ORIGINAL ARTICLE

# The role of amlycure in protecting liver from the hepatotoxic effects of anticancer agents and antitubercular therapy-A randomized controlled study. [Initial observations]

**Chintamani, JP Singh, Vinay Singhal, Mohil RS, Bhatnagar D**
Department of surgery Vardhman Mahavir Medical College Safdarjang Hospital New Delhi

**Background:** There are many known and unknown side effects of various agents used in the treatment of cancer and tuberculosis [1]. It is therefore imperative to understand and reduce the incidence of these toxic effects in order to avoid a scenario where the treatment becomes worse than the disease. The hepatotoxic effects of various anticancer agents used in the treatment of breast cancer as neo-adjuvant and adjuvant chemotherapy are well established .A majority of antitubercular agents also have hepatotoxic effects. The damage could vary from minor and reversible changes in the biochemical and physiological parameters to severe and often irreversible damage.

Herbal products like Amlycure DS have been demonstrated to have hepatoprotective action in various studies [2,3,4]. Against this background a study was contemplated to assess the hepatoprotective role of Amlycure-DS in patients of breast cancer receiving neo-adjuvant chemotherapy/adjuvant chemotherapy as one group and patients receiving antitubercular therapy in the other group. The effects were compared with a control group consisting of both breast cancer and tubercular patients who did not receive Amlycure DS along with their therapy.

**AIMS & OBJECTIVES** –

1. To study the incidence of hepato-toxicity in patients of breast cancer receiving CAF (cyclophosphamide, adriamycin, 5-fluouracil) regime along with Amlycure DS.
2. To study the incidence of hepatotoxic effects in patients receiving the antitubercular therapy (ATT) along with Amlycure DS.
3. To compare the toxicity in the two groups with the control group comprising of both tubercular and breast cancer patients on therapy without Amlycure DS.
4. To assess the hepatoprotective role of amlycure is paticnts of Ca breast/ tuberculosis who are receiving chemotherapy / ATT.

**Patients and Methods** – A total of 61 patients were included in the study. (31 patients with tuberculosis of lymph nodes, abdomen etc. and 30 patients with locally advanced breast cancer (LABC).

*Correspondence :*

**Dr. Chintamani**
DII/131 Kidwai Nagar (west)New Delhi- 110023 India.
E mail: chintamani7@rediffmail.com
Telephone:011-26886405

Diagnosis of breast cancer was confirmed by fine needle cytology (FNAC) / Tru-cut biopsy and patients received neo-adjuvant chemotherapy (three cycles of cyclophosphamide, adriamycin, 5-fluorouracil in standard doses i.e. CAF regime) **after the required investigations including the liver function tests.**

All tuberculosis patients were started on ATT for at least a period of six months.

Antitubercular treatment included

Cap. Ritampicin

Tab. INH

Tab. Ethambutol

Tab. Pyrazinamide

In standard doses for 1st 3 months and for next three months pyrazinamide was excluded.

Chemotherapy included – cyclophosphamide, Adriamycin, 5- Flurouracil in standard doses, 3 cycles were given at 3 weekly interval.

**Results**:

These patients (n=61) were divided into three groups

Group I –n= 21 patients (11 TB patients and 10 Ca breast patients). These patients were not given AmlycureDS

Group II – n= 20 TB patients and were given Amlycure for 3 months.

Group III – n=20 Ca breast patients and were given Amlycure for 3 months.

**Divisions of groups was random, every third patient was included in-group I.**

Liver function tests i.e. serum bilirubin, SGOT, SGPT was done before initiating treatment (i.e. ATT / Chemotherapy)

LFT was repeated at the completion of treatment i.e. after 6 months for TB patients and after 3 cycles of chemotherapy in Ca breast patients.

**Statistical Analyses**

Statistical analyses were performed using SPSS-10 statistical software. Statistical test employed was paired 't' test.

## Observation and Results

**Group I** – All patients had shown an increase in individual LFT parameters, after completion of treatment. When pretreatment LFT parameters were compared with post treatment LFT, it was found that mean of each individual LFT parameter was increased after treatment and this increase was found to be statistically significant (P <0.05)

**TABLE – I Group 1 (n=21)**

| | Mean | Std. Deviation | Std. Error Mean | Correlation | Sign. |
|---|---|---|---|---|---|
| Pair 1 PRESB | .848 | .3156 | .0689 | | |
| PSTSB | 1.11 | .585 | .128 | .879 | .000 |
| Pair 2 PRESGOT | 41.71 | 16.038 | 3.500 | | |
| PSTSGOT | 58.38 | 19.418 | 4.237 | .869 | .000 |
| Pair 3 PRESGPT | 39.14 | 11.612 | 2.534 | | |
| PSTSGPT | 55.10 | 14.936 | 3.259 | .555 | .009 |
| Pair 4 PREALK | 108.29 | 88.118 | 19.229 | | |
| PSTALK | 133.29 | 98.357 | 21.463 | .952 | .000 |

PRESB = pretreatment serum bilirubin
PSTSB = post treatment serum bilirubin
PRESGOT = Pre treatment SGOT
PSTSGOT = Post treatment SGOT
PRESGPT = Pre treatment SGPT
PSTSGPT = Post treatment SGPT
PREALK = Pre treatment alkaline phosphatase
PSTALK = Post treatment alkaline phosphatase

**Group 2 and 3**

All patients had shown a decrease in individual LFT parameter after completion of treatment. When pretreatment LFT parameter were compared with post treatment LFT, it was found that mean of each individual LFT parameter was decreased after treatment and this decrease in mean was statistically significant (P <0.05)

One patient from group 2 died during the study and therefore was excluded from analysis.

**TABLE – II Group 2 (n=19)**

| | Mean | Std. Deviation | Std. Error Mean | Correlation | Sign. |
|---|---|---|---|---|---|
| Pair 1 PRESB | 1.153 | .6168 | .1415 | | |
| PSTSB | .97 | .586 | .134 | .949 | .000 |
| Pair 2 PRESGOT | 54.42 | 20.543 | 4.713 | | |
| PSTSGOT | 45.68 | 16.279 | 3.735 | .858 | .000 |
| Pair 3 PRESGPT | 47.89 | 17.916 | 4.110 | | |
| PSTSGPT | 37.89 | 14.110 | 3.237 | .826 | .000 |
| Pair 4 PREALK | 139.21 | 124.065 | 28.462 | | |
| PSTALK | 96.68 | 94.242 | 21.621 | .905 | .000 |

**TABLE – III Group 3 (n=20)**

| | Mean | Std. Deviation | Std. Error Mean | Correlation | Sign. |
|---|---|---|---|---|---|
| Pair 1 PRESB | .925 | .3740 | .0836 | | |
| PSTSB | .70 | .152 | .034 | .176 | .459 |
| Pair 2 PRESGOT | 61.50 | 23.654 | 5.289 | | |
| PSTSGOT | 42.85 | 10.530 | 2.354 | .726 | .000 |
| Pair 3 PRESGPT | 61.10 | 25.674 | 5.741 | | |
| PSTSGPT | 41.30 | 11.411 | 2.552 | .453 | .045 |
| Pair 4 PREALK | 135.45 | 70.657 | 15.799 | | |
| PSTALK | 93.70 | 36.930 | 8.258 | .689 | .001 |

## Discussion

Hepatotoxicity is a known adverse effect of certain anticancer and antitubercular drugs although the change may not be clinically evident and be appreciated only after biochemical assessment of liver function tests [1].

In a published study involving [2,3] a group of patients on antitubercular treatment comprising of Rifampicin, isoniazid, pyrizinamide and ethambutol, Amlycure double strength (amlycure DS) was found to show notable improvement in appetite and none of the patients developed jaundice during the trial period of four months. The SGOT and SGPT levels were also observed to be within normal limits in the treated group. The group receiving ATT without Amlycure DS developed jaundice in 8%(n=50) of patients and the SGOT/ SGPT values were also on the higher side. Most of these patients were relieved of anorexia/nausea/malaise and liver tenderness at the end of third week in the trial group. No significant side effects were observed during the trial [2]. In the present study also the findings were similar and all patients showed a marked improvement in the feeling of well being.

In another study hepatic fatty changes were found to be absent in the subjects treated with alcohol and Bhuiamla (P.niruri), there was a complete reversal of abnormal liver function tests [3]

Amlycure or its constituents have been demonstrated to be effective in checking the antitubercular toxicity in another [4]. The drug was found to protect against thiacetamide induced toxicity, reverse resultant elevated levels of GOT, GPT and alkaline phosphatase in serum and reduced the activity of succinate dehydrogenase and ribonuclease and glucose 6 phosphatase. It was also found to increase the DNA contents due to protective effects of Picroliv [4]

The drug has also been reported to have anticholestatic effects and has also been reported to act as a cardio and hepatoprotective agent. It has been found to lower LDL/ Phospholipid ratio [5,6]

The proposed mechanism of AMD, with respect to regenerative and anti-degenerative effects on hepatocytes.

1. Prevents drug induced liver cell damage
2. Exerts safe anti-inflammatory action
3. Exerts anticholestatic effects.
4. Improves phagocytosis by the liver Kupffer cells.
5. Normalizes LFT.

In view of the multiplicity and complexity of liver proteins, it is obvious that no single test can establish the disturbances of liver fuctions, thus a number of parameters are employed for accurate diagnosis to assess the severity of damage to judge and evaluate the therapy. AmlycureDS or AMD (and its constituents) significantly reduce the serum bilirubin; check the central necrosis of the hepatocytes due to membrane stabilizing effects [6]. AMD has also been found to significantly reduce the enzymatic leakage of the SGPT, alkaline

phosphatase, inhibiting the glutathione depletion by exerting the antioxidant effects of glucosidic contents [6].

Important constituents of AMD include

- Bhuiamla(Phyllanthus niruri)
- Ravend chini (Rheum sps)
- Haritaki(Glyrrhiza glabra) etc.

**Conclusions**:

The initial observations of this ongoing study conducted at a tertiary care center reinforce the already established hepatoprotective role of amlycure DS,

The well-known hepatotoxic effects of antitubercular drugs and anticancer agents were significantly lower in patients receiving amlycure DS as compared to their counterparts that did not receive AMD.

There were additional beneficial effects in the form a generalized well being (euphoria), improvement in appetite and weight, which may be difficult to quantify.

There were no deleterious side effects observed in any patient with amlycure DS

Amlycure DS may be safely recommended along with any potentially hepatotoxic therapy.

***Although the study is small and in its early stages the observations suggest that patients who were receiving ATT / chemotherapy for cancer, co administration of amlycure DS was hepatoprotective.***

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