

Could garlic be an useful adjuvant therapy in adriamycin heart failure?

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Abstract

50 year old suffering from breast carcinoma, treated with adriamycin developed heart failure with 22.82% ejection fraction. Added garlic pearl to routine anti-failure measures for 9 months to achieve 51.6% ejection fraction.

Key word: Garlic pearl, antioxidants, ductal carcinoma of breast, adriamycin, cardiomyopathy.

Doxorubicin (DOX) is a highly effective antineoplastic antibiotic associated with a dose dependent acute or chronic cardiotoxicity in the form of transient or persistent arrhythmia, myocarditis, pericarditis, left ventricular or congestive heart failure. Recently, cellular evidence implicating cardiac mitochondria as key intracellular targets, both as sites of generation of highly reactive free radical intermediates as well as targets for the interference with cell calcium regulation and bioenergetic failure that are hallmarks of doxorubicin-induced cardiac failure¹.

Case Report

A 50 year old was suffering from invasive ductal carcinoma of left breast, undergone modified radical

mastectomy[25.09.2001] and received 6 cycles of 5-fluorouracil [600mg/m²] adriamycin [60mg/m²], cyclophosphamide [600mg/m²] and tamoxifen [10mg]. She presented with breathlessness, dry cough and palpitation on 27.05.2002. Chest skiagram showed cardiomegaly (Fig 1) confirmed by echocardiogram (Fig 2) with ejection fraction 22.82%. She was treated with routine digoxin, frusemide, carvedilol and losartan. Empirically, garlic pearl (Solus Pharma), containing garlic oil 0.25%w/w as herbal preparation was given twice a day along with salt restriction and low intensity exercises for 9 months. Repeat echocardiogram (Fig 3) revealed 51.63% ejection fraction. Patient was free from all previous symptoms and signs.

Fig 1: Cardiomegaly



Fig 2: Before therapy

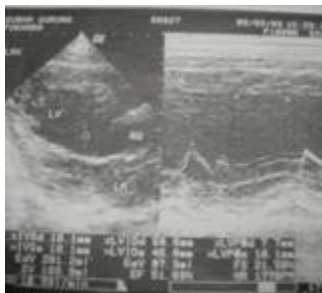


Fig 3: After therapy



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Table1: Echocardiographic evidence of improvement of Garlic therapy

Echo dimension	Before therapy[04.06.02]	After therapy[09.03.03]
EDv[ml]	161.0	201.2
ESv [ml]	124.3	97.3
EF[%]	22.82	51.63

Discussion

Adriamycin, an anthracycline antibiotic, is widely used in the treatment of a variety of human malignancies, including breast cancer, small cell lung cancer and acute leukaemia. Like other anticancer drugs, adriamycin also causes various toxic side effects. The commonest of which is dose dependent cardiotoxicity leading to acute or chronic heart failure. Myocardial damaged caused by adriamycin is mediated by formation of an iron-anthracycline complex that generates free radicals, which, in turn, damage plasma membrane and interferes with cytoskeleton structure.

Oxidative stress is major etiopathological factor in adriamycin induced cardiotoxicity. Adriamycin converted into its toxic, short-lived metabolite semiquinone in cardiomyocyte by myocardial CYP450 and flavin monooxygenases, which interacts with molecular oxygen and initiates a cascade of reaction, producing reactive oxygen species. The latter reacts with hydrogen peroxide to produce hydroxyl (OH•) radical. Reactive oxygen species react with lipids, protein and other cellular constituents to cause damage to mitochondria and cell membranes of cardiomyocytes². Relatively low amounts of endogenous antioxidant make myocardium vulnerable to oxidative stress injury. Chronic dose dependent oral administration of garlic [*S*-allylcysteine] has been reported to enhance endogenous antioxidants in myocardium which might have important direct cytoprotective effects, especially in event of oxidative stress injury. Experimentally, quinolinic acid induced oxidant injury on rat neuromuscular system revealed cytoprotective effects of garlic compound as follows:(a) scavenge free radicals; (b) decrease oxidative stress; and (c) preserve the myocardial activity of Cu, Zn-superoxide dismutase (Cu, Zn-SOD)³.

Considerable efforts have been made on using antioxidants and iron-chelators to protect heart against adriamycin toxicity. Initial attempts to use traditional antioxidants, like *N*-acetylcysteine and tocopherol in prevention of adriamycin cardiotoxicity, were not successful.

Dexrazoxane, the only drug presently approved by FDA to prevent adriamycin cardiotoxicity is an iron chelator and possesses potent antioxidant properties. But, due to high incidence of myelosuppression, its use has only been limited to advanced stages of malignant disorders⁴.

A lipid lowering agent probucol [250mg/m²] augments endogenous antioxidants, has been shown to offer protection against adriamycin cardiotoxicity. But probucol is not available in Nepal and is very expensive to import from abroad. Garlic, well known for its medicinal use since Vedic times, has been reported to have antioxidant properties. Recently, it has been shown that chronic intake of garlic enhanced super oxide dismutase and catalase in rat heart and shown protection against adriamycin cardiotoxicity⁵. Most recently, co-administration of a dihydrolipoamide compound, H-2545, having a 3-carboxamido-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrole moiety, was reported to exhibit antioxidant properties which accumulate in cell membranes, scavenging free radicals at site of formation, attenuates doxorubicin cardiotoxicity without interfering with its anticancer effects⁶.

Conclusion

We observed that antioxidant in the form of garlic capsule containing garlic oil 0.25%w/w as herbal preparation given empirically twice a day, along with other standard medicines for treatment of reversed adriamycin cardiotoxicity as evidenced clinically by symptom free state and echocardiographically by increase in left ventricular ejection fraction from 22.82% to 51.63% in 9 months. It might be interesting to explore the hidden benefits of Garlic in cardiac patients. Further large scale studies are required to establish the use of Garlic and look into the side effects or drug interactions if any.

References

- Wallace KB. Doxorubicin-induced cardiac mitochondrionopathy. *Pharmacol Toxicol.* 2003 Sep; 93(3):105-15.
- Sugioka K, Nakano M: Mechanism of Phospholipid peroxidation induced by ferric ion-ADP-adriamycin coordination complex. *Biochem Biophys Acta* 1982, 713(2):333-343.

3. Perez-Severiano F, Rodriguez-Perez M, Pedraza-Chaverri J, Maldonado PD, Medina-Campos ON, Ortiz-Plata A, Sanchez-Garcia A, Villeda-Hernandez J, Galvan-Arzate S, Aguilera P, Santamaria A. S-Allylcysteine, a garlic-derived antioxidant, ameliorates quinolinic acid-induced neurotoxicity and oxidative damage in rats. *Neurochem Int.* 2004 Dec; 45(8):1175-83.
4. Seifert CF, Nesser ME, Thompson DF: Dexrazoxane in the prevention of doxorubicin induced cardiotoxicity. *Ann Pharmacother* 1994, 28(9); 1063-1072.
5. Mukherjee S, Banerjee SK, Maulik M, Dinda AK, Talwar KK, Maulik SK. Protection against acute adriamycin-induced cardiotoxicity by garlic: role of endogenous antioxidants and inhibition of TNF-alpha expression. *BMC Pharmacol.* 2003 Dec 20; 3:16.
6. Deres P, Halmosi R, Toth A, Kovacs K, Palfi A, Habon T, Czopf L, Kalai T, Hideg K, Sumegi B, Toth K. Prevention of doxorubicin-induced acute cardiotoxicity by an experimental antioxidant compound. *J Cardiovasc Pharmacol.* 2005 Jan; 45(1):36-43.