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Place of Liv.52 as an Adjuvant to Chemotherapy of Malignant Diseases

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The past few years have witnessed a steady progress in the number of chemotherapeutic agents available for the treatment of malignant diseases. Some of these have been observed to be very efficacious in affording appreciable periods of remission or palliation. Unfortunately, the chemotherapeutic agents have many side effects, particularly bone marrow depression. This is one of the greatest limiting factors to the administration of a desired dosage over an optimum period. These side effects could to a certain extent be minimised by supportive measures such as periodic blood transfusion, administration of vitamins, iron, anabolic steroids, liver extracts and other haematinics.

The purpose of this study was to assess the usefulness of Liv.52 as an adjuvant to chemotherapeutic agents in minimising the haemopoietic depression; thus permitting a higher effective dose level of chemotherapeutic drugs.

MATERIAL AND METHODS

The study was undertaken in 3 stages. Initially a group of 26 patients of various types of malignancies was taken up. They were invariably in stages where surgery and/or radiotherapy was not feasible. All the cases selected were beyond the scope of useful radiotherapy. Since the purpose of this study was mainly to assess the value of Liv.52 as an adjuvant to chemotherapy, all the 26 cases were put on a chemotherapeutic regime. Of the 26 cases 21 were administered oral Liv.52 tablets 6 tablets per day (2 t.i.d.). Five patients were not administered Liv.52 and served as a control and those patients were, however, administered routine multivitamins and iron tablets.

The patients were assessed before, during and after treatment for sense of well-being, state of appetite, haemogram values, weight gain and state of bone marrow. On perusing the results it was observed that the beneficial or adjuvant effects of Liv.52 administration were not very significant.

It was presumed that if the dosage of Liv.52 was raised the fall in the haemogram values and other parameters of assessment may be reduced giving good haemopoietic tolerance of higher doses of chemotherapeutic agents.

In the second series 13 cases of different malignant diseases were taken up for chemotherapy. Nine cases were administered, as a supplement, Liv.52 tablets at a dosage of 9 tablets per day (3 t.i.d.). Liv.52 was withheld in 4 cases who received multivitamin and iron tablets with specific chemotherapeutic agents. The chemotherapeutic agents were parenteral mitomycin at 4 mg on alternate days in 9 cases; 4 mg biweekly in one case; 10 mg biweekly in 2 cases and cyclophosphomide 200 mg on alternate days in one. The total dosage of mitomycin achieved was over 100 mg in 5 cases; about 80 mg in 5 cases; 40 mg in one case; 30 mg in one case and the other patient discontinued cyclophosphomide therapy after 2200 mg.

Table 1

Remarks		Satis-factory	Discontinued	Poor	Satis-factory	Satis-factory	Poor	Satis-factory
Marrow	AT	Hypo	–	Acellular	Hypo	Hypo	Accellular	Hypo
	BT	Hypo	Hypo	Hypo	Hypo	Hypo	Hypo	Hypo
Platelet count	AT	104000	156000	135000	110000	118000	164000	162000
	BT	114000	159000	114000	140000	150000	167000	185000
Hb%	AT	60%	64%	40%	62%	57%	64%	65%
	BT	75%	60%	50%	70%	62%	70%	80%
RBC	AT	3.18	3.14	2.68	3.17	3.5	3.25	3.62
	BT	3.95	3.17	3.00	3.65	3.45	3.5	3.72
WBC	AT	5400	6200	2800	4000	3500	5800	5600
	BT	5000	5800	7100	6400	6400	11600	5800
General condition	AT	+	+	+	+	+	Poor	++
	BT	+	+	+	+	+	+	+
Weight	AT	37	44	37	54	52	48	52
	BT	43	46	37	55	52	50	52
Total dosage		70 mg	22000 mg	80 mg	100 mg	100 mg	30 mg	40 mg
Dosage		4 mg bi-weekly	20 mg alt. Days	4 mg alt. Days	4 mg alt. Days	4 mg alt. Days	10 mg bi-weekly	10 mg bi-weekly
Chemo-therapy		MMC with Liv.52	EXN with Liv.52	MMC with Liv.52	MMC with Liv.52	MMC with Liv.52	MMC	MMC with Liv.52
Disease		Tongue	Alveolus	Ca. Cervix	Ca. Larynx	Ca. Vallecule	Melanoma	Naso-pharynx
Sex/Age		M/55	F/39	F/50	M/43	M/42	F/63	M/30
Sl. No.		1.	2.	3.	4.	5.	6.	7.

Table 1 (Contd...)

Remarks		Satis-factory	Satis-factory	Satis-factory	Poor	Poor	Poor
Marrow	AT	Hypo	Hypo	Hypo	Hypo	Hypo	Acellular
	BT	Hypo	Hypo	Hypo	Hypo	Normal	Hypo
Platelet count	AT	148000	157000	152000	128000	600000	156000
	BT	164000	158000	168000	132000	174000	180000
Hb%	AT	68%	62%	65%	30%	40%	55%
	BT	70%	45%	55%	35%	70%	75%
RBC	AT	3.50	3.18	3.18	2.82	3.00	2.98
	BT	3.58	3.00	3.80	3.82	3.45	3.65
WBC	AT	7000	4000	4400	3800	6000	4200
	BT	6800	8200	5200	9400	7800	8000
General condition	AT	++	+	+	Poor	Poor	+
	BT	+	Poor	+	+	+	+
Weight	AT	48	48½	60	45	45	60
	BT	48	50	63	49	51	63
Total dosage		80 mg	80 mg	100 mg	76 mg	100 mg	100 mg
Dosage		4 mg. alt. Days	4 mg. alt. Days	4 mg. alt. Days	4 mg. alt. Days	4 mg. alt. Days	4 mg. alt. Days
Chemo-therapy		MMC with Liv.52	MMC with Liv.52	MMC with Liv.52	MMC with Liv.52	MMC with Liv.52	MMC with Liv.52
Disease		Semino-manx	Ca. Stomach	Ca. Breast	Ca. Cervix	Ca. Lungs	Ca. Cervix
Sex/Age		M/25	M/50	F/55	F/35	M/47	F/38
Sl. No.		8.	9.	10.	11.	12.	13.

Table 2

Remarks		Satis-factory	Poor	Satis-factory	Fair	Satis-factory	Poor	Satis-factory	Satis-factory	Satis-factory	Fair
Marrow	AT	Hypo	Acellular	Normal	Hypo	Normal	Hypo	Normal	Hypo	Hypo	Hypo
	BT	Hypo	Hypo	Normal	Hypo	Normal	Hypo	Hypo	Hypo	Hypo	Hypo
118000	AT	164000	152000	144000	114000	114000	156000	120000	175000	152000	112000
	BT	168000	167000	150000	124000	167000	165000	185000	168000	132000	124000
Hb%	AT	82%	54%	57%	60%	67%	58%	65%	60%	38%	40%
	BT	87%	60%	58%	80%	70%	70%	80%	65%	45%	45%
RBC	AT	3.20	2.90	3.05	3.16	3.32	2.90	3.52	3.20	2.82	3.00
	BT	3.48	3.38	3.12	4.20	3.35	3.50	3.70	3.80	3.82	3.40
WBC	AT	7200	4500	5800	7000	5800	7200	5600	4800	3800	7200
	BT	8600	7200	5200	10000	7000	11000	5800	5200	9400	8200
General condition	AT	++	+	++	+	++	+	++	++	Poor	+
	BT	++	++	+	+	+	+	+	+	++	+
Weight	AT	52	36	43	40	42	46	50	60	44	48
	BT	55	39	40	41	41	50	52	64	49	50
Total dosage		60 mg	60 mg	100 mg	10 g	100 mg	60 g	100 mg	100 mg	100 mg	100 mg
Dosage		4 mg. alt. Days	4 mg. alt. Days	10 mg bi-weekly	1 g bi-weekly	10 mg bi-weekly	10 mg bi-weekly	10 mg bi-weekly	10 mg bi-weekly	10 mg bi-weekly	10 mg bi-weekly
Chemo-therapy		MMC with Liv.52	MMC	MMC with Liv.52	EXN	MMC with Liv.52	MMC	MMC with Liv.52	MMC with Liv.52	MMC	MMC with Liv.52
Disease		Ca. larynx	Ca.oesophagus	Ca. Oesophagus	Ca. Tongue	Ca. Tongue	Ca. Cervix	Ca. Tonsil	Ca. Cervix	Ca. Breast.	Ca. Stomach
Sex/Age		M/50	M/50	M/48	M/45	M/38	M/50	M/30	M/35	M/50	M/50
Sl. No.		1.	2.	3.	4.	5.	6.	7.	8.	9.	10.

The patients were assessed again as in the first series. In addition sternal marrow smears were studied before and after treatment (vide Table 1). On analysing the results it was observed that there was a rapid deterioration in general condition of the patients and a rapid fall of haemogram values in the control group. The patients on Liv.52 showed an appreciable improvement in general condition, insignificant fall in the haemogram values, improved appetite and no deterioration in the sternal marrow smears. The patients were also observed to tolerate a higher dosage of the chemotherapeutic agent. It was also evident that increase of the dosage of Liv.52 to 3 tablets t.i.d. had a remarkable advantage, at the same time no untoward effects of Liv.52 due to increase in its dosage, were noticed.

In the third series a higher dosage of chemotherapy was aimed at with Liv.52 as an adjuvant. Of a series of 10 patients 6 were administered a total dose of 100 mg and 3 were given 60 mg of mitomycin. One case was given ten grams of cyclophosphomide. Five of the cases with a total dosage of 100 mg and one with 60 mg were administered Liv.52 tablets at 3 tablets t.i.d. In 4 patients, 2 were taken to a total dosage of 100 mg, one to a total dosage of 60 mg of mitomycin and one on cyclophosphomide upto 10 mg. Liv.52 was not administered. These served as controls.

Assessment of this series of patients, revealed that the patients on Liv.52 tablets tolerated the high dosage schedule very well (vide Table 2) whereas the patients who did not receive Liv.52 could not withstand the high dosage schedule.

CONCLUSION

The beneficial effect of Liv.52, an indigenous drug, in many diseases particularly those affecting the liver has been well documented. Its possible anabolic effects on cancer patients on radiotherapy have been reported. This study brings forward its beneficial effects as an adjuvant to chemetherapy of malignancy. The parameters such as haemogram, appetite and general condition of the patient are satisfactory yardsticks of the assessment of a patient's progress. These are influenced a great deal by the disease process itself and significantly also by the chemotherapeutic agents. The effect of the latter can be corrected to a certain extent by substitution therapy such as iron and vitamins. Some principles in Liv.52 appear to have either an adjuvant effect on the chemotherapeutic agent or stimulus to bone marrow. Studies on bone marrow *per se* however, were not contributory. The spectrum or sternal marrow smear depends on so many factors that the patterns were unpredictable.

It may be concluded that apart from the so many beneficial effects of Liv.52 described earlier, its usefulness in the general management of cancer patients on a chemotherapeutic regime is worth pursuing. Meanwhile efforts may be made to isolate the various active principles of Liv.52.