Abstract

Background: Survival rates over the years have remarkably improved in cancer patients. However, the incidence of chemotherapy associated toxicities impairs the quality of life (QOL). Post chemotherapy associated cognitive decline (chemobrain) is one such major complication whose prevalence is high in breast cancer survivors. Till now, no satisfactory animal model is available to screen this condition. Further, no interventions are found to be effective. Naringin (NAR), Rutin (RUT) possess neuroprotective and nootropic potential. Hence, we designed study to develop animal model with Doxorubicin (DOX) to induce chemobrain and to assess NAR and RUT against chemobrain.

Objectives: To develop suitable animal model for DOX-induced chemobrain by assessing the gender difference and suitability of female rats for studying chemobrain especially episodic and spatial memories. To assess flavonoids, NAR and RUT against DOX-induced chemobrain in developed models of chemobrain

Materials and methods: Preliminary studies evaluated effect of various inter trial intervals (ITI) on episodic memory in either sex and compared with donepezil (1 mg/kg, i.p.) following the optimization of ITI to assess gender difference. DOX was given to female rats at 2.5 mg/kg, i.p. once in five days for 10 cycles and cognitive functions were assessed by object recognition task (ORT) and Morris water maze (MWM). Biochemical and histological analyses were carried out. In-vitro neuroprotection studies were conducted.

Results: Female rats formed episodic memory with 2 h ITI whereas in case of males, it was upto 6 h. NAR and RUT showed procognitive effects for episodic memory. DOX induced cognitive deficits in female rats for episodic memory but not spatial in normal rats and flavonoids reversed deficits. In mammary cancer animals, both episodic and spatial memory were deteriorated and RUT but not NAR reversed episodic and spatial memory deficits at 50 mg/kg, p.o. Also haematological, biochemical and histological abnormalities due to DOX chemotherapy were averted by treatment with RUT.

Conclusion: RUT protected against DOX-induced chemobrain associated cognitive dysfunction and other organ related toxicities which can be a potential intervention to alleviate chemotherapy-induced cognitive deficits, i.e. chemobrain to improve QOL in cancer survivors.