

**Discussion**

In the brain, the autonomic nervous system regulates and maintains body function and responds to external stimuli. It consists of two mutually inhibitory subsystems: those nerves which activate tissues- the sympathetic or arousal system and those which slow structures down for rest and repair- the parasympathetic or quiescent system. The sympathetic is ergotropic that releases energy and the parasympathetic is trophotropic, which is conserving energy. The two sides of our autonomic system reflect the two main processes in life "growth" or "protection."

Perinatal hypoxia/ischemia is a major cause of cerebral palsy, mental retardation, epilepsy, various motor and behavioral disorders (Brown et al., 1974). Vulnerability of the neonatal rat brain to hypoxia/ischemia appears to peak at the end of the first postnatal week and then progressively diminish (Ikonomidou et al., 1989).

**Body weight and blood glucose level in the serum**

Maintaining blood glucose level continues to be important throughout the pregnancy, but it is particularly important during early developmental stage, when an embryo's organs are forming. Oxygen is needed by cells to break down glucose and produce energy. The oxygen requirement is more during embryonic development for all the tissues. Insufficient oxygen supply cause developmental abnormalities and birth defects. Thus hypoxia has a potential to cause damage to cells (Rulin et al., 2005). The results suggest that hypoxic stress for thirty minutes during four days old rats does not cause significant change in body weight and blood glucose level after one week. Also, it suggests that supplementation of 100% oxygen, epinephrine and glucose does not adversely affect the blood glucose level and body weight (Kypson &
Epinephrine stimulated mechanical performance and heart rate of hypoxic hearts, but decreased myocardial glycogen and ATP. Though glucose utilization remained unchanged, the release of lactate increased from hypoxic hearts treated with epinephrine. However, epinephrine failed to stimulate myocardial lipolysis in hypoxic hearts. These metabolic changes due to epinephrine would lead to accelerated depletion of energetic reserves in hypoxic heart and its earlier deterioration.

Neurotransmitters in the cerebral cortex and adrenals.

Hypoxia and/or ischemia in the neonatal rat have been used as a model for studying the mechanisms underlying the pathogenesis of human brain pathology during perinatal anoxia (Rice et al., 1981). Monoamine metabolites have been found to decrease in the extracellular fluid during hypoxia (Masuda & Ito, 1993; Richards et al., 1993; Sarna et al., 1990) and to increase during the recovery period (Damsma et al., 1990). Exposure of neonatal rats to transient hypoxia induces a prolong decrease of brain DA and 5-HT content as well as DA uptake activity (Hadjiconstantinou et al., 1990). Brain hypoxia/anoxia is associated with excessive unregulated release of neurotransmitters, especially Glu (Choi, 1988, 1990) and activation of their receptors. Glu has excitotoxic properties after its induced release. Hypoxic stress in the neonate induces significant changes in neurotransmitter activity and functioning of the hypothalamic-pituitary-adrenal axis. These alterations cause an impairment of cognition by interfering with working memory capacity, independently of nutritional status. The change in cognitive performance after administration of glucose, depend on the level of sympathetic activation, glucocorticoid secretion and pancreatic β-cell function, rather than simple fuelling of neural activity. The outcomes can be predicted by vulnerability in coping with stressful challenges, interacting with nutritional and
Stress exacerbates many neuropsychiatric disorders associated with prefrontal cortical (PFC) dysfunction. Stress also impairs the working memory functions of the PFC. Birnbaum et al., (1999) reported that stress increases NE release in PFC.

Increased NE and EPI content in the cerebral cortex and adrenals of experimental animals exposed to hypoxia and supplemented with epinephrine and oxygen (Hx; Hx+O; Hx+E+O; Hx+G+E+O). The results suggest that the supplementation of glucose to hypoxic rats and hypoxic rats treated with oxygen showed better regulation of altered NE and EPI content in the cerebral cortex and adrenals of other experimental groups. Our results support the decreased DA content in the Cerebral cortex of neonatal rats exposed to hypoxic stress. The increased content of DA, NE and EPI in the adrenals suggests the enhanced production of catecholamines in the under-hypoxic stress in neonatal rats. Cheung et al., (2001) reported that there were no differences in systemic or splanchnic oxygen extraction or consumption at any dose of dopamine or epinephrine.

Glutamate dehydrogenase activity in the cerebral cortex and liver

Enzymatic adaptations to hypoxia have shown that there is a change in affinity of enzymes involved in aerobic and anaerobic metabolism (Lushchac et al., 1997). Glutamate dehydrogenase is an enzyme which has a key role in the synthesis of D-glucose. In hypoxic state a shift in the dynamic equilibrium from tri phosphate to di-phosphate resulting from increased energy consumption partially contribute to the increase in enzyme activity (Mons et al., 1998, Hawkins et al., 1986). GDH induces an increase in extracellular glutamate levels in the CNS with subsequent development of excitotoxicity (Kostic et al., 1989). Glutamate, a major excitatory transmitter in the
brain, is most widely distributed in the central nervous system. Its malfunction has been implicated in major psychiatric disorders such as schizophrenia, drug addiction and depression (Pomara et al., 1992; Perry & Hansen 1990; Plaitakis et al., 1988; Rothstein et al., 1996).

Organ specific studies revealed that GDH activity is higher in the liver. Developmental changes of GDH in rat liver were reported by Iguchi et al., (1992). It is important to maintain low levels (1-3μM) of extracellular glutamate as excessive receptor stimulation or excessive ammonium generated by the glutamate dehydrogenase can lead to neural injury and/or death ("excitotoxicity"). Increased extracellular glutamate has also been implicated in the onset of neurodegeneration associated with hypoxic damage (stroke). The release in glutamate following hypoxia has been suggested to be due, at least in part, to a calcium-independent mechanism following the reversal of the neuronal glutamate uptake carrier (Szatkowski & Attwell, 1994). This increase in extracellular glutamate acts afterwards post-synaptically to increase cellular calcium levels with subsequent cell death.

GDH in the liver and cerebral cortex showed an enhanced activity in animals exposed to Hx, Hx+O, Hx+E+O, Hx+G+E+O. This suggests that the hypoxic stress causes an elevated glutamate release, which in turn can lead to glutamate toxicity. The supplementation of oxygen and epinephrine enhances the glutamate toxicity even administered along with glucose. When glucose is supplemented to Hx and Hx+O, the glutamate release is regulated towards C. This suggests that the glucose supplementation reduce the possibility for glutamate toxicity. Alterations in components of glutamergic system and glutamate metabolizing enzymes are considered with reference to mental disorders such as senile dementia of Alzheimer's type and schizophrenia (Boksha, 2004).
Acetylcholine esterase activity has been used as a marker for cholinergic activity (Goodman & Soliman, 1991). Acetylcholine esterase is the enzyme catalysing the degradation of acetylcholine into choline and acetyl CoA. Other evidence indicates that glucose and acetylcholine can interact during memory formation, raising the possibility that the memory-enhancing effects of postextinction trial glucose may ultimately involve a cholinergic mechanism. Extracellular and tissue ACh contents as well as choline activity are reported to be depressed during and after a hypoxic or ischemic insult (Beley et al., 1992). One mechanism by which glucose may enhance acetylcholine function is by serving as a precursor to this neurotransmitter in conditions of high acetylcholine demand. Acetylcholine is synthesized by the reaction of choline and acetyl-Co-A, and glucose serves as the main source of acetyl-Co-A (Quastel, 1978). Although high-affinity choline uptake is generally the rate-limiting step for acetylcholine synthesis (Simon et al., 1976), the availability of acetyl-CoA appears to be the rate-limiting step in certain conditions, including when cholinergic neurons are activated (Bielarczyk & Szutowicz, 1989).

The cholinergic innervation of the cerebral cortex has been extensively investigated because of its role in arousal, learning and memory (Olton et al., 1991; Metherate et al., 1992; Voytko et al., 1994). Cholinergic neurons in the nucleus basalis magnocellularis (NBM) and associated forebrain nuclei are the major sources of the extrinsic cholinergic innervation of the cortex (Mesulam et al., 1983). In the present study a significant increase in AChE activity in the muscle and significant decrease in the AChE activity in the cerebral cortex of Hx, Hx+O, Hx+O+E, Hx+G+E+O were observed.
In rodents, a small portion of the cortical cholinergic innervation is also derived from intrinsic neurons (Eckenstein & Baughman, 1983). The density of cholinergic terminals is particularly high in cortical layer (Houser et al., 1985). There is evidence that synaptic density is related to cognitive function (Eastwood et al., 1994). For instance, acquisition of cognitive tasks corresponds to an increase in the number of synapses in the motor cortex (Kleim et al., 1996) and a reduction in synaptic density in the frontal cortex in Alzheimer's disease is correlated with cognitive decline (DeKosky & Scheff, 1990; Terry et al., 1991). Therefore, it is reasonable to assume that the decline in cognitive function in aging is related to the diminution in cortical synaptic number in general and in particular to the decline in cholinergic synapses (Winkler et al., 1995). Enhanced AChE activity in the muscle explains that the acetylcholine released is utilized by the muscle under hypoxic stress, where there is increased demand for energy. AChE activity in the cerebral cortex is deprived, indicating an alteration in ACh synthesis that leads to impairment in behaviour and cognition. The muscles need more energy and an increased demand for glucose is generated under hypoxia. AChE activity increase in the muscle, which in turn leads to enhanced utilization of ACh leading to locomotory defects during hypoxia.

Adrenergic receptor (AR) of epinephrine, \( \alpha_2-, \beta-, \beta_1- \) AR

Adrenergic receptors can be subdivided into several distinct categories, based on pharmacological specificity and physiological actions. These include the \( \alpha_1, \alpha_2, \beta_1, \) and \( \beta_2- \) adrenergic receptor subtypes. Theoretically, the \( \beta \)-adrenergic effects of epinephrine would produce bronchodilation that could affect the distribution of ventilation. Because epinephrine activates both \( \alpha \) and \( \beta \)-receptors, both pulmonary vasoconstriction (\( \alpha \)) and vasodilation (\( \beta \)) are possible. Bucheler et al. (2002) reported
that the two functionally distinct α2-adrenergic receptor subtypes α2A and α2C, operate as presynaptic inhibitory receptors regulating neurotransmitter release in the mouse CNS. These distinct categories of receptors differ not only in their specificity for various ligands but also in their specificity for coupling to G proteins and thereby respond to different second messenger systems.

It was reported that hypoxic pulmonary vasoconstriction was attenuated by a β-adrenergic receptor–mediated vasodilation caused by reflex release of catecholamine from the adrenal gland and sympathetic nerves (David et al., 1997). Prior to the development of sympathetic nerve function, adrenal catecholamine plays a predominant role in enabling the neonate to survive hypoxia. Interference with the release of adrenal amines invariably increased mortality during hypoxia. In contrast, interference with sympathetic neural release of catecholamines did not affect the ability of 1-day-old rats to withstand hypoxia, indicating that survival during low PO2 conditions is not dependent on the sympathetic innervation at that stage of development. After functional development of the sympathetic nerves and disappearance of non-neurogenic adrenomedullary responses, the neonatal rats became partially dependent upon catecholamines derived from sympathetic terminals (Seidler & Slotkin 1985).

The present study suggests that hypoxia causes an up-regulation of epinephrine and β-adrenergic receptor in the cerebral cortex of hypoxic experimental groups and those treated with oxygen and epinephrine (Hx, Hx+O, Hx+E+O, Hx+G+E+O) whereas α2 showed a down regulation in the above experimental groups. The glucose supplementation to hypoxic neonatal rats and those treated with oxygen (Hx+G; Hx+G+O) showed a reversal of receptor activity of epinephrine, β2 and α2AR. Real-Time PCR results showed an up-regulation of β2-AR gene expression and a
down-regulation of \( \alpha_{2A} \)-AR which are in concordant with the receptor binding studies.

In the periphery, the adrenergic system plays an important role in regulating sympathetic function (Ani et al., 2006 a,b) and cardiovascular system. Increased sympathetic discharge to the heart increases the rate and force of contraction mediated through \( \beta_1 \) receptors. Circulating adrenaline also acts on cardiac tissue. In addition, it acts on \( \alpha_1 \) adrenoceptors in arterial smooth muscles, stimulating vasoconstriction, and on \( \beta_2 \) adrenoceptors in vascular beds of skeletal muscles, stimulating vasodilation. \( \beta_1 \) and \( \beta_2 \) receptors often coexist, but one subtype normally predominates. \( \beta_2 \) receptors mediate relaxation of smooth muscle (including vascular beds, bronchus, intestine and uterus); they mediate glycogenolysis and glucogenesis in the liver and regulate cell metabolism in skeletal muscles; they inhibit the activity of leukocytes and other blood cells; and they are found in the heart. The receptors are located presynaptically in nerves, where they facilitate neurotransmitter release and in the brain, where they regulate a variety of physiological processes. The \( \beta \)-adrenergic receptor stimulation evokes an increase in cAMP levels, which then activates cAMP dependent protein kinase through G proteins. Conversely, agonist activation of \( \alpha_2 \)-adrenergic receptor leads primarily to inhibition of cAMP via a distinct G protein, Gi (Bylund, 1988).

**Glutamate receptor binding parameters in the cerebral cortex of experimental neonatal rats**

Glucose in brain supplies energy essential for maintenance of the nervous system. Deficiency in glucose that results from hypoglycemia or ischemic insults can trigger neuronal injuries. Disturbance of ionic homeostasis results in membrane depolarization and massive release of neurotransmitters, including glutamate (Siesjo, 1988; Erecinska & Silver, 1989). Neurons can display many different kinds of
glutamate receptors on their surface, some of which are useful targets for treating neurologic diseases. Glutamate receptors can be divided into ionotropic and metabotropic receptors. Activation of ionotropic glutamergic receptors leads to greater permeability of the cell membrane to the sodium (Na+) and calcium (Ca2+) cations.

The extracellular accumulation of glutamate results in neuronal death by activating ionotropic glutamate receptors sensitive to NMDA or AMPA-kainate (Choi, 1988). In addition, neurons impaired of energy metabolism appear to be highly sensitive to excitotoxicity (Simon et al., 1984; Cebers et al., 1998). NMDA receptor antagonism appreciably affects both ventilatory phases of hypoxia. The inability to uphold ventilation in the depressant phase suggests that the NMDA glutamate-mediated pathway is operative in shaping the late hypoxic ventilatory response. The role of the glutamergic pathway is thus be extended beyond the hitherto recognized early ventilatory stimulation of hypoxia (Tarakanov et al., 2004). The contribution of glutamate to synaptic transmission, plasticity and development is well established; current evidence is based on diverse approaches to decipher function and malfunction of this principal transmitter (Riedel et al., 2003).

NMDA receptors are assembled from 5 subunits belonging to two families—NMDAR1 and NMDAR2. NMDAR2 family has four members—A, B, C, and D. Studies employing in situ hybridization and immunocytochemical techniques have shown that NR1 subunits are ubiquitously distributed throughout the central nervous system whereas the four NR2 subunits display differential expression patterns in several mammalian species including humans (Moriyoshi et al., 1991, Petralia et al., 1994, Rigby et al., 1996) In general, within the cerebral cortex, hippocampus, and cerebellum, NMDA receptors are mainly distributed in neuronal cell bodies and dendrites. NR1 and NR2 are also found intracellular membranes such as mitochondria
and rough endoplasmic reticulum whereas in synapses they appear to be limited to the postsynaptic membrane and density (Moriyoshi et al., 1991; Sheng et al., 1994).

It is studied that the mechanisms of amino acid release that occur in vivo upon oxidative stress, hypoxia or ischemia is frequently associated with the impairment of energy metabolism (Rego et al., 1996). Glutamate appears to be remarkably potent and rapidly acting neurotoxin. Exposure to 100μM glutamate for 5 min is enough to destroy large numbers of cultured cortical neurons. By the way, glutamate neurotoxicity is blocked by antagonist compounds and attenuated by antagonists added after glutamate exposure (Choi, 1990).

The results suggest that the glutamate receptors get overactivated during hypoxia in (Hx, Hx+O, Hx+E+O, Hx+G+E+O) and the toxicity can be reduced by the supplementation of glucose along with oxygen or without oxygen to the sufferers of hypoxic insult during early neonatal period. The Real-Time PCR study also supports this receptor data.

Intracellular free Ca²⁺ and reactive oxygen species (ROS) have been well documented as causative mediators of excitotoxicity (Choi, 1988; Lundgren et al., 1992; Coyle & Puttfarcken 1993; Li et al., 1998). However, administration of high glucose before hypoxic–ischemia has been reported to reduce brain damage (Kraft et al., 1990; Vannucci et al., 1996). Increasing glucose entry into neurons was shown to protect neurons from glutamate neurotoxicity (Ho et al., 1995), stroke or seizure (Lawrence et al., 1995, 1996), and mitochondrial toxins (Dash et al., 1996).

Hypoxia causes irreversible neuronal damage within a shorter period than ischemia, with both free radicals and glutamate suggested to be involved in tandem in the neurotoxicity induced by hypoxia, whereas glutamate alone is involved in ischemic neurotoxicity (Omata et al., 2000). NMDA neurotoxicity and oxidative stress have been well documented as mechanisms underlying hypoxic–ischemic brain
injuries. The neonatal rat administrated with high glucose is resistant to hypoxic-ischemic injuries (Palmer & Vannucci, 1993). Glucose entered into cells likely enhances mitochondrial potentials that play a central role in regulation of $[\text{Ca}^{2+}]_i$ and ROS. These in contrast to the beneficial effects of high glucose, systemic administration of glucose before ischemia emphasize brain damage in the adult animals after hypoxic–ischemic injuries (Sieber & Traystman, 1992; So et al., 1999).

**Second messenger cAMP in the cerebral cortex of experimental neonatal rats**

Hypoxia appears to activate adenylate cyclase directly and independent of any hormone-receptor interactions (Delpiano & Acker 1991). Biochemically, adrenergic receptors couple to several well-characterized signal transduction systems. Both $\beta_1$ and $\beta_2$-adrenergic receptors stimulate adenylyl cyclase (Emorine et al., 1989), whereas $\alpha_2$-adrenergic receptors have been classically shown to inhibit adenylyl cyclase in tissues (Ruffolo et al., 1988). Agonist activation of either the $\beta_1$ or $\beta_2$-adrenergic receptor subtype classically leads to the generation of cyclic adenosine monophosphate (cAMP) by stimulating the enzyme adenylyl cyclase; this pathway is mediated by the G protein Gs. Conversely, agonist activation of $\alpha_2$-adrenergic receptor leads primarily to inhibition of adenylyl cyclase via a distinct G protein, Gi (Bylund, 1988). Neurotransmitters, neuropeptides, chemokines and many other molecules signal through G protein-coupled receptors (GPCRs). Neonatal HI-induced brain damage is associated with specific changes in the GPCR desensitization machinery (Lombardi et al., 2004). The adrenergic receptor subtypes involved in cyclic AMP responses to norepinephrine showed a large response to both $\alpha_1$-receptor activation (increases in inositol phosphate accumulation) and $\alpha_2$-receptor activation (decreases in forskolin-stimulated cyclic AMP accumulation) were observed in slices
of rat cerebral cortex and primary neuronal and glial cultures from rat brain (Brian & Kenneth, 1991).

The functions of G protein-coupled receptors are subject to dynamic regulation by a number of mechanisms. Covalent modification of the receptor (i.e., phosphorylation by various kinases) has been implicated in the regulation of β-adrenergic receptor function (Sibley et al., 1987). Phosphorylation of β-adrenergic receptor is closely associated with impaired receptor function, (Benovic et al., 1985, 1986) correlating with a decreased ability to couple to its G protein Gs. The paradigm in which receptor phosphorylation reactions have been examined is the phenomenon known as desensitization. Desensitization refers to the attenuation of responsiveness to a drug or hormone in its continued presence. This phenomenon can markedly diminish the therapeutic efficacy and duration of action of a drug.

Second messenger assay showed that the cAMP gets significantly enhanced in the experimental groups of neonatal rats except Hx+G and Hx+G+O. This support the receptor data showing up-regulation of β-AR and glutamate and down regulation of α2-AR is mediated through cAMP pathway.

Electroencephalogram (EEG)

Neonatal electroencephalography presents some of the most difficult challenges in EEG interpretation. It differs significantly in many ways from EEG of neonate and older children. Technologically, acquisition of a neonatal EEG is significantly more difficult and different than an adult EEG. There are numerous features that are age-specific and change almost week-to-week in the preterm infant. Some features may be normal at one age and abnormal if they persist for several weeks. Many of these features also have different implications in neonates as compared to older individuals.
Seizures occur commonly in neonatal intensive care units and they are the important clinical evidence for CNS diseases in the newborn including brain hemorrhage, stroke, meningitis and hypoxic-ischemic encephalopathy (Stephen et al., 2005). A seizure is the most frequent sign of neurological dysfunction in the neonate. Since seizures are the only sign of a central nervous system disorder, their recognition is very important. O’Meara et al., (1995) reported that several infants had electrographic seizures with reduced or no clinical manifestations.

Although infants have been noted to have greater relative right or left frontal EEG as early as the neonatal period, other ways in which these newborns differ have not been reported (Field et al., 2002). EEG measured during the neonatal period helps to analyze behavioral, physiological and biochemical changes of the individual as well as predict the possibility of neurodegenerative defects. A clinical seizure was considered to arise from a specific epileptic basis if it occurred simultaneously and was consistently synchronized to an electrographic seizure displayed on the coincident EEG. Many parts of the brain are immature at birth. This immaturity implies selective vulnerability, as well as selective resistance to specific disease processes. Rapid brain growth imposes rigid constraints. Therefore, an event that interferes with the developmental cascade has the potential for long term effects. In newborn rats, seizures inhibit brain protein synthesis (Jorgensen et al., 1986), reduce brain size and delay developmental milestones (Wasterlain et al., 1990, Holmes et al., 1998). Recurrent seizures during the neonatal period also result in deficits in learning and memory when animals are studied as adults, despite lack of cell loss (Neill et al., 1996). Neonatal seizures arise focally and often become generalized. Seizures contain rhythmic activity that can vary in frequency from approximately 0.5 to 8 Hz and this activity is often very sharp (Stephen et al., 2005). Generalized spike and wave activity
that is often seen in older children and adults is extremely rare in neonates (Clancy, 1995).

**Behavioural activities of the experimental neonatal rats using Elevated Plus-Maze and Open-Field Test.**

The differences in the anxiety and locomotor-related behavioural activities observed in the experimental groups of rats predict the chance for occurrence of significant behavioural abnormalities as a result of hypoxic impact. Neonatal hypoxia-ischemia in the preterm human leads to selective injury to the subcortical developing white matter, which results in periventricular leukomalacia (PVL), a condition associated with abnormal neurodevelopment. Maturation-dependent vulnerability of late oligodendrocyte progenitors is thought to account for the cellular basis of this condition. A high frequency of cognitive and sensory deficits with decreasing gestational age suggests pervasive abnormalities of cortical development. In a neonatal rat model of hypoxic-ischemic injury that produces the characteristic pattern of subcortical injury associated with human PVL, selective sub plate neuron death is seen. The premature sub plate neuron death occurs after thalamic axons have reached their targets in cortex. Sub plate neuron cell death in PVL provides another mechanism for abnormal neurodevelopment and deficits in motor function after neonatal hypoxia-ischemia (Patrick *et al.*, 2003).

Elevated Plus-Maze test is used to test a drug's anxiogenic or anxiolytic properties, memory impairment and general motor activities (Shah & Treit, 2004). The following parameters were measured to analyse the behavioural changes of the experimental rats using elevated plus-maze: open arm entry, closed arm entry, percentage arm entry, total arm entry, time spent in open arm, time spent in closed
arm, percentage of time spent in open arm, head dipping, stretched attend posture and grooming. Open field test is used to measure the locomotor activity of experimental animals to determine the drug effects (Halina & Roza, 2006). The response of experimental animal groups to crossing, time of walk, resting time, episodes of rearings, head sniffing and washing were measured.

The results showed that the experimental rats exhibit significant abnormalities in its behavioural pattern which may be due to cortical neuronal damage as a result of hypoxic stress. Supplementation of oxygen and epinephrine separately and in combination or along with glucose (as the traditional way of resuscitation practiced) seem to produce anxiogenic behaviour in the neonates exposed to hypoxia. The glucose supplemented to hypoxic and hypoxic rats oxygen treated showed a behavioural pattern very similar to control. Thus our study suggests the supplementation of glucose first alone or together with oxygen can regulate the possible anxiogenic and locomotory defect shown in neonates after hypoxic insult.

Cerebral palsy (CP) means "brain paralysis" refers to motor or postural abnormalities that are noted during early development. These anomalies are thought to be associated with prenatal, perinatal or postnatal events of varying etiologies (often multifactorial in nature). CP generally is considered to be a static encephalopathy that is non-progressive in nature. However, the clinical expression of CP is subjected to change as children and their developing nervous systems mature. Despite advances in neonatal care, CP remains a significant clinical problem (Papile et al., 1978). Brain injury due to vascular insufficiency depends on various factors at the time of injury, including vascular distribution to the brain, efficiency of cerebral blood flow and regulation of blood flow, and biochemical response of brain tissue to decreased oxygenation (Singhi et al., 2003).
Thus our results suggest that the traditional way of administration of epinephrine and oxygen currently practiced as part of initial resuscitation cause an adverse effect in the hypoxic stress. The sequence of treatment followed is without any scientific basis. Glucose administration prior to oxygen and epinephrine treatment has shown recovery from hypoxic damage to the brain. However, epinephrine treatment to glucose treated hypoxic rat model did not show that effective recovery. The neurotransmitters, neurotransmitter synthesizing enzymes, receptor binding parameters and Real-Time PCR studies support these findings. Also, brain activity measurements by EEG and behavioural studies confirm these results. These corrective measures from the molecular study brought to practice will lead to maintain healthy and intellectual life during later developmental stages. This will have immense clinical significance in neonatal care.