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Effect of tamoxifen on lipid metabolizing enzymes in women with breast cancer

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Tamoxifen, a synthetic antioestrogen, is widely used in the treatment of breast cancer. This study was designed to understand the modulation of plasma lipids and lipid metabolising enzymes in untreated subjects and 6 months tamoxifen treated subjects.

One hundred and thirty five (104 postmenopausal, 31 premenopausal) consecutively-treated healthy women with resectable breast cancer were recruited from the Government General Hospital (Chennai, India) through their physicians according to a process approved by the hospital ethical review board. Blood samples were drawn from all patients before commencing tamoxifen therapy, and after 3 and 6 months of tamoxifen therapy (20 mg twice a day). Plasma cholesterol [Total cholesterol (TC), ester cholesterol (EC), free cholesterol (FC)] and triglycerides (TG) were estimated by the method of Parekh & Jung (1970); Leffler & McDougald (1963) and Rice (1970) respectively. Whereas, the activities of total lipase (TL), lecithin : cholesterol acyltransferase (LCAT) and lipoprotein lipase (LPL) were assayed by the respective method of Bier (1955); Hitz *et al.*, (1983) and Schmidt (1974). The results are shown for the six-months in Table 1.

After tamoxifen treatment the levels of TC and FC were significantly decreased *($P < 0.001$)*; similar decreases were noted in TL and LPL activity whereas the levels of EC, TG and LCAT were significantly increased in postmenopausal women receiving tamoxifen.

On tamoxifen administration plasma TG level is inversely proportional to the LPL activity which may be due to competitive inhibition of HDL (Bani *et al* 1986). The lipid lowering potential of tamoxifen is significant in postmenopausal than premenopausal women. Tamoxifen-treated patients showed a marked elevated plasma LCAT activity compared with untreated breast cancer patients. The corresponding increase in the level of EC with concomitant decrease in FC was also observed in these patients. These changes were thought to be due to an oestrogenic effect of tamoxifen in the liver-stimulation of apo A-I, an activator of the enzyme LCAT (Love *et al* 1991). The increased EC and LCAT activity and decreased FC in plasma indirectly control the rapid multiplication of the already proliferating cells, suggesting that tamoxifen may retard cell proliferation through the above mechanism.

Table 1. Analysis of plasma lipids in women receiving therapeutic doses of tamoxifen (20 mg, twice daily) for 6 months

Parameter	Premenopausal		Postmenopausal	
	Control (n=31)	Treated (n=27)	Control (n=104)	Treated (n=82)
TC (mg/dl)	203.09 ± 17.44	193.09 ± 16.97#	228.73 ± 13.11	189.71 ± 14.74*
FC (mg/dl)	74.63 ± 6.84	56.85 ± 4.72*	100.86 ± 8.51	56.50 ± 4.79*
EC (mg/dl)	131.46 ± 8.43	136.24 ± 8.71#	127.87 ± 8.42	133.21 ± 10.53*
TG (mg/dl)	171.58 ± 10.34	178.91 ± 11.67*	184.32 ± 13.51	203.07 ± 16.35*
TL (nM-p-nitrophenol /ml plasma/hr)	6.29 ± 0.83	5.83 ± 0.54	7.13 ± 0.74	4.93 ± 0.47*
LCAT (nM cholesterol/ml plasma/hr)	48.36 ± 4.30	52.39 ± 5.84#	45.86 ± 5.07	55.41 ± 4.79*
LPL (μM Free fatty acids/ml plasma/hr)	4.68 ± 0.51	4.26 ± 0.49#	4.27 ± 0.52	3.71 ± 0.31*

* Significant from pretreatment level at $P < 0.001$
\# Significant from pretreatment level at $P < 0.01$

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