Role of Extracellular Superoxide Dismutase in Normal Pregnancy

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Summary

Nitric Oxide (NO) may be involved in the maintenance of both low placental vascular tone and uterine quiescence during pregnancy. Extracellular superoxide dismutase (Ec SOD) has been identified as a major regulator of NO bioavailability within the lung, and its expression within both murine uterus and placenta has been reported. We planned to study the effect of normal pregnancy on EC-SOD levels in 35 normal pregnant and 35 healthy adults in the age group 19-36 years. EC-SOD levels were significantly lower in normal pregnant women as compared to controls ($p<0.001$) suggesting the role of EC-SOD as modulator of NO activity during pregnancy.

Introduction

Recent studies indicate that extracellular superoxide dismutase (EC-SOD) may not be as scarce in some tissues as was initially believed. EC-SOD is the major isoenzyme of SOD in the umbilical cord and is a major source of SOD activity in uterus (Sandstrom, 1994). In addition, EC-SOD is highly expressed in blood vessels. EC-SOD is primarily located in the extracellular matrix of tissues (99% of EC-SOD) with only 1% of EC-SOD found in serum (Sandstrom, 1993). The observation that EC-SOD exists in high concentrations in arteries suggests that it has a particularly important role in blood vessels (Oury, 1996). Also, superoxide will be scavenged leading to a higher balance of nitric oxide, which can then signal smooth muscle relaxation, neurotransmission or other important intracellular signal. EC-SOD is a predominant form of SOD in the uterus, as in arteries and may play an important role in modulating nitric oxide dependent relaxation (sandstorm, 1994 and Conrad, 1993). The present study was therefore planned to study the effect of normal pregnancy on EC-SOD levels.

Methods

Thirty five normal pregnant (primigravida) women (aged 19-36 years) with normal blood pressure, in the third trimester were selected. 35 age matched healthy volunteers served as control. Each subject had blood sampled on one occasion. Serum was separated on centrifugation and assayed within 24 hours. Serum SOD levels were estimated according to method of Misra and Fridovich, (1972) on the basis of ability of SOD to inhibit the autooxidation of epinephrine to adrenochrome at pH 10.5. Statistical significance was assessed by Student't t-test.

Results

There were no significant differences in patient ages between the 2 study groups: healthy volunteer, 26.8 ± 4.2 years; healthy pregnant, 24.1 ± 4.0 years. The EC-SOD levels in normal pregnant group were significantly lower than those levels in healthy nonpregnant group ($p < 0.001$ Table I).

Table I : EC-SOD in various groups (mean ± SD, EU/L)

	Nonpregnant (n=35)	Pregnant (n=35)
EC-SOD	256 + 6.95	184.5 ± 6.12

Discussion

Free radicals, by their unstable and transient nature are difficult to measure directly. Their tendency to cause lipid peroxidation has been used as an indirect measure. Markers of lipid peroxidation have been found to rise during the progression of normal pregnancy, with greater rises seen in association with pregnancy-induced hypertension (Ishihara, 1978). Knowledge of the responses of other antioxidant systems in pregnant and in pregnancy-induced hypertension is limited. Increased serum antioxidant activity has been documented during normal pregnancy (Cranfield, 1979). In this study examination of antioxidant status in pregnancy has been extended. In normal pregnancy women the superoxide dismutase activity was reduced. It could be due to reduced enzyme production, implying reduced intracellular oxidative stress, or enzyme in activation.

EC-SOD is present in human placentae, uterus and at the site of placental implantation. The level of SOD activity (unclassified iso-form) in the placenta ha however, been shown to increase during the progression of pregnancy (Sekibs, 1979). Recent studies indicate that EC-SOD exists in high concentrations in organs that contain large amounts of smooth muscle and considering the well-documented role of nitric oxide in mediating relaxation of smooth muscle (Oury, 1996) particularly in the vasculature, and the high reactivity of nitric oxide with superoxide to produce the toxic peroxy nitrite among it is likely that EC-SOD has a pivotal role in regulating these processes in vessels. Scavenging of extracellular superoxide by EC-SOD is likely to play an important role in mediating these nitric oxide responses (Sandstrom 1993 and Sekibs, 1979). Therefore, EC-SOD may play an important role in modulating nitric oxide dependent relaxation of the uterus and the development of hypertension as a predominant symptoms in preeclampsia indicates that nitric oxide and superoxide may play a role in this disease.

References

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