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Sperm transcript dysregulation: Possible role in recurrent pregnancy loss

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Introduction: With a host of accepted etiologies for recurrent pregnancy loss (RPL), the current focus has been shifted towards analysing the paternal factors as more than just mere vectors for transmission of genetic information. The non-genomic paternal delivery of spermatozoal mRNA transcripts is retained for translation of proteins for early embryonic development.

Aim: The current study was designed with an aim to analyse the dysregulation in sperm transcriptome and correlate with ROS and DFI values.

Material/methods: Semen samples from 75 male partners of couples with RPL and 30 healthy controls with proven fertility were obtained. Semen analysis was assessed by WHO (2010) criteria. Sperm RNA was isolated from the semen samples, reverse transcribed and q-PCR analysis was performed. Reactive oxygen species (ROS) levels were assessed by chemiluminescence and sperm chromatin structure assay (SCSA) was performed by flow cytometry.

Results: The mean DFI of male partners of couples with RPL (36.47) was significantly ($p < .0001$) higher as compared to controls (25.32). The DFI in all the patients was seen to be >30 against fertile controls ($p < .0001$). The mean ROS level was seen to be higher (>25) and calculated as 176.36 RLU/sec/million sperm. The seminal ROS values and DFI will be correlated with dysregulation in sperm transcripts.

Conclusion: The dysregulation in the levels of these hidden messengers can be established as an adjunct to routine semen analysis. Adoption of various lifestyle measures like yoga and meditation can be used for correcting sperm mRNA dysregulation by normalising ROS values.

Conflicts of interest

The authors have none to declare.

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Effects of yoga based lifestyle intervention on genomic instability in major depressive disorder patients: A randomized controlled trial

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Background: Modern lifestyle is responsible for high rates of major depressive disorder (MDD) and associated co-morbidities including suicidality and metabolic syndrome. Genomic instability and consequent cellular aging, associated with psychosocial stress and unhealthy lifestyle is linked to pathogenesis of MDD. This study evaluated effects of yoga based lifestyle modification program (YLMP) on 8OH2dG, reactive oxygen species (ROS), total antioxidant capacity (TAC), telomerase activity, depression symptoms, and lifestyle factors.

Methods: Fifty-six men and women with MDD were randomized to either YLMP group or routine medical therapy (RMT group) for 12 weeks. Primary outcomes were levels of 8OH2dG, ROS, TAC and telomerase activity in peripheral blood, and scores of Beck Depression Inventory II (BDI-II). Secondary outcomes included lifestyle-related factors. Data were analyzed for within-group and between-group changes.

Results: YMLP group showed increase in the measures of telomerase activity ($p = 0.02$) and TAC levels ($p = 0.005$) and decreases in the measures of 8OH2dG and ROS (both $p < 0.001$). Moreover, statistically significant between-group changes were observed between YLMP and RMT (all $p < 0.01$)). There was a significant reduction in BDI-II score in the YLMP group (−15.7 score, $p = 0.0013$) but not in RMT group (−5.2 score, $p = 0.44$); the between-group difference was significant ($p = 0.04$).

Conclusion: In this RCT, yoga based lifestyle modification program group demonstrated balanced oxidative stress with the consequent decrease in both DNA damage and telomere attrition. These findings are suggestive of reductions in genomic instability and reversal of accelerated cellular aging in MDD patients.

Conflicts of interest

The authors have none to declare.

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Influence of 5-HTTLPR genotype on adverse life events, oxidative stress, clinical severity and response to yoga based lifestyle intervention in major depressive disorder patients

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Background: Major depressive disorder (MDD) is associated with short (S) and a long (L) variants of serotonin transporter-linked polymorphic region (5-HTTLPR) in SLC6A4 gene and oxidative stress. The aim of this study was to understand moderation by an interaction between 5-HTTLPR, adverse life events (ALE) and oxidative stress on severity of depression and yoga based lifestyle intervention (YBLI) in MDD.

Methods: From 95 MDD cases, we collected ALE data, HAM-D 17 score, and blood samples to determine 5-HTTLPR genotype and oxidative stress, measured by reactive oxygen species (ROS) and total antioxidant capacity (TAC). 41cases were also analyzed before and after YBLI.

Results: Compared to LL group, SS/SL group individuals showed increased HAM-D score as a function of ALE ($r = .41$, $p = .007$), which correlated positively with ROS levels ($r = .31$, $p = .040$) and negatively with TAC levels ($r = -.351$, $p = .042$), as well as reduced TAC ($r = -.31$, $p = .041$) and increased ROS ($r = .30$, $p = .016$) as a function of ALE. Both SS/SL and LL-groups responded to YBLI with significant decreases in HAM-D score and levels of ROS and significant increases in levels of TAC (all $p < .001$) and showed change in Ham-D score as a function of ALE ($r = -.45$, $p = .008$), ROS ($r = -.44$, $p = .010$), and TAC ($r = .39$, $p = .018$).

Conclusions: ALE and oxidative stress alter MDD severity as a function of 5-HTTLPR genotype and their interactions may have a role in severity of MDD. YBLI is beneficial in MDD irrespective of 5-HTTLPR genotype, but the baseline adverse life events and oxidative stress influence the extent of clinical benefit.

Conflicts of interest

The authors have none to declare.

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Ovarian tissue cryopreservation as an option for fertility preservation in young unmarried girls suffering from cancer

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Introduction: Due to various social and economic reasons women in the reproductive age group delay their marriage and the age of bearing their first child. This leads to an important health problem, as women steadily lose their oocytes from birth to menopause, with an accelerated loss of oocyte quantity and quality from the age of 35 years onwards. The situation becomes grim when a unmarried girl is diagnosed with cancer. Fertility preservation presents a peculiar challenge in young unmarried girls suffering from malignancies. It is now well established that the chemotherapy and/or radiotherapy is gonadotoxic and hence the need for preservation of fertility. The multiple factors affecting the fertility potential include the drug or size/location of the radiation field, dose, method of administration, disease, age and sex of the patient, and combination chemotherapy and pretreatment fertility of the patient. The ovarian cortex contains primordial follicles which are undifferentiated and not active metabolically.

Materials and methods: The primordial follicles in the ovarian cortex can be cryopreserved by offering ovarian cortex freezing as a method of fertility preservation. The ovarian tissue is obtained by performing laparoscopy on the same day. The cryopreserved ovarian cortical tissue is intended to be thawed and implanted after completion of chemotherapy and/or radiotherapy.

Result and conclusion: This method of ovarian tissue cryopreservation can be offered as a method of fertility preservation to children who survive childhood malignancies. In young unmarried girls suffering from cancer where in vitro-fertilization-embryo transfer (IVF-ET) is contraindicated, ovarian tissue cryopreservation and transplantation could become the technique of choice in the future.

Conflicts of interest

The author has none to declare.

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Association of *pai-1* promoter sequence variations in idiopathic avascular necrosis of head of femur

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Background: Avascular necrosis of femur head (ANFH) is considered a multifactorial disorder mainly associated with intravascular thrombosis or occlusion of already meager femoral head blood supply. Pertinent to its etiology, lot of causative factors have been elucidated in literature but derangement in fibrinolytic mechanism have been focused with more concern. Though various genes and genetic factors play role in maintaining harmony in coagulation and fibrinolytic system, *PAI-1* gene plays a crucial role. Hence aim of our study was to find out any polymorphism in this gene in respect to AVN hip.

Methods: Two SNPs of the *PAI-1* gene (rs2227631, −844G/A; rs 1799889, −675 4G/5G) were genotyped in 12 patients diagnosed with idiopathic AVN of head of femur and 13 control subjects, using direct sequencing. Subsequently, association analysis was performed for the genotyped SNPs.

Results: In −844G/A genotype GG (normal) was found in 10/13 controls and 10/12 cases (AVN). Similarly, GA (polymorphism) was noticed in 3/13 controls and 2/12 cases (AVN). Also in −674 4G/5G genotype: 4G/4G (normal) was found in 3/13 controls, 4G/5G in 4/13 controls, and 4G/4G + A in 6/13 controls while 4G/4G in 4/12 cases, 4G/5G in 2/12 & 4G/4G + A in 6/12 cases of AVN. Hence, cases and controls had equal frequency of polymorphism association of *PAI-1* gene.

Conclusion: Equal frequency of genetic polymorphism of *PAI-1* gene in cases and controls, suggests that sequence variation in promoter region is not associated with AVN. However, larger study group is warranted to validate our findings.

Conflicts of interest

The authors have none to declare.

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Molecular diagnosis of sickle cell anaemia based on SNPs in β-globin gene

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Introduction: Sickle cell anaemia is an autosomal recessive disorder caused by a point mutation in the 6th codon of the β-globin gene on chromosome 11. The substitution of a single amino acid (glutamic acid → valine) decreases the solubility of the deoxyhaemoglobin molecule making the erythrocytes assume irregular shapes. The sickled erythrocytes become trapped in the microcirculation and cause damage to multiple organs.

Aims and objective: To standardize a DNA based diagnosis of sickle cell anaemia in adolescent tribal girls of selected regions of Odisha so as to create awareness among the tribal communities to avoid consanguineous marriages.

Materials and methods: 40 Blood samples were collected from microscopically diagnosed cases of sickle cell anaemia in adolescent tribal girls who were from western Odisha. The blood samples were collected in 0.1% EDTA treated vials and stored in fridge till DNA isolation. DNA isolation was done from 200 μl of blood from each sample using the conventional phenol–chloroform method. Primers were designed from human β-globin gene using Primer 3 software. Primers were then synthesized commercially. PCR amplification, Sanger sequencing and analysis was done using BIOEDIT sequence editor.

Results: A DNA based detection of sickle cell anaemia could be done, thus showing mutation after the 6th codon where the nucleotide 'A' has mutated to 'T', i.e., adenine is replaced by thymine.