Dietary Supplement in Management of End-Stage Hepatocellular Carcinoma

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Annual Incidence of HCC in SAARC Countries

- In Bangladesh 1.3/100,000 in males and 1.3/100,000 in females
- In India 2.24/100,000 in males and 0.96/100,000 in females
- In Pakistan 0.7/100,000 in males and 0.8/100,000 in females
- In Sri Lanka 0.8/100,000 in males and 0.5/100,000 in females

Globally HCC is the 2nd commonest cancer

Dhir et. al Indian Gastroenterol 2007
Gloomy Side of HCC in Bangladesh

HCC 3rd commonest cancer in Bangladesh next to lungs and stomach cancers

Karim, (Mahtab) et al EJOHG 2012
Chowdhury et al JCMCTA 2009
Bari et al. Bangladesh Oncology J 2009
HBV Related HCC: Past and Present in Bangladesh

- Chowdhury et al JCMCTA 2009
- Mahtab et. al. Hepatol Int (Suppl) 2009
- Karim et. al. Korean J Hepatol (Suppl) 2011
Incidence of especially end-stage HCC rising in Bangladesh as in other developing countries of Asia-Pacific

Due to recent development of diagnostic approaches, especially imaging techniques and comparatively better economic conditions, increasing number of HCC patients are attending physicians

Almost nothing can be done to these patients, either due to end-stage liver disease or technical or financial limitations

‘Nothing To Do’ approach is adopted by attending physicians to manage end-stage HCC

Patients and their relatives are advised to accept ‘death’ at homely condition
Unfortunate Reality!

- In Bangladesh >80% HCC unresectable at diagnosis
- Globally mean age of HBV related HCC 59.87 yrs
- In Bangladesh 41.92 yrs; 18 yrs earlier
- Early detection of HCC Improves cure rate from 5% to 80%
- Must look for ‘home grown’ solution for management of advanced cases
Current Focus

New Therapeutic Option for HBV

Therapeutic potential of a combined hepatitis B virus surface and core antigen vaccine in patients with chronic hepatitis B

Mamun Al-Mahtab · Sheikh Mohammad Fazle Akbar · Julio Cesar Aguilar · Md. Helal Uddin · Md. Sakirul Islam Khan · Salimur Rahman

- 1st therapeutic vaccine against any chronic disease
- Phase III complete; safe and superior to Peg-IFN
- Awaiting publication
Early Prediction of HCC

- Single nucleotide polymorphism in IL28B gene in HBV-HCC (complete)

Discovery and Validation of DNA Hypomethylation Biomarkers for Liver Cancer Using HRM-Specific Probes

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Abstract

Management of End-Stage HCC

- Antigen-pulsed dendritic cell therapy for end-stage HBV-HCC (ongoing)
- Dietary supplements in end-stage HCC (ongoing)
Alternative Management Strategy for Advanced HCC in Resource-Constrained Countries

Role of Food Supplements in HCC

- Improved prognosis of post-operative HCC by functional food
  Matsui et al. J Hepatol 2002

- Increase survival and decreased disease progression of advanced liver diseases by nutrient supplement
  Vilar Gomez et al. BMJ Open 2011

- Improve liver function in HCC by late evening snack
  Morihara et al. Hepatol Res 2012

- Branched chain amino acid in HCC
  Nishikawa et al. World J Gastroenterol 2012

Inference

Food supplement may have positive impact in management of liver cirrhosis and HCC
Aims and Objectives

Development of insights about efficacy of food supplement in patients with end-stage HCC

Role of food supplement, if any, in the management of advanced and end-stage HCC

What remains to be clarified
ONCOXIN®: Glycyrrhizinic Acid Plus Green Tea Extract

Composition of ONCOXIN®

100 ml of ONCOXIN contains

- Glycine: 2000 mg
- Glucosamine: 2000 mg
- Malic acid: 1200 mg
- Arginine: 640 mg
- Cystine: 204 mg
- Mono-ammonium glycyrrhizinate: 200 mg
- Ascorbic acid: 200 mg
- Sodium methylparaben: 120 mg
- Zinc sulphate: 100 mg
- Green tea extract: 80 mg
- Calcium pantothenate: 25 mg
- Pyridoxine: 12 mg
- Manganese sulphate: 4 mg
- Cinnamon extract: 3 mg
- Folic acid: 400 microgm
- Cyanocobalamin: 2 microgm

Follow-up was done monthly or when patient expired

Catalysis SL, Madrid, Spain

ONCOXIN® syrup: 25 ml, twice daily for 3 months
ONCOXIN® capsule: 1 cap, thrice daily for 3 months
ONCOXIN® Induced Reduced Viability

Best effect with 1:10 to 1:100 dilution

Arriazu et al J Hepatol (Suppl) 2012
Toxicity seen only with 1:10 dilution. 1:50 to 1:100 dilutions are safe.

ONCOXIN® Safe to Healthy Mouse Hepatocytes

Arriazu et al J Hepatol (Suppl) 2012
Study Population

- End-stage HCC 60
  (Abandoned by Physicians, Oncologists, Hepatologists)
- BCLC C & D
- Performance status (KPSI) 20-30%

- Patients receiving supplement 30
- No supplement 30 (control)
Another Way to Look at Patients!

Patients receiving supplement 30
(Patients with HOPE)

No supplement 30 (Control)
(Patient without HOPE; waiting for DEATH)

Influence of ‘HOPE’
### Effect of ONCOXIN® on Patient Survival

<table>
<thead>
<tr>
<th>Survival after study commencement</th>
<th>HCC patients receiving ONCOXIN®</th>
<th>HCC patients receiving no ONCOXIN®</th>
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<tbody>
<tr>
<td>2 months</td>
<td>15/30 (50%)</td>
<td>3/30 (12%)</td>
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<tr>
<td>&gt;6 months</td>
<td>4/30 (13.3%)</td>
<td>0/30 (0%)</td>
</tr>
</tbody>
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**Quality of life**
- KPSI increased in patients receiving ONCOXIN®
- Decreased KPSI control patients

*Leung et al. American J Gastroenterol 2005*
*Cabibbo et al. World J Hepatol 2013*

**Median survival in HCC 3 months**
Survival 0.7-1.8 month in end-stage HCC
Mr. DH
- Male, 65 yrs., Retd.
- HCV
- PST: 3, BCLC: C
- AFP: 15
- KPSI: 40%
- Diffuse HCC

At Base line

Mr. DH
- AFP: 7
- KPSI: 60%
- Diffuse HCC

At 1 year

A Happy Patient!!
5. Mahtab MA, Akbar SMF, Rahman S. Role of dietary supplement and sorafineb in the management of end-stage HCC patients. EASL HCC Summit 2014, Abstract vol, 199

- Selected as ‘top 10 best paper’ at 4th Asia-Pacific Primary Liver Cancer Expert (APPLE) Meeting, Busan, 2013
- Oral presentation at 7th Annual Conference of SAARC Federation of Oncology, Dhaka, 2012
- Oral presentation at 8th Annual Conference of SAARC Federation of Oncology, Katmandu, 2013
Increased survival of patients with end-stage hepatocellular carcinoma due to intake of ONCOXIN®, a dietary supplement

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Conclusions

- ONCOXIN®, a dietary supplement, seems to be an effective management strategy for end-stage HCC
- This study has inspired optimism about multi-centre clinical trial
- In addition ONCOXIN® with surafenib may exhibit better and added management strategy for end-stage HCC
- Finally, ONCOXIN® may be a drug of choice for advanced HCC in resource-constrained countries of Asia-Pacific region
Not the Bangladesh We Dream of!

This is a much greater menace than HBV or HCC that threatens our stability!!
What’s happening in Bangladesh?

Self-assured commentators who saw Bangladesh as a “basket case” not many years ago could not have expected that the country would jump out of the basket and start sprinting ahead even as expressions of sympathy and pity were pouring in. This informative Lancet Series on Bangladesh helps to explain what nature of the struggle for independence of Bangladesh, particularly in focusing on the contrast with West Pakistan, that made it possible to make an effective political translation towards empowering women.

The causation of this move towards gender equity cannot but remain somewhat speculative, but its

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I declare that I have no conflicts of interest.