositis resolved or discharge .
Outcomes	Hospital durationMucositisDuration of PNDuration of neutropaenia
Notes	Follow up: 24 recruited, 8 withdrew.12- Oral glutamine group (four withdrew)12- Control group (four withdrew).
Allocation concealment	B
Study	**Jimenez 1999**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	62 BMT patients.
Interventions	Randomisation:19 - 22.5% BCAA* + 20%LCT 26 - 45% BCAA* + 20%LCT*17- 45% BCAA*+ 20%MCT*/ LCT*
Outcomes	Hospital durationDuration of MucositisDuration of PNLipid metabolismNutritional assessment parameters.
Notes	(Original paper in Spanish)
Allocation concealment	B
Study	**Lenssen 1987**
Methods	Randomised controlled trial.Method of randomisation is truly random.
Participants	40 recruited.BMT type: 40 Allogeneic Disease type: 40 Haem malignancyAge median(range) years:23% BCAA*, PN = 28.5 (18-48)45% BCAA*, PN = 28.5 (18-49)
Interventions	Randomisation:20 - 23%BCAA* (PN) 20 - 45% BCAA*(PN)Start criteria: pre BMT (day not specified)Stop criteria: oral protein >10g/day.
Outcomes	Graft versus host disease
Notes	Follow up: 40 recruited, 21 withdrew.20 - 23%BCAA* (PN) (9 withdrew.)20 - 45% BCAA*(PN) (12 withdrew.)
Allocation concealment	A
Study	**Lenssen 1998**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	512 recruited.BMT type: 419 Allogeneic/ 93 Autologous Disease type: 512 Haem malignancyAge mean + (range) years:Standard PN Lipid group = 35 (0.5-65) PN+ low dose lipid group = 35 (0.4 -67).
Interventions	Randomisation:253 Standard PN Lipid259 Low dose PN Lipid Start criteria: oral energy intake < basal requirementsStop criteria: oral energy intake >10kcals/kg/day.
Outcomes	Graft versus host disease.Death by day 60 and day 150 post BMT.
Notes	Follow up: 512 recruited, 43 withdrew.253 Standard PN (20 withdrew)259 Low dose PN Lipid(23 withdrew)
Allocation concealment	B
Study	**Lough 1990**
Methods	Randomised controlled trial.Method of randomisation is truly random.
Participants	29 recruited.BMT type: 17 Allogeneic/12 AutologousDisease type: 29 Haem malignancyAge range (14-44yrs)
Interventions	Randomisation:14 PN 15 IV Hydration.Start criteria: day+1 after BMT until Stop criteria: 15 days after BMT?
Outcomes	Change in body weight
Notes	Follow up: 29 randomised,14 PN (4 excluded from analysis).15 IV (none excluded)
Allocation concealment	A
Study	**MacBurney 1994**

Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	43 recruitedBMT type: 43 Allogeneic Disease type: not specifiedAge range: not specified
Interventions	Randomisation:22 PN+ Glutamine (0.57g/kg/day21 Standard PN (no glutamine)Start criteria: day+1 after BMTStop criteria: oral intake > 50% energy requirements for 3 days.
Outcomes	Hospital durationSurvival
Notes	Small sub report from Ziegler's 1992 study.Cost is the main outcome reported.
Allocation concealment	B
Study	**Malhotra 1996**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	45 recruited.BMT type: not specified Disease type: not specifiedAge range: not specified
Interventions	Randomisation:Elemental diet Normal ad lib diet.Start criteria - 72 hours pre high dose therapy.Stop criteria: not stated.
Outcomes	MucositisNauseaDiarrhoeaSugar absorption tests for gastro-duodenal permeability, small bowel absorption and small bowel permeability.
Notes	Abstract report only.
Allocation concealment	B
Study	**Mulder 1989**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	22 recruited.BMT type: 22 AutologousDisease type: 22 solid tumourAge (range) years:PN group = 28-54yrsEN group = 21- 56 yrs.
Interventions	Randomisation:11 PN 11 PN+ENStart criteria:day + 4 after BMTStop criteria: leukocyte count > 1x 109.
Outcomes	Hospital durationChange in body weightSurvival
Notes	There were no losses to follow up.
Allocation concealment	B
Study	**Muscaritoli 1998**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	66 recruited.BMT type: 66 Allogeneic Disease type: 66 Haem malignancyAge mean(range) years:Glucose based PN = 30.5 (15-47)Lipid based PN = 29.1 (16-44)
Interventions	Randomisation:35 PN Glucose 31 PN LipidStart criteria - day +1 after BMT.Stop criteria - day + 16 after BMT.
Outcomes	Hospital durationChange in body weight.Graft versus host diseaseSurvival
Notes	Follow up : 66 recruited, 6 withdrew.35 PN Glucose (4 withdrew)31 PN Lipid (2 withdrew)
Allocation concealment	B
Study	**Scheltinga 1991**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	20 recruited.BMT type: 20 AllogeneicDisease type: 20 Haem malignancyAge(years)- mean(SEM)PN + Glutamine - 36+/-3Standard PN - 33+/-3
Interventions	Randomisation:10 PN+Glutamine (0.57g/kg/day)10 Standard PN (no glutamine)Start criteria: day+1 after BMTStop criteria: oral intake > 50% energy requirements for 3 days.
Outcomes	Hospital durationChange in body weight.Duration of PN
Notes	There were no losses to follow up.Small sub report from Ziegler's 1992 study.
Allocation concealment	B
Study	**Schloerb 1993**
Methods	Randomised controlled trial.Method of randomisation is truly random.
Participants	29 recruited.BMT type: 13 Allogeneic/ 16 AutologousDisease type: 26 Haem malignancy3 Solid tumourAge (years) - mean (range)PN + Glutamine 35.6(19-55)Standard PN - 37.6 (19-55)
Interventions	Randomisation:16 PN+ Glutamine (2830mg glutamine/100ml)13 Standard PN (no glutamine)Start criteria - unclearStop criteria - oral intake >50% energy requirements.
Outcomes	Hospital durationMucositisChange in body weight.Duration of PNGraft versus host

	diseaseNeutropaeniaPositive blood cultures
Notes	There were no losses to follow up.
Allocation concealment	A
Study	**Schloerb 1999**
Methods	Randomised controlled trial.Method of randomisation is truly random.
Participants	66 recruited.BMT type:19 Allogeneic/ 47 Autologous Disease type: 43 Haem maligancy23 Solid tumourAge: all > 17yrs.
Interventions	Randomisation:35 Oral Glutamine,10g x 3 /day.33 Oral/PN Glycine, 10g x 3/day. Start criteria: unclear. Stop criteria: oral intake >50% energy requirement.
Outcomes	Hospital durationMucositisChange in body weight.SurvivalDuration of PN
Notes	There were no losses to follow up.
Allocation concealment	A
Study	**Szeluga 1987**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	65 recruited. 61 participated.BMT type: 46 Allogeneic/ 15 Autologous Disease type: 45 Haem malignancy16 other miscellany of disorders.Age (years) PN = 21 > 19yrs, 10 < 19yrs.EN group = 21 > 19yrs, 9 < 19yrs.
Interventions	Randomisation:31PN 30 EN(4 withdrew)Start criteria: day before BMTStop criteria: 28 days after BMT
Outcomes	Hospital durationDuration of PNChange in body weight.NeutropaeniaGraft versus host diseaseSurvival
Notes	65 recruited. 61 participated, 4 withdrew. 57 could be evaluated at day 28.27 PN group (4 treatment failures).30 EN group. (7 received PN).Although 7 failed enteral feeds and received PN their outcomes were included in the EN group analysis.However 2 from the PN group were crossed at some stage into the EN group and were included in the EN group analysis . Consequently numbers for each outcome presented are unclear and none can be used.
Allocation concealment	B
Study	**Weisdorf 1987**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	137 recruited.BMT type:104 Allogeneic/ 32 AutologousDisease type:118 Haem malignancy8 Solid tumour3 Inherited disorder5 Haem abnormalities1 other malignancy2 unaccounted Age - years, mean (+/-SD) for PN group = 20 (+/- 12.9) IV hydration = 18.3 (+/- 12.9)
Interventions	Randomisation:71 PN 66 IV Hydration.Start criteria: 7 days before BMT.Stop criteria: 4 weeks post BMT.
Outcomes	Hospital durationChange in body weight.Survival
Notes	Difficulty extracting data from paper.There were no apparent losses to follow up.
Allocation concealment	B
Study	**Young 1993**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	23 recruited.BMT type: 23 Allogeneic Disease type: 23 Haem malignancyAge (yrs) (mean (range):PN + Glutamine = 36 (20-49)Standard PN = 30 (22-44)
Interventions	Randomisation:13 PN + Glutamine (0.57g glutamine/kg/day)10 Standard PN Start criteria : Day + 1 after BMT.Stop criteria : oral intake >50% energy requirements.
Outcomes	Hospital durationDuration of PN
Notes	There were no losses to follow up.Small report from Ziegler's 1992 study.Main outcome reported is mood.
Allocation concealment	A
Study	**Young 1997**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	20 recruitedBMT type:20 AllogeneicDisease type: not specifiedAge: not specified Allogeneic BMT patients.Age - not specified
Interventions	Randomisation:10 PN 10 ENStart criteria: weight loss >10% nutritional requirements inadequate.Stop criteria:not stated.
Outcomes	Duration of feeding (PN/EN_Change in body weight.
Notes	Follow up: 20 recrutied, 5 withdrew.10 PN 10 EN (5 withdrew)Abstract version only.

Allocation concealment	B
Study	**Ziegler 1992**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	45 recruited.BMT type: 45 Allogeneic Disease type: 45 Haem malignancyAge (years) - mean (range)PN + Glutamine - 32.1(20-48)Standard PN - 35.5(20-49)
Interventions	Randomisation:24 PN+ Glutamine (0.57g/kg/day)21 Standard PN (no glutamine).Start criteria: day+1 after BMTStop criteria: oral intake > 50% energy requirements for 3 days.
Outcomes	Hospital durationDuration of PNMucositiisNeutropaeniaGraft versus host diseasePositive blood culturesSurvival
Notes	Follow up: 45 recruited.24 PN + Glutamine - 2 were not followed up for hospital duration but were for all other outcomes reported.21 Standard PN - (1 withdrew)Note a number of studies are sub reports of this main study and they will not be included in the analysis.
Allocation concealment	A
Study	**Ziegler 1998**
Methods	Randomised controlled trial.Method of randomisation is not clear.
Participants	20 recruited.BMT type: 20 Allogeneic Disease type: 20 Haem malignancyAge (years) - mean (+/- SE)PN + Glutamine - 36 (+/- 3Standard PN - 35 (+/-3)
Interventions	Randomisation:9 PN+ Glutamine (0.57g/kg/day)11 Standard PN (no glutamine).Start criteria - day+1 after BMTStop criteria - not stated
Outcomes	Duration of PNNeutropaeniaClinical infection
Notes	There were no losses to follow up.Small report from Ziegler's main 1992 study.Main outcome reported effect on circulating lymphocytes.
Allocation concealment	B

Characteristics of excluded studies

Study	Reason for exclusion
Clemens 1997	This is not a randomised controlled trial.
Cohen 1996	This is not a report of a randomised controlled trial but single case report.
Ford 1992	The study does not include bone marrow transplant patients.
Klein 1994	This is not a report of a randomised controlled trial.
Lipman 1991a	This is not a report of a randomised controlled trial but a report of a review of clinical trials of nutrition support in Cancer patients.
Mercadante 1998	This is not a report of a randomised controlled trial but a report on the benefits of enteral nutrition versus parenteral nutrition for oncology patients.
Mobrahan 1992	This is not a report of a randomised controlled trial but instead a report on the potential benefits of glutamine for Bone Marrow Transplant patients.
Ramsay 1981	This randomised controlled trial did not use any form or type of nutrition support as its intervention.
Reiffers 1996	This randomised controlled trial did not use any form or type of nutrition support as its intervention.
Sax 1992	This is not a report of a randomised controlled trial but a comment report of a randomised controlled trial (Ziegler 1992) that compared glutamine supplemented PN with standard PN.
Souba 1993	This is not a report of a randomised controlled trial but a comment report of other randomised controlled trials that have compared glutamine supplemented PN with standard PN.

ADDITIONAL TABLES

Table 01 Summary table - Quality of studies assessed

Study ID	Randomisation	Allocation conceal	Double blind	Participants masked	Clinicians masked	Assessors masked
Anderson 1998	Truly random	Adequate	Yes	Yes	Yes	Yes
Jebb 1995	Unclear	Unclear	Yes	Yes	Yes	Yes
Schloerb 1999	Truly random	Adequate	Yes	Yes	Yes	Yes

Coghlin Dickson 2000	Unclear	Unclear	Yes	Yes	Unclear	Unclear
Brown 1998	Truly random	Adequate	Yes	Yes	Yes	Yes
Schloerb 1993	Truly random	Adequate	Yes	Yes	Yes	Yes
Ziegler 1992	Unclear	Adequate	Yes	Yes	Yes	Uncertain
Lough 1990	Truly random	Adequate	No	No	No	No
Weisdorf 1987	Unclear	Unclear	No	Uncertain	Uncertain	Uncertain
Szeluga 1987	Unclear	Unclear	No	Uncertain	Uncertain	Uncertain
Young 1997	Unclear	Unclear	No	Uncertain	Uncertain	Uncertain
Cope 1997	Unclear	Unclear	No	Uncertain	Uncertain	Uncertain
Macburney 1994	Unclear	Unclear	Yes	Yes	Yes	Yes
Scheltinga 1991	Unclear	Unclear	Yes	Yes	Yes	Uncertain
Young 1993	Unclear	Unclear	Yes	Yes	Yes	Yes
Ziegler 1998	Unclear	Unclear	Yes	Uncertain	Uncertain	Uncertain
Charhuas 1997	Unclear	Unclear	Yes	Yes	Yes	Yes
Mulder 1989	Unclear	Unclear	No	Uncertain	Uncertain	Uncertain
Lenssen 1998	Unclear	Unclear	Uncertain	Uncertain	Uncertain	Uncertain
Aldamiz 1996	Unclear	Unclear	Uncertain	Uncertain	Uncertain	Uncertain
Lenssen 1987	Truly random	Adequate	Yes	Yes	Yes	Yes
Jimenez 1999						
Malhotra 1996	Unclear	Unclear	Uncertain	Uncertain	Uncertain	Uncertain
Muscaritoli 1998	Unclear	Unclear	No	No	No	Uncertain

REFERENCES

References to studies included in this review

Aldamiz 1996 *{published data only}*

Aldamiz EL, Bachiller MP, Ariz MC, Gimenez A, Barcia MJ, Marin M. Continuous versus cyclic parenteral nutrition during bone marrow transplantation: Assessment and follow-up. Clin Nutr 1996;15(6):333-6.

Anderson 1998 *{published data only}*

Anderson PM, Ramsay NK, Shu XO, Rydholm N, Rogosheske J, Nicklow R et al. Effect of low-dose oral glutamine on painful stomatitis during bone marrow transplantation. Bone Marrow Transplant 1998;22(4):339-44.

Brown 1998 *{published data only}*

Brown SA, Goringe A, Fegan C, Davies SV, Giddings J, Whittaker JA et al. Parenteral glutamine protects hepatic function during bone marrow transplantation. Bone Marrow Transplant 1998;22(3):281-4.

Charuhas 1997 *{published data only}*

Charuhas PM, Fosberg KL, Bruemmer B, Aker SN, Leisenring W, Seidel K, Sullivan KM. A double-blind randomized trial comparing outpatient parenteral nutrition with intravenous hydration: effect on resumption of oral intake after marrow transplantation. J Parenter Enteral Nutr 1997;21(3):157-61.

Coghlin Dickson 2000 *{published data only}*

Coghlin Dickson T, Wong RM, Negrin RS, Shizuru JA, Johnston LJ, Hu WW et al. Effect of oral glutamine supplementation during bone marrow transplantation. Journal of Parenteral and Enteral Nutrition 2000;24(2):61-6.

Cope 1997 *{published data only}*

Cope FO. Prophylactic enteral support to BMT patients reduces length of hospital stay, improves GI integrity and nutritional status, and reduces intake requirements required for positive outcome. In: Proc Annu Meet Am Soc Clin Oncol. 1997.

Jebb 1995 *{published data only}*

Jebb SA, Marcus R, Elia M. A pilot study of oral glutamine supplementation in patients receiving bone marrow transplants. Clin Nutr 1995;14(3):162-5.

Jimenez 1999 *{published data only}*

Jimenez JF, Ortiz LC, Garcia GJ, Garnacho MJ, Rodriguez FJ, Espigado TI. Prospective, comparative study of different amino acid and lipid solutions in the parenteral nutrition of patients subjected to a bone marrow transplantation. Nutricion Hospitalaria 1999;14(2):57-66.

Lenssen 1987 *{published data only}*

Lenssen P, Cheney CL, Aker SN, Cunningham BA, Darbinian J, Gauvreau JM, Barale KV. Intravenous branched chain amino acid trial in marrow transplant recipients. J Parenter Enteral Nutr 1987;11(2):112-8.

Lenssen 1998 *{published data only}*

Lenssen P, Bruemmer BA, Bowden RA, Gooley T, Aker SN, Mattson D. Intravenous lipid dose and incidence of bacteremia and fungemia in patients undergoing bone marrow transplantation. Am J Clin Nutr 1998;67(5):927-33.

Lough 1990 *{published data only}*

Lough M, Watkins R, Campbell M, Carr K, Burnett A, Shenkin A. Parenteral nutrition in bone marrow transplantation. Clinical Nutrition 1990;9(2):97-101.

MacBurney 1994 *{published data only}*

MacBurney M, Young LS, Ziegler TR, Wilmore DW. A cost-evaluation of glutamine-supplemented parenteral nutrition in adult bone marrow transplant patients. J Am Diet Assoc 1994;94(11):1263-6.

Malhotra 1996 *{published and unpublished data}*

Malhotra D, DeMeo D, Kruger A, Rooney D, Holmes E, Poe L et al. Oral elemental nutrition improves gastrointestinal integrity in patients undergoing bone marrow transplantation. In: Proceedings of Asco Vol. Vol. 15. 1996:450.

Mulder 1989 *{published data only}*

Mulder PO, Bouman JG, Gietema JA, Van Rijsbergen H, Mulder NH, Van der Geest S, de Vries EG. Hyperalimentation in autologous bone marrow transplantation for solid tumors. Comparison of total parenteral versus partial parenteral plus enteral nutrition. Cancer 1989;64(10):2045-52.

Muscaritoli 1998 *{published data only}*

Muscaritoli M, Conversano L, Torelli GF, Arcese W, Capria S, Cangiano C et al. Clinical and metabolic effects of different parenteral nutrition regimens in patients undergoing allogeneic bone marrow transplantation. Transplantation 1998;66(5):610-6.

Scheltinga 1991 *{published data only}*

Scheltinga MR, Young LS, Benfell K, Bye RL, Ziegler TR, Santos AA et al. Glutamine-enriched intravenous feedings attenuate extracellular fluid expansion after a standard stress. Annals of Surgery 1991;214(4):385-95.

Schloerb 1993 *{published data only}*

Schloerb PR, Amare M. Total parenteral nutrition with glutamine in bone marrow transplantation and other clinical applications (a randomized double-blind study). J Parenter Enteral Nutr 1993;17(5):407-13.

Schloerb 1999 *{published data only}*

Schloerb PR, Skikne BS. Oral and parenteral glutamine in bone marrow transplantation: a randomized, double-blind study. J Parenter Enteral Nutr 1999;23(3):117-22.

Szeluga 1987 *{published data only}*

Szeluga DJ, Stuart RK, Brookmeyer R, Utermohlen V, Santos GW. Nutritional support of bone marrow transplant recipients: a prospective, randomized clinical trial comparing total parenteral nutrition to an enteral feeding program. Cancer Res 1987;47(12):3309-16.

Weisdorf 1987 *{published data only}*

Weisdorf SA, Lysne J, Wind D, Haake RJ, Sharp HL, Goldman A et al. Positive effect of prophylactic total parenteral nutrition on long-term outcome of bone marrow transplantation. Transplantation 1987;43(6):833-8.

Young 1993 *{published data only}*

Young LS, Bye R, Scheltinga M, Ziegler TR, Jacobs DO, Wilmore DW. Patients receiving glutamine-supplemented intravenous feedings report an improvement in mood. J Parenter Enteral Nutr 1993;17(5):422-7.

Young 1997 *{published and unpublished data}*

Young M, Stanford J, Walker DJ, Frost G. Preliminary report of the efficacy of nasogastric feeding in allogeneic adult bone marrow transplant patients. 1997.

Ziegler 1992 *{published data only}*

Ziegler TR, Young LS, Benfell K, Scheltinga M, Hortos K, Bye R et al. Clinical and metabolic efficacy of glutamine-supplemented parenteral nutrition after bone marrow transplantation. A randomized, double-blind, controlled study. Ann Intern Med 1992;116(10):821-8.

Ziegler 1998 *{published data only}*

Ziegler TR, Bye RL, Persinger RL, Young LS, Antin JH, Wilmore DW. Effects of glutamine supplementation on circulating lymphocytes after bone marrow transplantation: a pilot study. Am J Med Sci 1998;315(1):4-10.

** indicates the major publication for the study*

References to studies excluded from this review

Clemens 1997

Clemens MR, Waladkhani AR, Bublitz K, Ehninger G, Gey KF. Supplementation with antioxidants prior to bone marrow transplantation. Wien Klin Wochenschr 1997;109(19):771-6.

Cohen 1996

Cohen D. Nutrition management of gastrointestinal graft-versus-host disease following bone marrow transplantation. Support Line 1996;5:13-5.

Ford 1992

Ford EG. Clinical comparison of tolerance to elemental or polymeric enteral feedings in the postoperative patient. Journal of the American College of Nutrition 1992;11(1):11-6.

Klein 1994

Klein S, Koretz RL. Nutrition support in patients with cancer: what do the data really show?. Nutrition in Clinical Practice 1994;9(3):91-100.

Lipman 1991a

Lipman TO. Grains or veins: Is enteral nutrition really better than parenteral nutrition? A look at the evidence.

Journal of Parenteral and Enteral Nutrition 1998;60(22 / 3):167-82.

Mercadante 1998

Mercadante S. Parenteral versus enteral nutrition in cancer patients: Indications and practice. Supportive Care in Cancer 1998;6(2):85-93.

Mobrahan 1992

Mobrahan S. Glutamine: A conditionally essential nutrient or another nutritional puzzle. Nutrition Reviews 1992;50(11):331-3.

Ramsay 1981

Ramsay N. Prevention of graft versus host disease (GVHD) in bone marrow transplantation (BMT) recipients: A randomized study. In: Proc Am Assoc Cancer Res. 1981.

Reiffers 1996

Reiffers J. Allogeneic vs autologous stem cell transplantation vs chemotherapy in patients with acute myeloid leukemia in first remission: the BGMT 87 study. Leukemia 1996;10(12):1874-82.

Sax 1992

Sax HC. Clinical and metabolic efficacy of glutamine-supplemented parenteral nutrition after bone marrow transplantation. A randomized, double-blind, controlled study. J Parenter Enteral Nutr 1992;16(6):589-90.

Souba 1993

Souba WW. Total parenteral nutrition with glutamine in bone marrow transplantation and other clinical applications. J Parenter Enteral Nutr 1993;17(5):403.

Additional references

Herrmann 1993

Herrmann VM, Petruska PJ. Nutrition support in bone marrow transplant recipients. Ntr Clin Pract 1993;8(1):19-27.

Iestra 1999

Iestra JA, Fibbe WE, Zwinderman AH, Romijn JA, Kromhout D. Parenteral nutrition following intensive cytotoxic therapy: an exploratory study on the need for parenteral nutrition after various treatment approaches for haematological malignancies. Bone Marrow Transplant 1999;23(9):933-9.

Klein 1994

Klein S, Koretz RL. Nutrition support in patients with cancer: what do the data really show?. Nutrition in Clinical Practice 1994;9(3):91-100.

Kudsk 1994

Kudsk KA. Gut mucosal nutritional support- enteral nutrition as primary therapy after multiple system trauma. Gut 1994;suppl 1:S52-4.

Lipman 1991b

Lipman T. Clinical trials of nutrition support in cancer, parenteral and enteral therapy. Haematology/Oncology Clinics of North America 1991;5(1):91-101.

Mercadante 1998

Mercadante S. Parenteral versus enteral nutrition in cancer patients: indications and practice. Support Care

Cancer 1998;6(2):85-93.

Mulrow 1997

Mulrow CD, Oxman AD, editors. Cochrane Reviewer's Handbook 3.0.2. Oxford: The Cochrane Collaboration, 1997.

Papadopoulou 1997

Papadopoulou A, MacDonald A, Williams MD, Darbyshire PJ, Booth IW. Enteral nutrition after bone marrow transplantation. Arch Dis Child 1997;77(2):131-6.

Rickard 1980

Rickard KA. Effectiveness of enteral and parenteral nutrition in the nutritional management of children with Wilm's tumour. Clinical Nutrition 1980;33:2622-9.

Weisdorf 1984

Weisdorf S, Hofland C, Harvey LS, Teasley K, Schissel K, McGlave PB et al. Total parenteral nutrition in bone marrow transplantation : A clinical evaluation. Journal of Paediatric Gastroenterology and Nutrition 1984;3:95-100.

GRAPHS

Graphs and Tables

To view a graph or table, click on the outcome title of the summary table below.

01 Oral Glutamine v Oral Placebo Studies

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Mean duration (+/-SD) of time in hospital (e.g. admission to discharge or from day '0' to discharge).	4	333	Weighted Mean Difference (Fixed) 95% CI	-2.39 [-6.11, 1.34]
02 Mean(+/-SD) number of days patients had some degree of mucositis from start to end of study.	4	333	Weighted Mean Difference (Fixed) 95% CI	Not estimable
03 Number of patients who developed line infections from start to end of study.	4	333	Peto Odds Ratio 95% CI	Not estimable
04 Difference in mean % change in body weight from start to end of the study between the trial groups.	4	325	Weighted Mean Difference (Fixed) 95% CI	5.73 [-7.09, 18.55]
05 Mean duration (+/-SD) that nutritional intervention is given as PN.	4	333	Weighted Mean Difference (Fixed) 95% CI	-1.00 [-4.42, 2.43]
06 Number of patients who developed > grade 2 graft versus host disease (GVHD).	4	333	Peto Odds Ratio 95% CI	Not estimable
07 Number of days(+/-SD) to achieve normal neutrophil level (>0.5 X 10/9/l) after day 0 of BMT.	4	333	Weighted Mean Difference (Fixed) 95% CI	6.82 [1.67, 11.98]
08 Actual numbers of patients who have completed the study and survived to the 100th day post BMT.	4	333	Peto Odds Ratio 95% CI	1.73 [0.95, 3.17]
09 Actual number of patients who have completed the study and survived beyond day 100 post BMT.	4	333	Peto Odds Ratio 95% CI	Not estimable
10 Number with positive blood cultures	1	66	Peto Odds Ratio 95% CI	1.18 [0.39, 3.62]

02 PN + Glutamine v Standard PN

Outcome title	No. of studies	No. of participants	Statistical method	Effect size

01 Mean duration(+/-SD) of time in hospital (e.g. admission to discharge or from day 0 to discharge home).	3	103	Weighted Mean Difference (Fixed) 95% CI	-6.62 [-9.77, -3.47]
02 Mean(+/-SD) cumulative mucositis score	3	107	Weighted Mean Difference (Fixed) 95% CI	-0.18 [-0.69, 0.32]
03 Number of patients who developed line infections from start to end of study.	3	108	Peto Odds Ratio 95% CI	Not estimable
04 Difference in mean % change in body weight from start to end of the study between the trial groups.	3	105	Weighted Mean Difference (Fixed) 95% CI	-0.34 [-1.40, 0.72]
05 Mean duration (+/-SD) that nutritional intervention is given.	3	107	Weighted Mean Difference (Fixed) 95% CI	-0.41 [-4.00, 3.17]
06 Number of patients who developed >/=grade 2 graft versus host disease (GVHD).	3	107	Peto Odds Ratio 95% CI	0.57 [0.18, 1.83]
07 Number of days(+/-SD) to achieve normal neutrophil level (>0.5 X 10/9/l) after day 0 of BMT.	3	104	Weighted Mean Difference (Fixed) 95% CI	0.57 [-1.63, 2.76]
08 Actual numbers of patients who have completed the study and survived to the 100th day post BMT.	3	107	Peto Odds Ratio 95% CI	0.69 [0.16, 2.97]
10 Number of patients with positive blood cultures	3	107	Peto Odds Ratio 95% CI	0.23 [0.08, 0.65]

03 PN v IV Hydration

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Mean duration (+/-SD) of time in hospital (e.g. from discharge admission to discharge or day 0 to discharge).	2	166	Weighted Mean Difference (Fixed) 95% CI	Not estimable
02 Mean(+/-SD) number of days patients had some degree of mucositis from start to end of study.	2	166	Weighted Mean Difference (Fixed) 95% CI	Not estimable
03 Number of patients who developed line infections from start to end of study.	2	162	Peto Odds Ratio 95% CI	21.23 [4.15, 108.73]
04 Difference in mean % change in body weight from start to end of the study between the trial groups.	2	162	Weighted Mean Difference (Fixed) 95% CI	2.76 [1.26, 4.26]
05 Mean duration (+/-SD) that nutritional intervention is given.	2	166	Weighted Mean Difference (Fixed) 95% CI	Not estimable
06 Number of patients who developed > grade 2 graft versus host disease (GVHD).	2	166	Peto Odds Ratio 95% CI	Not estimable
07 Number of days(+/-SD) to achieve normal neutrophil level (>0.5 X 10/9/l) after day 0 of BMT.	2	166	Weighted Mean Difference (Fixed) 95% CI	Not estimable
08 Actual numbers of patients who have completed the study and survived to the 100th day post BMT.	2	166	Peto Odds Ratio 95% CI	Not estimable
09 Actual number of patients who survived to day 200 post BMT.	2	166	Peto Odds Ratio 95% CI	2.10 [0.48, 9.18]
10 Mean % change in albumin	2	162	Weighted Mean Difference (Fixed) 95% CI	-5.93 [-9.90, -1.96]

04 PN v Enteral feeding studies

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Mean duration (+/-SD) of time in hospital (e.g. from admission to discharge or day 0 to discharge).	3	144	Weighted Mean Difference (Fixed) 95% CI	Not estimable

02 Mean(+/-SD) number of days patients had some degree of mucositis from start to end of study.	3	144	Weighted Mean Difference (Fixed) 95% CI	Not estimable
03 Number of patients who developed line infections from start to end of study.	3	144	Peto Odds Ratio 95% CI	Not estimable
04 Difference in mean % change in body weight from start to end of the study between the trial groups.	3	144	Weighted Mean Difference (Fixed) 95% CI	Not estimable
05 Mean duration (+/-SD) that nutritional intervention is given.	3	144	Weighted Mean Difference (Fixed) 95% CI	Not estimable
06 Number of patients who developed > grade 2 graft versus host disease (GVHD).	3	144	Peto Odds Ratio 95% CI	Not estimable
07 Number of days(+/-SD) to achieve normal neutrophil level (>0.5 X 10/9/l) after day 0 of BMT.	3	144	Weighted Mean Difference (Fixed) 95% CI	Not estimable
08 Actual numbers of patients who have completed the study and survived to the 100th day post BMT.	3	144	Peto Odds Ratio 95% CI	Not estimable
09 Actual number of patients who have completed the study and survived beyond day 200 post BMT.	3	144	Peto Odds Ratio 95% CI	Not estimable

COVER SHEET

Nutrition support for bone marrow transplant patients

Reviewer(s)	Murray SM, Pindoria S
Contribution of Reviewer(s)	Information not supplied by reviewer
Issue protocol first published	2001 issue 1
Issue review first published	2002 issue 2
Date of last minor amendment	28 May 2002
Date of last substantive amendment	23 February 2002
Most recent changes	Information not supplied by reviewer
Date new studies sought but none found	Information not supplied by reviewer
Date new studies found but not yet included/excluded	Information not supplied by reviewer
Date new studies found and included/excluded	Information not supplied by reviewer
Date reviewers' conclusions section amended	Information not supplied by reviewer
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Cochrane Library number	CD002920
Editorial group	Cochrane Pain, Palliative Care and Supportive Care Group
Editorial group code	SYMPT

SYNOPSIS

Bone marrow transplant patients who are given parenteral nutrition with additional glutamine are likely to have a reduced rate

of infections and leave hospital earlier.

Bone marrow transplant patients can experience prolonged poor appetite with vomiting and diarrhoea. Malnutrition is a consequence. To prevent this, patients can receive nutritious fluids orally or via a nasogastric tube, or intravenously as parenteral nutrition. The benefits of either route are unclear. Studies were found that compared these interventions but missing data prevented proper assessment of the benefits. The limited data available indicated that patients with an inadequate food intake, unable to tolerate oral or tube feeding, are likely to go home earlier if they receive parenteral nutrition with additional glutamine compared to standard parenteral nutrition without additional glutamine.

KEYWORDS

Human; Bone Marrow Transplantation[*adverse effects]; *Enteral Nutrition; Nutrition Disorders[etiology][*prevention & control]; *Parenteral Nutrition; Randomized Controlled Trials