Effects of Silymarin on Nonalcoholic Fatty Liver Disease patients, A Pilot Study

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SRI LANKA CLINICAL TRIALS REGISTRY

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19th June 2017

Dr. Md. Ayub Al Mamun
Associate Professor
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Dear Dr. Mamun,

Sri Lanka Clinical Trials Registry – Trial Registration Confirmation Letter

Scientific Title: Efficacy of Silymarin (Milk Thistle fruit extract) compared to placebo in improving liver fibrosis in patients with non-alcoholic fatty liver disease, a Pilot Study

Application no: APPL/ 2017/022

Thank you for submitting your clinical trial to the Sri Lanka Clinical Trials Registry. I am pleased to inform you that your trial has been registered. The registration details are as follows:

Registration No: SLCTR/ 2017/016

Date of Registration: 19th June 2017

The SLCTR is a Primary Registry linked to the WHO International Clinical Trials Registry Platform (WHO - ICTRP). The SLCTR registered trials can be accessed via the WHO - ICTRP website.

Please note the following, which are requirements of the WHO.

1. Maintenance of trial records: Please note that you are requested to
    a. Notify the SLCTR of the actual date of commencement of the trial
    b. Send updates of trial progress at 6 months following registration, and yearly thereafter until the trial is completed
    c. Notify the SLCTR of any changes to protocol
    d. Send details of publications (if any) which will be linked / uploaded in the SLCTR website
2. Deletion of the trial from the registry: once registered, no clinical trial may be deleted from the SLCTR.

We wish you well in your research efforts.

Yours sincerely

Prof. Colvin Goonaratna
Chairperson
Sri Lanka Clinical Trials Registry Committee

Introduction

- Nonalcoholic fatty liver disease **(NAFLD)** is the 3rd most common liver disease in world.

- In Bangladesh, the prevalence of NAFLD ranges from 4% to 18.4% in general population.

- **Silymarin,** the active extract of milk thistle an antioxidant was used from classical Greece to treat liver diseases to protect the liver against toxins.


Silybin®
Silymarin 140 mg
Hepatoprotective
Silybin®
Silymarin 140 mg

Study Objective

In this study we had assessed the improvement of hepatic fibrosis after taking different doses of Silymarin by **Fibroscan Score**.

Patient Selection

Inclusion criteria

1. Ultrasonography of hepatobilliary system suggests Fatty Liver

Exclusion criteria

1. Co-infection with HBV or HCV

Methods

- N =50 in each group (total=200 in 4 groups)

- All patients got appropriate diet and lifestyle modification and appropriate treatment for co-morbid diseases.

- Along with this Group 1 was given Placebo and Group 2, 3 and 4 were given Cap Silymarin 280mg, 420mg and 560mg daily for 6 months respectively

- Primary end point: After 6 month of treatment
- Secondary end point: Patient safety

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Month	0	6
Group 1 (N = 50)	**Placebo**	
Group 2 (N = 50)	**Cap Silymarin 280mg**	
Group 3 (N = 50)	**Cap Silymarin 420mg**	
Group 4 (N = 50)	**Cap Silymarin 560mg**	

Drug Dosing

Group 1 : Placebo daily for 6 month

Group 2 : Cap Silymarin 140 mg 2 cap (single dose) daily for 6 month

Group 3 : Cap Silymarin 140 mg 3 cap (single dose) daily for 6 month

Group 4 : Cap Silymarin 140 mg 4 cap (single dose) daily for 6 month

Results

Table 1: Baseline demographics and disease characteristics

Characteristic	Group 1 (N=10)	Group 2 (N=10)	Group 3 (N=10)	Group 4 (N=10)
Male	3 (30%)	4(40%)	6 (60%)	5(50%)
Age, years(range)	22-60	18-58	21-63	19-58
SGPT(range)IU/ml	9-138	11- 119	7-161	16-230
SGOT(range)IU/ml	12-159	10-90	11-100	11-120-
DM	2 (20%)	3 (30%)	3 (30%)	2 (20%)
HTN	1 (10%)	2 (20%)	0 (0%)	1 (10%)
Hypothyroidism	2 (20%)	3 (30%)	2 (20%)	2 (20%)
IHD	0(0%)	0 (0%)	1 (10%)	0 (0%)
Fibroscan, Kappa, (range)	3.1-6.4	3.9-8.1	4.3-11.8	4.8-26.6

Table 2: Fibroscan Score before and after treatment

Group 1		Group 2		Group 3		Group 4	
Before	After	Before	After	Before	After	Before	After
3.3	3.7	5.2	4.8	7.1	4.2	4.9	4.8
5.9	5.6	4.8	3.5	6.6	5.5	6.8	6.1
4.9	4.3	5.9	5.3	8.7	5.4	6.6	4
4.3	4.2	6.8	5.8	10.3	7.6	5.4	4.8
3.8	3.8	5.6	5.4	5.3	4.4	10.4	6.8
5.8	5.3	8.1	4.3	10.8	5.1	26.6	10.2
5.3	5.3	7.1	5.8	11.8	10.7	5.1	4
5.8	3.5	3.9	3.3	4.8	4.1	6.6	4
6.4	5.9	6.1	5.6	5.9	5.2	6.8	7.1
4.1	3.3	6.1	6.3	4.3	3.5	4.8	5.7

Table 3: EFFECTS OF SILYMARIN ON DIFFERENT DOSES

Group No	Before treatment Mean(SD)	After treatment Mean(SD)	P value
Group 1	4.96(1.04)	4.49(0.95)	0.73
Group 2	5.96(1.19)	5.01(1.01)	0.024
Group 3	7.56(2.67)	5.57(1.01)	0.007
Group 4	8.4(6.6)	5.7(1.93)	0.130

Discussion

Nonalcoholic fatty liver disease **(NAFLD)** patients treated with appropriate diet and lifestyle modification and appropriate treatment for co-morbid diseases and Cap Silymarin 420mg daily for 6 months shows best result(p=0.004) on the basis of **Fibroscan Score** improvement.

Conclusion

Newer drugs for the treatment of NAFLD is very frustrating.

On the basis of Fibroscan Score improvement with Silymarin shows promising results.

Definite comment can be made after completion of the study.

Thank you