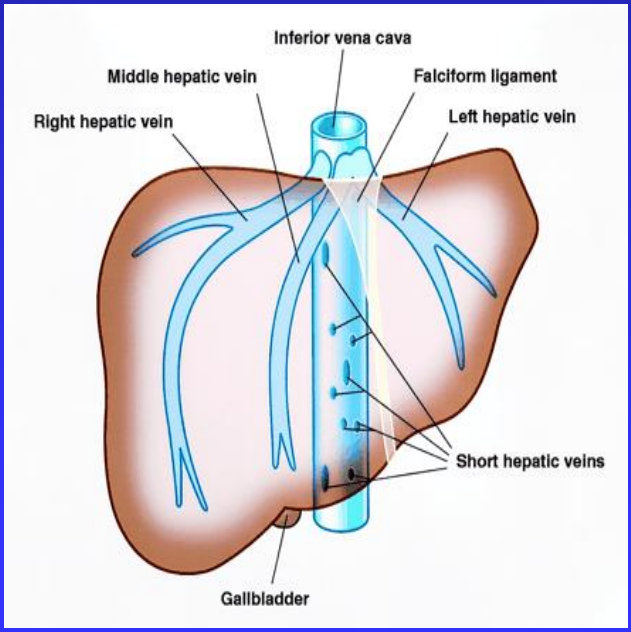
Nutrition and Liver Disease



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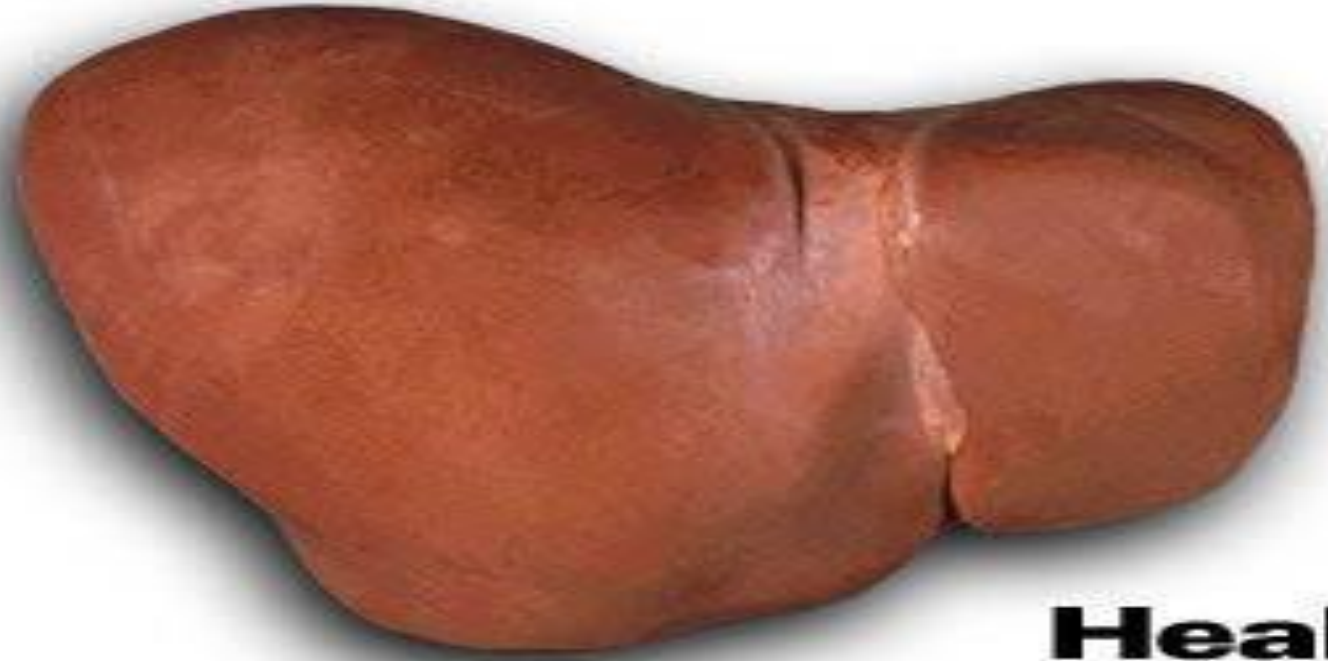
Areas Covered

- Malnutrition & liver disease
- Metabolism & liver disease
- Nutrition in compensated liver disease
  - Nutrition in HCV undergoing antiviral treatment
  - Nutrition in NAFLD
- Nutrition in decompensated liver disease & transplant
- BCAA & future developments
- Problem solving/ Case study
- Summary of Dietary Intervention

Increased alcohol consumption and obesity causing more ALD, NAFLD



Healthy

Cirrhosis

Malnutrition in liver disease

- Malnutrition- 65-90% cirrhosis + 100% waiting for a transplant - severity malnutrition correlates with pse, ascites, hepatorenal, post olt morbity/ mortality

- Aim to be as well nourished as possible to prevent further nutrient and muscle depletion, correct malnutrition, improve qol, decrease risk infection

- Assessment of nutritional status in all patients

Malnutrition

Causes of Malnutrition	Etiology
Decreased Intake	Secondary to gastroparesis, tense ascites, small bowel dysmobility and bacterial overgrowth. Increased proinflammatory cytokines Zinc/ Mg deficiency Sodium restriction
Anorexia, nausea, early satiety, abdo pain Altered taste Unpalatable Diets Constipation	
Increased Losses	
Hyperglycaemia	Insulin resistance
Malabsorption of fat and fat sol vits Intestinal losses of protein¸low protein synthesis	Seen in severe cholestasis as intraluminal bile salts are reduced. Pancreatic insufficiency in ALD Increased protein loss from paracenthesis.
Altered Metabolism/ Expenditure	
Glucose storage is reduced Decrease protein synthesis Increase fat metabolism Gluconeogenesis is active	Increase catabolic hormores Lack of glycogen stores.

Altered metabolism (fat supplies 75%cals instead of 35%)

CHO	▪ ↑ Catabolic hormones(as not degraded by liver)& gluconeogenesis ▪ ↓ Post prandial gluc storage ▪ ↓ Glycogen stores (accelerated starvation)
Protein	▪ ↓ Protein synthesis ▪ ↑ Resistance to anabolic hormones Lower BCAA to AA ratio
Fat (preferred fuel)	▪ Nocturnal fat metabolism- impaired synthesis PUFA from EFA (Cabre 93)

Assessment of Nutritional Status

- Use simple bedside nutrition screening tool and anthropometry to assess under-nutrition (ESPEN 09)
- NPT tool asks the ascitic patient 3 simple questions = NPT score
- Symptoms that affect eating & Diet History
- Anthropometry- TSF, MAMC, Grip strength, Dry wt, BMI. Aim >10th C

Albumin is not a good indicator of nutritional status in liver disease

Compensated cirrhosis

Nutrient requirements → 25-35kcal/kg

(ESPEN 97) → 1-1.2gm prot/Kg

- Hep C

BMI >30 less response to antivirals

Aim BMI 20-25 prior to and while on treatment

?? Caffeine helps decrease progression liver disease

NAFLD Dietary Aims

- ✓ 5% weight loss initially then aim for 0.5-1Kg/ wk & 10% over 1 yr
- ✓ Adequate protein
- ✓ High fibre & low sat fat
- ✓ Monitor waist circumference, BMI, Wt
- ✓ 30-60 mins moderate exercise daily to improve insulin sensitivity

(National Heart and Lung Institute, NIH, USA)

Expand on rationale

Nutrition in Decompensated Liver Disease

Nutrient requirements → 35-40kcal/kg

(ESPEN 2006) → 1.2-1.5gm Protein/Kg

Aim 60-70% cals complex + refined CHO

Obese use - adjusted wt for Kcals, For protein use actual wt x 75%

- High Protein High calorie diet +/-Tube feeding +/- ONS . Use concentrated feeds if fluid overloaded

- ONS can increase nutrition status and survival in alcoholic hepatitis (ESPEN 06)

- Tube feeding in cirrhosis improves nutritional status, liver function and decreases rate complications and improves survival (ESPEN 06)

Estimating Dry Weight
(Mendenhall 1992)

	Ascites	Oedema
Minimal	2.2 Kg	1 Kg
Moderate	6.0Kg	5 Kg
Severe	14Kg	10 Kg

Ask patient their pre ascitic weight

Nutrition Support

- Oral/ ONS/NG- 1.25-2cal/ml, high N2 to energy ratio
  - ONS recommended (ESPEN 06 Grade B)
- TF - If unable to meets reqs orally (ESPEN 06)
  - Oesophageal varices not a contraindication to fine bore Ng (ESPEN 06)
  - Overnight TF helps decrease fasting period
  - Concentrated whole protein feeds if ascites
- In ALF commence artificial nutrition if unlikely to resume normal nutrition within 5-7 days (ESPEN 09)
- Use IV gluc2-3gm/kg if fasting >12 hrs (ESPEN 09)
- Avoid PEG/ PN if possible

Nutrition Support

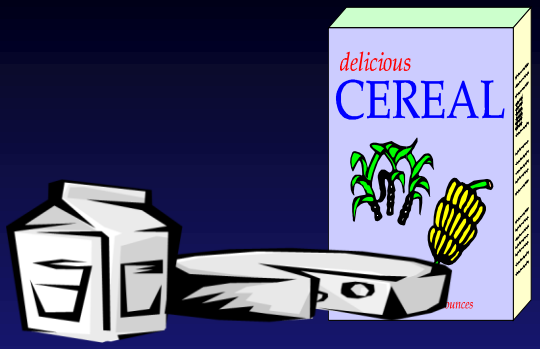
- DM control- Gluc intolerance, insulin resistance
- Use PN in moderate or severely malnourished cirrhosis who cannot be fed either orally or enterally or if fasting > 72 hrs (ESPEN 09)
- Important to have a late evening carbohydrate snack (Plank 2008 Hepatology)

PN associated Liver Disease (PNALD)

- Results from intestinal failure, underlying liver disease, cancer, surgery together with length of time on PN
- 40-55% steatosis in adults, after 2/52 on PN. Reversible, rarely progresses (increase ALP, GGT)
- 2-30% cholestasis, Commences after 3/52 on PN, slow to resolve
- Prevent by using cyclical PN, fat <1gm/kg,use mix fat types

  (Some research on choline oral/iv improving steatosis but not commercially avail)

Snacks

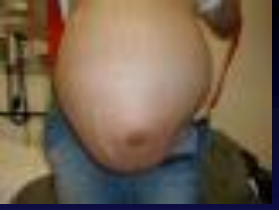


- 6-7 meals/ snacks /day
- 50gm CHO late evening snack

Increase CHO oxidation rate

Decrease lipid and protein oxidation

- Improves Nitrogen balance
- Can be food or supplement drink



NAS Diet 80-100mmol (2gm)

Only fluid restrict if Na<120-125mmol/L

- ORAL
- No salt cooking/table
- Up to 100gm hard cheese/wk (1oz cheese =10mmol)
- Up to 4 slices bread /day (1 slice bread =6mmol)
- Limit processed foods/ salty foods(sauces, soup, crisps, cured meats, sports drinks)

Often give HPHC d/s if losing dry wt or undernourished

- FEED/ ONS
- Avoid low Na feeds, use HPHC feed and ONS

Nutrison Protein Plus 48mmol/L, *Ensure plus* 10.4 mmol/200ml

If require fluid restriction use 2cal/ml feed

Portosystemic Encephalopathy

- No protein restrictions
- Reduced muscle mass may predispose to or exacerbate PSE
- Evenly distribute protein over day
- HPHC diet +/- ONS +/- Tube feeding

Steatorrhea

- No fat restrictions unless symptom relief then use MCT

Micronutrients in Liver Disease
Water Soluble Vitamins

- Aim to correct any deficiences Diagnosis of defic can be difficult (Plauth 09
- B1 100mg TDS x 1/12 + multi vit prior to feeding ALD+/- Mg, Phos ,Zn
- Multivitamin all ESLD(ASPEN 05 & manuel dietetic practice)
- Caution with Hep C. Vit E can increase viral replication (Yanno 2007)
- Hep C pats on Interferon & Riboviron can decrease vit B and Fe levels

Fat Soluble Vitamins

- Fat sol vits practice varies in centres- no policies
- NB Cholestatic disease + ALD with pancreatic insuffic (snachez 06)
- Vit K- look at prothrombin time. 10mg od. Repeated doses not warrented if response to intial use is unsatisfactory
- Vit E, PIVENS trial 2009
- Insufficient info to make sound recommendations on how much to supplement

(avail ADEK = 5667iu vit A mainly retinol, 400iu D, 150iu E, 150microgm K)

Micronutrients

Vitamin D & Ca

- 92% ESLD low vit D (Arteh et al 2009)
- 1gm Ca + 800 IU vit D
- If osteoporosis 1.2-1.5gm/d Ca (Antonio et al 2006)
- Post OLT bone loss 1.4-24% mainly 1st 3-6/12 post OLT but stable at 1 yr post OLT

Minerals & Trace Elements

- **Zn** low

Zn supple assoc with improved gluc disposal in cirhotics & defic may contribute to impaired IGT/ DM

Conflict results Zn trials to decrease hepatic encephal

May decrease fibrosis in NASH(Matsuoka 09)

May improve outcome Hep C (Kang 05)

- **Copper** often high so don't take more than standard multivit but can be low in NASH

- **Fe/ Copper**. Haemachromatosis & Wilsons can have excess

- **Manganese** high as excretion altered (choi 05)

- **Antioxidants**. No evidence to support or refute use in liver disease (Cochrane 2010)

Nutrition & Liver Transplant (OLT)

- Better outcome post OLT if BMI 18.5-35
  (andree et al 2009)
- ? NG/NJ post OLT 3 options
- Oral/TF 12-24 hrs post OLT (ESPEN 06)
- TF can decrease complication rate and cost, is preferable to PN
- Long Term

Safe Food advice

24% Dm post OLT

Prednisilone >5mg/d =Vit D 800iu + 1gm ca

70% Hypertension

Excessive wt gain

Branched Chain Amino Acids

Valine, Leucine, Isoleucine

- ↓ BCAA : AAA ratio in liver disease (3.5:1 → 1:1)
- ↑ aromatic AA, proposed cause of HE, acting as 'false neurotransmitters'
- Correction of amino acid ratio may improve HE
- ? BCAAs support muscle glutamine synthesis, thereby ammonia detoxification
- Older studies showed BCAA may ↑ muscle synthesis, ↓ catabolism & potentially promote more rapid recovery from HE

BCAA - the evidence

1. Encephalopathy

- Consider using BCAA if on TF and encephalopathy grade 3-4 arises (ESPEN 09-grade A)

vs

- No convincing evidence to support the use of BCAA for patients with hepatic encephalopathy (Cochrane 2003)

2. Clinical outcome

- BCAA improve clinical outcome in advanced cirrhosis (ESPEN 06- grade B) but noted lack of long term studies + improve nut status (Charlton 2006)
- Long term BCAA decrease progression of hepatic failure (Etsushi et al 2009)-given to Child Class A dx.

- Paeds- pre OLT, BCAA increase body cell mass–(ESPEN 06 grade B)

- **Products** – Neither avail in Eire currently

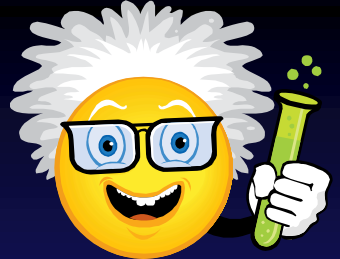
1. *Fresubin Hepa* complete sip/ tube feed - 44% BCAA

2. *Hepatical* (SHS) complete powder 31% BCAA)

- LOLA increases glutamine available enabling muscle to detoxify ammonia

- ? Modifying gut flora

Future Developments



- **Pre and Probiotics** (Cochrane 08 no clear evidence but offer promise need RCT)
- **Immune modulating** formula
- **Fish oils**-recommended for *Sirolimus* induced hyperlipideamia Need trials to determine efficacy in OLT in general

- **Glutamine** (? Helps pre OLT if PSE (ASPEN conf 2010)
  ALF not recommended - Post OLT no data)

- **CAM** - potential risk immune modulation in OLT, hepatotoxicity

35% use USA, 65% use in Germany- results inconclusive

- ✓ Silymarin (milk thistle) trials in NASH & hep C. Safe , no interference with drugs
- ✓ Curcummin has potential in HCC

Case study/ Problem solving

- 68 ♂ **with ALD cirrhotic ,who lives alone**
- Weight 59.3kg Ht 1.64m
- Mild ascites, encephalopathy Grade 2, pleural effusions

Ques 1: What do you need to do to undertake a nutritional assessment ?

Nutrition Assessment

- Normal Wt - 66kg
- Estimated dry wt 59.3 - 2.2= 57.1kg
- % weight loss 13%
- Est dBMI – 21kg/m^2 MUAC 5^{th} – 10^{th} C
- TST 10^{th} – 25^{th} C MAMC 5^{th} – 10^{th} C
- Hand Grip strength = 8.9kg = 22% of normal

Case study/ Problem solving

Ques 2: What are his calorie and protein requirements for weight maintenance ?

Calories	**Protein**
A) 1800kcals	A) 86-114gm
B) 2000Kcals	B) 68-86gm
C) 2500kcals	C) 114-125gm

Answer : 35-40kcal/kg dry wt + 1.2-1.5gm prot /kg

2000kcals + 68-86gm protein- additional 400kcal for wt gain

Case study/ Problem solving

Requirements approx 2000kcal + 68-86 gm protein

Ques 3: What would be a suitable nutritional care plan considering he has ascites and encephalopathy ?

Care Plan

A) Low protein low salt diet + ONS

B) Low salt high protein diet + ONS

C) Low protein tube feed

Answer: B

Ques 4 :What else do you need to consider in the plan ?

✓B1 50gm CHO Bedtime snack ? NG

✓ONS high protein eg *Fresubin Protein Energy*

Challenges with encephalopathic Pts

- Pt forgetting to eat
- Pt asleep when meals delivered and not woken
- No food chart
- Pt unable to tell you what he has had
- ? accuracy of Pts answers
- Pt answering the same to all questions
- Junior Drs asking for a low protein diet

2nd Admission Mr P.

- ↑ oedema and ascites, oesophageal varices, PSE,confused
- Reasonable appetite, dislikes ONS. Intake met 65% requirements. On OLT waiting list
- ↓ in MUAC & TSF , MAMC<5thC , BMI 20

Ques 5: What would be a suitable nutritional care plan ?

A) NG feed overnight with special low sodium feed eg *Nutrison low sodium*

B) NG Feed overnight with high protein normal sodium feed eg *Nutrison protein plus,Jevity plus HP, fresubi HP Energy*

C) Strict low sodium diet + high protein ONS

D) Ng feed 18 hours per day + diet as tolerated

Answer: B

Question 6: **Before** you start feeding what do you need to do ?

Refeeding syndrome is defined as severe fluid and electrolyte shifts in malnourished patients precipitated by the introduction of nutrition

- It can lead to a severe drop in **phosphate**, **potassium** and **magnesium** concentrations in plasma.
- The fall in plasma concentrations is largely due to a shift into cells coinciding with commencement of anabolism.
- These shifts lead to cardiac, respiratory, hepatic, neuromuscular, renal, metabolic, haematological and gastrointestinal problems.

Refeeding Syndrome

1. **Identify the risk:** moderate, high, severely high
(From the NICE guidelines 2006)

2. **Monitor K, Po4, Mg** during first wk of refeeding and twice weekly thereafter

3. **Moderate** risk Start feed at less than 50% target rate feed
High risk start 10kcal/kg , increase slowly over 4-7 days
Severely high risk start 5kcal/kg increase slowly to meet requirements over 4-7 days

4. Meet full requirements of **fluid, electrolytes, vitamins** from day 1

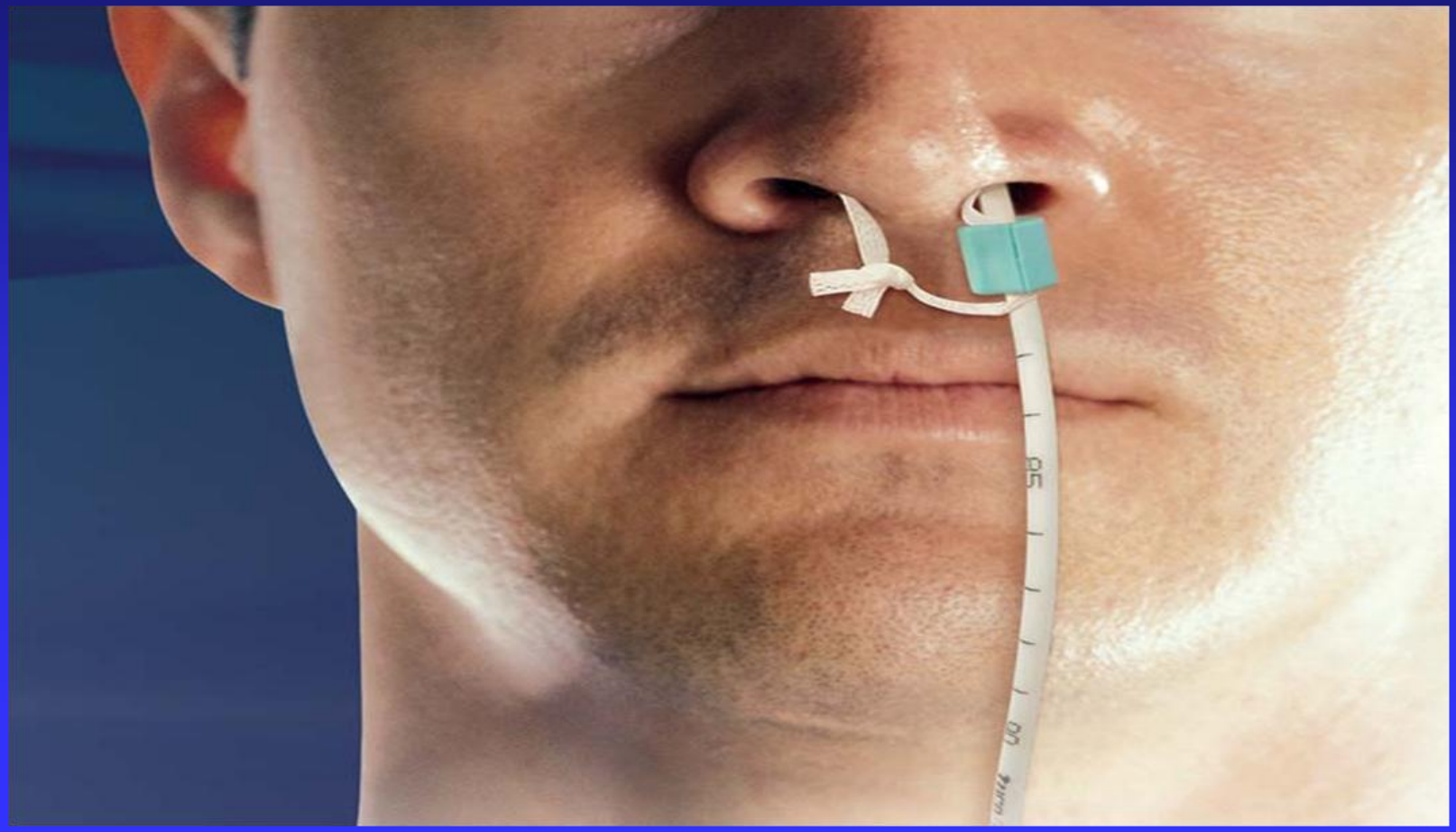
5. **High & severely high risk** B1 100mg TDS + B complex + multivitamin or IV pabrinex 1 and 2 for 3/7 with additrace and solvito IV if on parenteral nutrition

Ques 7: If patient is pulling out the NG what options do you have ?

A) Use TPN
B) Use a Nasal bridle
C) Insert PEG for feeding
D) Put on IV saline

Answer B: Consider using a nasal bridle

Nasal Bridles



Summary of Dietary Intervention

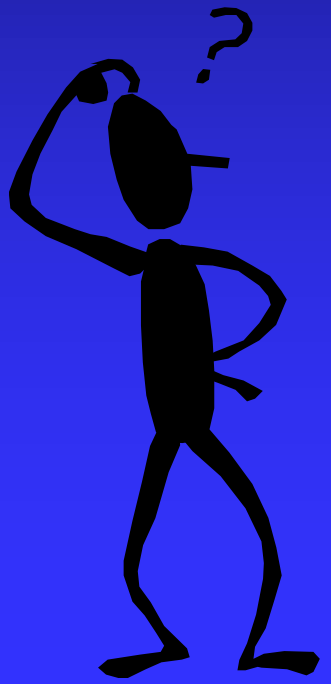
Compensated Hep C, NAFLD	**ESLD - don't over restrict**
✓Aim BMI 20-25 gradual weight loss ✓Adequate prot, high fibre low sat fat ✓30-60 mins moderate exercise daily to improve insulin sensitivity	✓ HPHC + bed time snack + ONS ✓ If ascites aim NAS 80-100mmol ✓ If need NG 1.5-2cal/ml feed – varices not a contraindication ✓Vitamins and minerals

Liver Transplant

✓ Oral / enteral — Initially HPHC +/- DM + food safety advice

✓Long term weight managment, chol, food safety, vit D & Ca

Any Questions ?



Reading

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- **Weimann A et al ESPEN Guidelines on Enteral and Parenteral Nutrition: Surgery including Organ Transplantation. *Clinical Nutrition* 2006;25:224-244**
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PSE-additional info

- Nitrogenous products from muscle breakdown exacerbate HE
- Muscle detoxifies ammonia by conversion to glutamine

Reduced muscle mass may predispose to or exacerbate HE

- Direct link between PEM and worsening HE (4-9)
- Cirrhotic patients need 1.2–1.3g protein/kg/day to remain in positive N_2 balance (11)

BCAA- proposed action

1. Stimulation of hepatic regeneration
2. Improves LFTs and biochemical profiles
3. Reverses malnutrition by providing sufficient protein, reducing anorexia assoc with hepatocellular failure, inhibiting protein degradation, and enhancing protein synthesis
4. Prevention of progressive hepatic failure and HE

Short term → Achieve positive nitrogen balance & increased nutritional status

Long term → Improved liver function

BCAA- additional info

- Some RCT's suggest LT supplementation with oral BCAA's is useful in slowing progression of hepatic failure & prolonging event free survival (15,16).
- BCAA's are associated with ↑ hepatic protein synthesis. Their use in HE is controversial.
- ESPEN 2006
  - 'BCAA - enriched formulae should be used in patients with HE arising during enteral nutrition'
  - 'Oral BCAA supplementation can improve clinical outcome in advanced cirrhosis'
- Cochrane review 2008
  - Not enough evidence to advocate using BCAAs with HE Pts

New treatments for PSE-additional info

- Modification of gut flora
  - Use of probiotics / fermentable fibre (23-26)
  - As an alternative to lactulose (25-26)
- Molecular adsorbent re-circulating system (MARS) and Single Pass Albumin Dialysis (SPAD)
- L-Ornithine L-Aspartate (LOLA)
  - ? Increase the removal of N_3 from the blood by stimulating urea and glutamine synthesis

Refeeding syndrome-categories

- **Moderate risk:**
- Patient has **one or more** of the following:
  - Very little intake for greater than 5 days
  - Unintentional weight loss greater than 10% within the previous 3-6 months.
  - BMI <18.5kg/m^2.
- **High risk:**
- Patient has any **one** of the following:
  - BMI <16kg/m^2.
  - Unintentional weight loss >15% in the last 3-6 months.
  - Very little or no food for >10 days.
  - Low levels of potassium, phosphate and magnesium before feeding.
- **Or if the patient has two or more of the following:**
  - BMI <18.5kg/m^2.
  - Unintentional weight loss >10% in the last 3-6 months.
  - Very little or no food intake for >5 days.
  - History of alcohol abuse.
  - Use of drugs including insulin, chemotherapy, antacids or diuretics.
- **Severely high risk:**
  - BMI <14kg/m^2.
  - Negligible intake for greater than 15 days.

Pattern of Malnutrition in Liver Disease

	Muscle wasting	Loss Fat stores	Reduced synthetic function
Alcohol	**severe**	mild	**moderate**
Viral	**moderate**	**moderate**	mild
PBC	**severe**	**severe**	mild
PSC	**moderate**	mild	mild