Age dependent impairment of angiogenesis &its association with alterations in vessel density ,inflammatory respone and growth factor expression

Lamiaa Mohammad Shawky Bakry

Angiogenesis is the creation of new blood vessels from preexistingone that may occurs either physiologically or pathologically.Angiogenesis is facilitated via administration of angiogenic growthfactors, recombinant human vascular endothelial growth factor 165 wasused in this study (rh VEGF165).This work was done to study the effect of aging on angiogenesis inischemic vascular diseases and the effect of administration of rhVEGF165 on angiogenesis in both young and old animal group models.Three groups ofNZW rabbits were studied in this work:Group 1:10NZW rabbits were used as control.Group 2:Operative resection of one femoral artery of one hind limb toproduce ischemia of the medial group muscles was performed in 10NZWrabbits of this group to stimulate the angiogenic cascade.Group 3:Operative resection of one femoral artery of one hind limb toproduce ischemia of the medial group muscles was performed in 10NZWrabbits of this group to stimulate the angiogenic cascade and thenadministration of rh VEGF 165 (500 ug) intra-arterial on tenthpostoperative day.Specific angiography was done at forty days postoperatively whichrevealed that the number of angiogenic blood vessels visible in rabbitsshowed lower number of collaterals in old ischemic group than in youngischemic group.Treatment with rh VEGF165 induced significant increase inangiographic blood vessels in the ischemic medial thigh muscles in bothgroups although it was still higher of angiographic score in young groupthan in old group.The following immunohistochemical and histochemical techniqueswere used to detect the capillary density, T-lymphocytes and sites ofinflammation and phagocytosis in ischemic tissues before and afterTreatment with rh VEGF 165:1-Immunoperoxidase staining CD 31:To detect capillary density (the average number of angiogenicblood vessels I 10 high power field).2- Immunoperoxidase staining CD 3.To detect T-lymphocytes (the average number of T-lymphocytes110 high power field) in the obtained tissue.3- Alkaline phosphatase staining:To detect sites of inflammation and phagocytosis in the ischemictissue.The results obtained can be summarized as follows:Immunocytochemical results:Capillary density: (the average number of angiogenic blood vesselsIhigh power field):Group1: (control group):Showed lower number of blood capillaries.Group 2:(ischemic group):Showed higher number of blood capillaries (angiogenic bloodvessels) than in group 1, and

the capillary density was higher in youngischemic animals than in old animals.Group 3: (treated group):Showed an increase in number of blood capillaries (angiogenicblood vessels) than in group 2 in both young and old animals afterinjection of rh VEGF 165, and the capillary density was higher in youngtreated -animals than in old treated animals.T-lymphocytes: (the average number of T -lymphocytes /10 high powerfield):Group 1: (control group):Showed no T lym~hocyte infiltration in normal tissue.Group 2:(ischemic group):Showed infiltrating T-lymphocytes in ischemic tissues in both oldand young groups, and the number of infiltrating T-lymphocytes washigher in young ischemic animals than in old animals .Group 3: (treated group):Showed increased number of T-lymphocyte infiltration than ingroup 2, in both young and old animals after Treatment with rh VEGF165, and the number of infiltrating T-lymphocytes was higher in youngtreated animals than in old treated animals.Histochemical results:Alkaline phosphatase staining : (demonstrated sites of inflammationand phagocytosis /high power field) .Groupl: (control group):Showed no alkaline phosphatase staining.Group 2:(ischemic group):Showed alkaline phosphatase staining in ischemic tissues in bothold and young groups, and the sites of inflammation and phagocytosiswere higher in young ischemic animals than in old animals.Group 3: (treated group):Showed a decrease in sites of alkaline phosphatase staining than ingroup 2, in both young and old animals, after Treatment with rh VEGF165Conclusion:Angiogenesis responsible for collateral development in limbischemia is impaired with aging. However, advanced age does notprevent augmentation of collateral vessel development in response toexogenous angiogenic cytokines.