Continuous infusion of doxorubicin has been a strategy to reduce cardiotoxicity. Epirubicin is another anthracycline in common clinical use. However, evidence is lacking regarding whether this strategy can reduce cardiotoxicity of epirubicin without compromising antineoplastic efficacy" Yang et al (2017).

Abstract:

BACKGROUND: Continuous infusion of doxorubicin has been a strategy to reduce cardiotoxicity. Epirubicin is another anthracycline in common clinical use. However, evidence is lacking regarding whether this strategy can reduce cardiotoxicity of epirubicin without compromising antineoplastic efficacy.

DESIGN AND METHODS: Healthy rats were randomized into groups: epirubicin (8 mg/kg) delivered intraperitoneally via micro osmotic pumps (MOP), epirubicin (8 mg/kg) by intraperitoneal (IP) bolus injection, and placebo control. Blood samples were collected for analyzing biomarkers of myocardial injury and pharmacokinetics. At chosen times, sub-groups of animals were sacrificed for histopathology. A mouse breast cancer cell line (4T1), stably transfected with luciferase, was orthotopically allografted in female mice, and treated in three groups as described above for the rats. Tumor growth was monitored by measuring tumor size as well as bioluminescence.

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RESULTS: Delivery by IP bolus and by MOP achieved essentially the same area under the curve of epirubicin plasma concentration time profile. Blood biomarkers showed that the degree of myocardial injury in MOP group was lower than that of IP group. Histopathology showed that there was less eosinophilic enhancement, interstitial hemorrhage and necrotizing muscle atrophy in MOP group than IP group. In the orthotopic breast cancer allograft mouse model, the antineoplastic effect of epirubicin by MOP was not different from that by IP as measured by tumor weights or by in vivo bioluminescence.

CONCLUSION: Slow delivery of epirubicin by MOP reduced cardiotoxicity without compromising the antineoplastic effect compared to IP bolus delivery. These in vivo data support our previous clinical data that continuous intravenous infusion of epirubicin using micro infusion pumps over 48-96 hours had less cardiotoxicity than intravenous bolus injections. However, whether multiple doses of epirubicin given by MOP result in a lower magnitude of long term cardiomyopathy remains to be further investigated.

Reference:

Yang, F., Lei, Q., Li, L., He, J.C., Zeng, J., Luo, C., Yeung, S.J. and Yang, R. (2017) Delivery of epirubicin via slow infusion as a strategy to mitigate chemotherapy-induced cardiotoxicity. PLoS One. 12(11), p.e0188025. eCollection 2017.

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