

A STUDY OF THE EFFECT OF MATERNAL SMOKING DURING PREGNANCY ON CORD BLOOD ERYTHROPOIETIN

Thesis

Submitted in partial fulfillment
of Master Degree in Pediatrics



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Acknowledgment

Thanks to God.

I wish to express my sincere gratitude and deepest thanks and respect to **Dr. Ismail Sadek Ismail**, Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for his valuable advice and wise supervision through out every part of this work.

I also would like to express my endless gratitude, respect and the sincere thanks to **Dr. Mohamed Nasr El-Din El-Barbary**, Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for his kind, exceptional care and support helping me to perform this work in a proper order. He devoted a lot of his time to guide and revise this work.

I would like to express my deepest thanks and respect to **Dr. Hala Ahmed Talkhan**, Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her great help in the laboratory part of this work.

I would like also to thank the co-operated obstetricians and smoker mothers for their co-operation during questionnaire and taking cord blood samples from the neonatal umbilical cord.



List of Abbreviation

AcT H	: Adrenocorticotrophic hormone
ATP	: Adenosin Triphosphate
Bo	: Unlabelled antigen
%B/T	: Maximum binding
cAMP	: Cyclic Adenosin Monophosphate
cGMP	: Cyclic Glucose monophosphate
CNS	: Central Nervous System
CoHb	: Carboxyhaemoglobin
cPM	: Calucate the mean counts per minute
DapA	: Dihydroxy phenyl acetic acid.
DL	: Decileter
DM	: Diabetes mellitus
DoPEG	: Dihydroxyphenyl glycol.
DSL	: Diagnostic System Laboratories.
E	: Epinephrine
Epo	: Erythropoietin
Gest. Age	: Gestational Age
GM	: Gram
Gp I	: Group one
Gp II	: Group two
Gp II	: Group three

Hb	: Haemoglobin
IBR	: Infant behaviour record
I UGR	: Intrauterine growth retardation.
6-KetoPGE₂	: 6 - Keto prostaglandin E ₂
6-KetoPGF_{1α}	: 6 - Keto prostaglandin F _{1α}
Lta	: L - Thyroxin
Mao	: Mono amine oxidase
MDI	: Mental developmental index
ML	: Melli letter
Mu	: Melli unit
NE	: Norepinephrine
NSB	: Non specific binding
PDI	: Psychomotor developmental index
PG	: Prostaglandin
PG E_I	: Prostaglandin E _I
PGI₂	: Prostacyclin
RIA	: Radio immuno assay
SGA	: Small for gestational age
SIDS	: Sudden infant death syndrome
TFP	: Trifluoperazine

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Introduction and Aim of the Work

Introduction :

Erythropoietin is the primary hormone controlling erythropoiesis in both adults and fetuses [Finne and Halversen, S. 1992].

Erythropoietin hormone cannot cross the placenta, its synthesis is regulated by hypoxia so its increase in fetal plasma is indicative of fetal hypoxemia [Petri, E.J. et al., 1989].

Smoking during pregnancy is associated with adverse long-term effects on pregnancy such as increased frequency of fetal mortality [Lindblad, A., et al., 1988].

The fetuses of cigarette smoker mothers have decreased placental intervillous blood flow, increased fetal heart rate and increased level of carboxyhaemoglobin [Varvariguo, A. et al., 1994].

Tobacco smoke contains over 500 compound, the two main constituents exerting harmful effects on the fetus are carbon monoxide and nicotine [Abel, F.L., 1982].

Aim of the work :

The aim of this work is assessment of cord blood erythropoietin as an indicator of chronic fetal hypoxia to detect the effect of smoking during pregnancy on the fetus.

Review

I. PREVELENCE AND PATTERNS OF SMOKING

Smoking is among the most widely researched topics in the area of teratology reflecting in part the significant number of women who smoke during pregnancy.

The data collected during the late 1980s and early 1990s have reported relatively consistent findings with respect to numbers and trends.

In Canada, the results of a recent national survey by Health and Welfare indicated that the general prevalence of smoking by people 15 years of age and older was declining among all age groups (Health and welfare Canada's Health promotion survey 1988 where as 41% of the adult were smokers in the 1970s decade declined to 30% in the last decade in males, while in females the declining is lesser than males as their percentage of smoking declined from 32% to 29% only particularly German to the topic at hand is that among women of reproductive age, there was essentially no change in the proportion smoking during this decade, approximately one third smoked on a regular base . In fact, a 1992 press released from Ottawa said, for the first time in any western country, in this particular age (> 15 years old) group the number of women who smoked outnumbered similar aged men revealed that the prevalence of the use by women of reproductive age is similar to other countries such as United States [National Institute of the Drug abuse 1990 and 1991 and Cnattingius 1989 for example in United States the 1990 National Household survey on drug abuse showed that 31% of women between the ages of 18-34 years smoked at least one pack of cigarettes, a day.

One of the most striking aspects of smoking habits and gender has to do with the proportion of heavy smokers (one pack a day or more) for example in Canada, the relative increase in the proportion of heavy smokers during the past decade was 37% for men versus 57% for women and the relevance of this observation noted that one of the predictors for continued smoking during pregnancy was the amount smoked before pregnancy, as many of the smokers switch to cigarettes, with lower nicotine content but counteract this potential benefit by smoking more [Cnattingius, 1985].

Cigarette use by pregnant women in non-ghetto urban regions generally had been found to range from 22-28% and in the perinatal prospective study among volunteer, primarily the percentage of heavy smokers diminished from 12% in the year before pregnancy to 7% in the first trimester and 6% in the 3rd trimester but in light smokers (<one pack/day) and 90% of heavy smokers continued to smoke to some degree after their pregnancies were confirmed but this decline of smoking in pregnancy is rapidly retained to the previous level before pregnancy after about one month from labour. This occurs usually with light smokers but the heavy smokers continue declining even after birth and this may be due to the concern that the mothers had about smoking effect on nursing (including second hand smoke) [Stewart and Dunkley, 1985 and Secker walker et al., 1992]. This is of obvious benefits for the mother and in terms of second hand smoke. Exposure for the child from a counseling perspective the knowledge that there is a fair probability that the reduction during pregnancy will persist beyond the birth of the baby providing an additional motivation for the smoker to reduce her habit before becoming pregnant.

II. MATERNAL SMOKING AND BEHAVIOR CHANGES IN THE NEONATE

1) Auditory change :

There are a number of reports about relationships between maternal smoking during pregnancy and altered behavior. These findings suggest auditory system involvement in the perinatal cigarette exposure was associated with decreased auditory habituation in 3-6 day old babies an indicator of nervous system integrity, showing decreased auditory responsiveness [Picone et al., 1982 & Fried and Makin 1987].

2) Autonomic nervous system, reflexes, limb movement and posture :

Fried et al., 1987 examined infants of smoker mothers and control of non smokers at ages of 9 days and 30 days age and they found that at younger age the features distinguishing the babies born to smokers from non smokers were an increased incidence of tremors and some lightened motor reflexes and at 30 days age, aspects of muscle tonus differentiated the two groups with increased tonic and heightened motor reflexivity noted in the smoking group and the hypertonicity remained statistically associated after controlling for birth weight indicating that the relationship was not the result of reduced fetal growth and there is also associated increased startles and tremor, with maternal smoking in the 30 days old infants and together with hypertonicity suggesting the increased nervous system excitation.

3) Hyperactivity in young children :

Several reports have linked maternal smoking with hyperactivity in young children [Nichols and Chen, 1981], and poor orientation and impaired attention in a vigilance task [Streissguth et al., 1984] further more recent research had demonstrated that habituation and recovery of attention such as appear to be affected in infants born to smokers is a better predictor of childhood cognitive competence than traditional infant developmental tests [Bornstein and Sigman, 1986]. However even if we make the reasonable assumption that development is a continuous process with common substrates underlying behavioral performances, such as a cause and effect postulates at this stage highly speculative, further more, the impact of the child's environment on behavior must not be relegated to a minor role [Sameroff and Chandler, 1975].

Some observations in babies of smoker mothers :

The instrument used in most research centers to examine the relationship between maternal smoking and the effects in the baby has been the Bayley scales of mental and motor development 1969 which is divided into three components.

1) The mental developmental index (MDI) :

Which assesses sensory perceptual abilities, early acquisition of the object constancy, memory, problem solving and vocalization.

2) Psychomotor developmental index (PDI) :

Examines gross and fine motor movements.

3) Infant behavior record (IBR) :

Evaluates the infant attitudes, interests and temperament.

Beter and Fried, 1993 use these scales in their study and demonstrated that cigarette use contributed significantly to the prediction of MDI scores, the average MDI of the babies born to the non smokers was 109.5 whereas the average score of the toddlers born to heavy smokers was 96.6 with the average for babies born to light smokers being intermediate, furthermore when examining the negative relationship between maternal smoking and infants MDI values, 39% of the heavy smokers had infants with scores less than 85 (more than one standard deviation below the mean) by contrast to 6% of the remaining subjects. But no relationship was detected between the PDI and maternal smoking and importantly there was a significant negative association between auditory-related items on the IBR and in utero exposure to cigarette smoke.

Fried and Watkinson 1988 use Bayley test and Reynell developmental language scale 1977, which used in the assessment instrument measures language comprehension and expression, at that age smoking during pregnancy was associated with auditory-related behavior as measured by IBR of Bayley, but maternal smoking no longer contributed a unique significant explanation of variance of MDI or the two Reynell language scores.

The children born to the heavy smokers scored more poorly on all measurements compared with the children of lighter smokers but factors other than maternal smoking statistically overwhelmed the smoking effect this in part related to the fact that outcome used at this age were relatively global in nature and did not focus on various components of behavior as the child gets older, postnatal factors play an increasing role in determining the child's performance and it becomes crucial to examine subtle