Doctoral thesis

Hipohormonal Pregnancy Untill 36\textsuperscript{th} gestational week

Boundary, insights and controversies in obstetric practice.

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Objectives - The practical relevance of the problem studied

Hipohormonal pregnancy is an entity of obstetric pathology less investigated in textbooks.

We started with the idea of Mr Univ. Dr. Mihai B. Braila, scientific leader of my thesis and student of Mr. Prof. Univ. Dr. Traian Rebedea both from “Romanian Obstetric School” of Prof. Univ. Dr. Eugene Aburel, that this type of pathology is more common in obstetric practice than one might think initially as a completely separate entity from a number of other serious diseases in practice and described in the literature.

Hipohormonal task is actually a subtle entity or we could even call it perverse of obstetrical pathology that often escapes diagnosis and therapy practitioner in obstetrics, and other serious pathology who have in context hormonal ovarian – placenta insufficiency - in fact the decisive cause placental and / or gestational yellow body. This goal was actually my PhD thesis focusing on research of the hipohormonale pregnancy besides other etiopathogenic obstetric causes.

I excluded from my study any other cause which could lead to an abortion during the first two trimesters of the pregnancy or a premature birth (between 29-37 SG).

To come up with arguments we studied clinical – paraclinical parameters in pregnancy during four years, from 2006 to 2009, the most important elements were represented by: clinical examination, ultrasonography, normal hematological examinations, special plasma laboratory determinations (beta HCG, progesterone, unconjugated estriol).

In all these determinations on the addressed case, we found a significant decrease in the analyzed hormone markers, despite the fact that we have not found another foeto-maternal pathology coexistent.

These determinations have been much reduced in the analyzed groups in four years and therefore I followed their evolution with or without appropriate prescribed treatment.

The hipohormonal pregnancy, in the first quarter I found a significant decrease of beta-HCG plasma, progesterone plasma, estradiol plasma and subsequently of progesterone. These findings led me to be every year hipohormonal pregnancy lots that we have pursued and directed.

All this is revealed by my clinical – paraclinical research, in which I have shown that the proportion of hipohormonal pregnancy is at least 20% of obstetric pathology.

The hipohormonal pregnancy should not be overemphasized nor underestimated as my studies are present in a number of other underlying gestation conditions. I am also interested only in the hipohormonal pregnancy as hormone deficiency on pregnancy maintenance in the first two quarters, the 3rd quarter and to date.

Another objective of my thesis was an alternative therapy usually applied by clinicians in both the prevention of abortion and premature birth.

This therapy has proven effect in both groups studied by me, a number of cases coming to give birth to term.

Arguments on the objectives and practical importance of the topic studied are actually revealed during my thesis dissertation.

I was not interested in my studies of specialty spectacular aspects such as preeclampsia / eclampsia, praevia placenta, utero – placental apoplexy, uterine rupture, maternal cardiovascular and haematological, renal disease, diabetes, morbid obesity, which I am sure that can often accompany hipohormonal pregnancy.
Hipohormonal pregnancy is therefore a reality and if you want to deny it, avoid the prescription of hormonal progestagen medication to any pregnant who attends the consultation in order to maintain the pregnancy.

A given drug dose progestogens more or less elevated in pregnancy without evidence that it is a hipohormonal pregnancy is a non – meaning both scientific and practical material. Such therapy administered paraclinical uncontrolled can lead to a delay of a possible miscarriage or premature birth of poor biological fetuses quality with chromosomal aberrations and / or other abnormalities revealed by the imaging issues in my dissertation.

These were the reasons for which I ventured to address the practical aim of my dissertation, hipohormonal pregnancy, under the guidance of my scientific coordinator, Univ. Dr. Mihai B. Braila.

**Hipohormonal pregnancy. Boundary, insights and controversies in obstetric practice.**

During the 280 days of gestation in obstetric practice we may encounter outstanding situations of which clinical – paraclinical substrate we cannot be sure without laboratory explorations with a high degree of specificity.

In this context, I accepted the task of practical study of hipohormonal pregnancy relying on three important markers during the nine months of pregnancy:
- Progesterone
- Unconjugated estriol
- Beta HCG

These three markers are important for the evolution of the pregnancy from the first weeks until term. The synthesis and movement of discharge into the maternal – fetal, these three hormones maintain pregnancy maintenance, evolution and uterus development and of the feto – placental unit.

In clinical practice we often face the lack of synthesis and secretion of these hormones reason why abortion and premature births appear from unexplained causes and are often not found at clinical examination and laboratory exploration or any favorable decisive cases.

Hipohormonal pregnancy is a concept which I have introduced into practice with my teacher Prof. Dr. Mihai B. Braila from the practical realities when numerous colleagues administrate in cases of imminent threat or abortion, in cases of threat or imminent preterm birth different predominant hormonal drugs, antispasmodics, antiocitocics. The goal is tokoliza beneficiary being both fetus and mother.

In the studies we have done both in the case of abortion and premature birth I decided on the basis of laboratory research, coupled with clinical and ultrasound to determine the impact of the failure of the gestational yellow body and of gestational trophoblastic placental in the pregnancy development on women who have infertility / habitual abortions and premature births, single or repeated.

Progesterone is the steroid hormone with 21 carbon atoms produced by the cells of the gestational yellow body in the first 8-10 weeks of gestation, after its synthesis is determinated by the placenta. Progesterone has close links with the development and regression of the yellow body, endometrium and myometrium over the short generative development of the biorhythm but also with the debut of ovoimplantation and subsequent the development of pregnancy. This phenomenon is explained by the paraclinical explorations, in pregnancy that recently recorded a gradual rise in plasma progesterone often a hundred times more than in the level prior to the installation of the pregnancy. Plasma progesterone concentration is also much higher in twins and / or multiple pregnancy compared with single pregnancy.
The uterus is the most important target organ of progesterone in both non-pregnant and during pregnancy. Progesterone makes the mucous uterine transformation (endometrium) in a pseudo - rich tissue in the secretory glands (secretory phase of endometrial cycle), for facilitating installation of blastocyst implanted pregnancy. Currently is known that progesterone is involved even on the local immunological factors in the area of implantation or the product design ovoimplantation inhibiting rejection phenomena (fertilized egg / ovular heterogref the site of nidation / maternal host organism). Normal levels of progesterone in the onset of any task will facilitate the process of ovoimplantation and the development of gestation in the first weeks. It is known that in the first trimester of pregnancy the plasmic level of progesterone should be between 32.6 to 140 nmol / l in the second trimester of pregnancy between 62-262 nmol / l in the third trimester of 206-728 nmol / l. As a conversion factor after the laboratory data nmol / lx 0.314 ng / ml ng / ml x 3.18 = nmol / l. Breakpoints in the failure of progesterone are related to hipohormonal pregnancy are those below 16 nmol / l (unviable pregnancy, pregnancy stopped from evolution, miscarriage) and between 16 and 32 nmol / l (premature birth, pregnancy disease).

These values were evaluated in the studied cases by me both in terms of unique or repeat miscarriages and premature births in the single or repeating. This hormone insufficiency put it in the first 10 to 12 due to insufficient progesterone of the yellow gestational body, blood progesterone determinations cases are conclusive both clinical (progression to an abortion) and therapeutic (progestin hormone therapy is administered insufficient both in quantity and the time of administration / late). Progestin treatment in such cases has done nothing but cause a late hipohormonal miscarriage already formed.

This situation we encountered both in cases of abortion in the second trimester of pregnancy and in premature births (between 28-37 SG).

Unconjugated estriol (E3) is the estrogen hormone predominantly in the blood and urine of the pregnant women. Most of the circulating unconjugated estriol is product of the feto – placental unit resulting from precursors (16 alpha hydroxy – dehydroepiandrosteron) synthesized in the fetal adrenals and transformed into estriol by the fetal liver and placenta due process flavoring. Normal production of this hormone is an indicator of the feto – placental unit integrity and intrauterine fetal wellbeing. During normal fetal development unconjugated estriol production gradually increases reaching a maximum in week 36 of the pregnancy.

Sequential monitoring of unconjugated estriol levels in pregnancies with increased risk for me was more important than determining the clinical value of this hormone in the isolated pregnant prosecution. Such low levels of unconjugated estriol, which I have determined in my research, coupled with low levels of progesterone led me to believe that it is a hipohormonal pregnancy suggestive for the product conception suffering and / or fetus to term.

I guided my pursuing cases where these values resulted unconjugated estriol value from the 27 week of pregnancy.

Unconjugated estriol lower values I found in all hipohormonal pregnancy analyzed situations in which I found a number of fetal – placental abnormalities of types: fetal death „in utero”, preeclampsia, malformed fetuses, anencefals fetuses, conjoined fetuses.

I should mention that the determination of isolated unconjugated estriol have less practical value only when associated with plasmatic progesterone determinations, determinations of beta-HCG and ultrasound examination in detail. I was able to correlate these data with determination and possible placental sulphatase obtained by genetic amniocentesis. In fact this was not the objective of my dissertation, the hipohormonal pregnancy is not after my studies a chromosomal aberration or a fetal – maternal genetic native.
Beta HCG or human chorionic gonadotropin, is the hormone present in normal blood and urine only during pregnancy. It is synthesized by placental tissue from early primitive trophoblast when implantation serves to support the gestational yellow body in the first weeks of pregnancy. This beta HCG is composed of two subunits alpha and beta united through a noncovalent link. Alpha subunit has an identical homologous of the subunit pituitary glycoprotein hormones structure (FSH, LH, TSH). Beta subunit is specific to each of these different hormones and giving them specific biological activities. Determination of beta-HCG can still serve in the diagnosis and monitoring of normal pregnancies, in the diagnosis and monitoring of gestational trophoblastic disease (hidatiform mola, invasive mola, coriocarcinom), the monitoring results of early fertilization in vitro in the prenatal screening Langdon – Down syndrome / trisomy 21, Edwards syndrome / trisomy 18, (have utility in the first trimester, weeks 10 to 14, their presence causing the therapeutic – triggering, therapeutic abortion, the practice known as double test or triple test).

In my study I am interested in the implication of beta-HCG hipohormonal pregnancy especially within the first trimester of pregnancy knowing that the maximum concentration is achieved in accordance with the table between weeks 8-12.

We found that production of this hormone decreases steadily to 20 weeks, reaching a concentration of 1 / 5 - 1 / 20 of maximum concentration in the first trimester after remaining in the plate to term.

In my study I have not pursued by the determinations performed in pregnancy (beta hCG, unconjugated estriol, progesterone) simply highlight the hipohormonal pregnancy as clinical entity encountered in obstetric practice in the form of abortion or premature birth.

Also I mention that I found the standard therapeutic procedures in different situations (gestagenic hormones antispasmodic, antiocitocics, diverse tokolitics) without substantive question about hipohormonal pregnancies (pregnancies characterized in particular by a significant decrease in beta-hCG, unconjugated estriol and progesterone, which were essentially the objective of my dissertation).

I was interested in three hormonal abnormalities especially in terms of practical work when in almost all situations the threat is of miscarriage or premature birth, and doctors administered progestogens and derived from progesterone, antiocitocics, antispasmodics, but without the usually performed hormonal doses to demonstrate obvious hipohormonal cause and therefore the appropriate therapeutic indication.

There are authors who do not take account of hipohormonal pregnancy but instead manages to prevent miscarriage and premature birth with hormonal drugs (Utrogestan, Aref, Duphaston, Gravibinon, Gravibinan, etc.) believing that such products can maintain pregnancy to term contributions.

Without an accurate diagnosis of pathogenic on abortion or premature birth, except hipohormonal pregnancy this treatment has no effect and / or it is useless in terms of both biomedical and material (these drugs have a high cost with regard to managing the constant to 32 SG).

Also say that in the normal course of pregnancy interruption this treatment may bring more disadvantages than benefits (delay the evacuation of a genetically altered product design, which once expelled without having known his biological quality can be a handicap to the family and society).

**Materials and methods**

Personal study and my own contributions start in 2006 and was extended for a period of 4 years (2006-2009).
This study I conducted in the Obstetrics Clinic II - Gynecology Clinic Emergency Hospital Craiova, clinical head Prof. Univ. Dr Mihai B. Braila, leader of my dissertation.

In this study I analyzed clinical cases of pregnant women admitted on which was systematically done in addition to normal ultrasound and laboratory investigations (blood count, blood group, RH, platelets, fibrinogen, Quick time, Howell time, glucose, urea, creatinins, uric acid, urine test) the specific investigations of my research respectively qualitative determinations (immunological test for pregnancy) and especially the quantitative plasma (determination of beta HCG, progesterone, unconjugated estriol after 27 gestational weeks).

Studied groups during the 4 years were required full clinical examination, paraclinical investigation, resolved obstetrical or by medical therapy administered (tokolitic, antispasmodic).

Group I included cases of abortion (threat, imminent, pending abortion, incomplete abortion) in the first (0-12 SG) and second trimester of gestation (12-28 SG) in which all data that estimated the current episode were detected and recorded at admission and a history of repeating miscarriage or pregnancies stopped from evolving, excluding other obvious cause of any other local, genital, general machinery and systems, mechanical causes, infectious, endocrine, genetic.

Group II consisted of cases of premature birth (threat, imminent) between 29 and 37 gestational weeks. In the case report forms have been recorded all data from current episode at admission, and any history of infertility, habitual abortion or repeating, single or repeating premature births, on single fetuses, twins or multiple pregnancies. I had studied a few cases of twins or multiple natural pregnancies or reproduced by artificial insemination or fertilization in vitro.

The two groups have reported the study in addition to specific laboratory explorations and treatments to maintain the pregnancy hormone medication (Aref, Utrogestan, Duphaston, Alilestrenol, Gravibinan, Gravibinon), beta-mimetic medication (Gynipral, Salbutamol, Pre-Odd ritodrine, Brycanil / terbutaline), usual antispasmodic medication (No - Spa Scobutil) antiprostaglandinics (aspirin, indomethacin), magnesium sulfate, and lately ocitocics receptor inhibitors such Atosiban / Tractocile. This last preparation introduced in recent years on the market I administrated in both hipohormonal pregnancies much wanted in the second trimester (after 25 SG) and especially the threat of premature birth (between 29-32 SG) not having hipohormonal pregnancies in the study cases between 33-37 SG.

I want to mention that in the hipohormonal pregnancies studied I preferred to lead tokolitic alternative therapy while maintaining constant hormone progesterone medication (Aref, Utrogestan) by continuing therapy after 32 SG magnesium sulphate, antispasmodics, such as No - Spa or Scobutil, beta mimetics such Brycanil, Gynipral, Salbutamol, and in some cases antiprostaglandinics thrombophilia and hipohormonal pregnancy I managed low weight molecular heparin injection (Clexan, Fraxiparin etc.).

In my study I took the following parameters:
- Patient Age
- Place of origin (urban, rural).
- Job, profession (intellectual, worker, farmer, student) vis a vis the socio-economic, family and employment.
- Gestational age at admission.
- Gestation and parity.
- Personal obstetrical history
- Personal history various pathological (infectious diseases, heart diseases, kidney disease, system / connective tissue diseases, genital / utero – gonads malformations, injuries, directly related pelvic – genital and abdominal injuries etc.).
Ultrasound and laboratory tests carried out (common and specific)
Conducted medical and obstetrical treatment / surgery.
Subsequent evolution and in some cases remote paraclinical subsequently
tracking investigation appropriate to the biological stage of life.

Group I
Miscarriage cases in the first and second trimester, in which we have observed a
significant decrease in the determinations of beta HCG and progesterone levels. Subnormal
HCG beta values to justify the existence of a hipohormonal pregnancy were below the
minimum value of the pregnancy week and reference interval (HCG mU.I. / ml).
Determination of progesterone plasma.
These values were determined in the same groups of patients admitted with abortion in
the first and second trimester which were concomitant with beta HCG and plasma
progesterone dosing.
What I can say is that many of these patients with abortions in the first and second
trimester were both hospitalized in the clinic for following of the course of pregnancy,
hormonal treatment while administered laboratory examinations being much easier to perform
than the rest of the abortions recorded in observation sheets and the register of abortions, but
that could not be caught in the study, leaving hospital good – willingly at the specialists
direction.
The fact is that many of these cases benefited of pregnancy maintenance treatment,
both hormonal (predominantly Utrogestan Aref or at various doses), treatment with
magnesium sulphate, Brycanil Gynipral, No - Spa or Scobutil. I mention that to those who
had a hipohormonal pregnancy the treatment was effective, with women benefiting from the
development of the pregnancy to term as subsequently improved. Doses of these drugs have
been directed by the attending physician and head of the clinic (I am talking about Aref doses
administered both orally and intra – vaginally, leading in some cases to about 1600 mg / 8
tablets per day with special beneficial effects). The same considerations can be made on
Utrogestan medicine. These preparations were the linchpin of treatment hipohormonal
pregnancy in situations of imminent threat of abortion in the first two trimesters of pregnancy.
Doing a clinical computing – statistical study on the total number of abortions during
the four years taken in the study (2006-2009) I concluded that a total of 1149 abortion cases
admitted in our clinic show the following:
Abortions overall studied during the four years that have made plasma dosages of beta
HCG and progesterone serum to prove the presence of a hipohormonal pregnancy numbers
were 440 (38.2%) of the total number of abortions recorded in the first two trimesters (1149).
Of these in the first trimester we saw a total of 86 cases (19.5%) and in the second trimester a
total of 52 cases (11.8%) of the total group of 440 cases investigated simultaneously for beta
HCG and plasma progesterone. They are labeled in my work as hipohormonal pregnancies
in the first two trimesters. Overall the number of hipohormonal pregnancies, studied by myself
in the above-mentioned period, was in the first two trimesters of 138 cases from a number of
440 cases studied from a total of 1149 cases of abortions admitted to Obstetrics and
Compared to the total number of abortions admitted and resolved the incidence of
pregnancies studied, 440, representing 38.2% and the incidence of hipohormonal pregnancies
was 31.3%, that means 138 cases studied, and 12% of the total number of abortions admitted.
The fact that these percentages are very different analyzed groups and that in almost
all cases of abortion in the first two trimesters of pregnancy it is administrated progesterone
hormone medication more or less in excess proves that in reality the obstetrician physician
takes notice almost always treatment of a possible hipohormonal pregnancy even if this is not
argued as in my research with the laboratory to laboratory exploration (at least the determination of beta-HCG and progesterone plasma in dynamics).

Group II consists in cases of premature birth (threat, imminent) between 29 and 37 gestational weeks. In the case report forms have been recorded all current episode data at admission, and any history of infertility, habitual abortion or repeating, single or repeating premature births, the single fetuses, twins or multiple pregnancies. I had studied a few cases of twins or multiple pregnancies natural or reproduced by artificial insemination or fertilization in vitro. I was interested in determining the predominant unconjugated estriol as a marker of fetal activity - described placental Dickfaluzzi since 1962 under the name of „feto – placental unity”.

Unconjugated estriol (E3) is the predominant estrogen hormone in the blood and urine of the pregnant women. Most of the circulating estriol is a unit of feto – placental result of 16 – alpha – hydroxy – dehydroepiandrosterone, a precursor, synthesized in the fetal adrenals and converted to estriol by fetal liver and placenta. Normal production of this hormone is from about 27 to termen/40 SG, a fundamental indicator of the integrity of feto – placental and fetal wellbeing.

Most circulating estriol is composed of conjugated forms that are excreted in urine, unconjugated estriol is generally present only at a rate of 9%. During normal development of fetal estriol production gradually increases reaching a maximum around the age of 36 SG. Sequential monitoring estriol levels in pregnancies examined by me has had an important clinical value in the dynamic tests carried out more than in isolation.

The fact to which I added the determination of plasma progesterone, allowed me to intervene therapeutically in the cases studied in group II. I mention that while the lower levels of estriol permanently reduce the possibility of an abrupt rise to conclusion fetal suffering more or less serious that can lead to intrauterine fetal death. The concomitant determination of progesterone plasma and unconjugated estriol we have made in the context of these cases demonstrate the importance of hipohormonal pregnancy to circumscribe a more accurate, appropriate and effective conduct in maintaining the pregnancy to term not being the case of fetuses with affected genetic / chromosomal viability or otherwise, malformed fetuses, which is the primary discharge conduct of pregnancy or reproductive failure to maintain a schedule.

The inclusion of this distribution is important both in terms of exploration made and I mean the determination of unconjugated estriol and progesterone in plasma, related to the usual investigations and treatment indications given tokolitic respectively pro – gestational progesterone and its derivatives only administered in group II, 29-33 SG, and the other preparations such as magnesium sulfate, beta mimetics (Gynipral, Brycanil, salbutamol), antispasmodics (No - Spa Scobutil) and lately ocitocics inhibitors (Atosiban / Tractocile), which could be administered in both groups. Mention that treating physicians have given antiprostaglandinics (aspirin, indomethacin), and in some cases with hematological disorders or low molecular collagen weight, heparin (Clexan, Fraxiparină). The administration had no direct connection with the treatment on the hipohormonal pregnancy studied, but had a
beneficial effect on pathological manifestations of avoiding any type of maternal thromboembolism, complications sometimes prognosis infaust feto – maternal.

Determination of unconjugated estriol plasma.

Determination of plasma progesterone.

During the pregnancy a majority of the clinical – laboratory trials often performed progressively increase progesterone concentrations reaching approximately 100 times higher than its constant level prior to pregnancy. The uterus during the pregnancy is the most important target organ of progesterone and I refer particularly to the myometrium. Progesterone has an inhibitory tocolitic effect on the uterine musculature and during the pregnancy is synthesized in excess by the placenta. It is a fact well known by all the clinicians that well secreted progesterone by the placenta leads to a much easier to – term carried pregnancies without the risk of miscarriage or premature births. Csapo in 1962 was the one who first introduced the „theory of progesterone blockage”; on maintaining pregnancy and labor determinism. The presence of progesterone in natural or artificial excess by exogenous administration is guarantee to maintain the pregnancy without any pre-existing disease or concomitant specific feto – maternal.

Hipohormonal pregnancy between 29-37 SG was highlighted by me on the two studied groups, A and B.

Results, Discussion

In this study we analyzed clinical cases of pregnant women admitted systematically, they were carried out besides ultrasound and paraclinical normal laboratory investigations (blood count, blood group - RH, platelets, fibrinogen, Quick time for Howell, glucose, urea, creatinin, acid uric urine) and specific investigations of my research that qualitative measurements (immunological test for pregnancy) and especially the quantitative plasma (determination of beta HCG, progesterone, unconjugated estriol after 27 gestational weeks).

Studied groups during the 4 years were required full clinical examination, paraclinical investigation, resolved obstetrical or medical therapy administered (tokolitic, antispasmodic).

Group I included cases of abortion (threat, imminent) in the first and second trimester of pregnancy at which all data have estimated that the current outbreak was detected and recorded at admission, and repeating history of miscarriage or terminated pregnancy evolving, excluding other obvious cause of any other local, genital, general machinery and systems, mechanical causes, infectious, endocrine, genetic.

Group II consisted of cases of premature birth (threat, imminent) between 29 and 37 gestational weeks. In the case report forms have been recorded all current episode data at admission, and any history of infertility, habitual abortion or repeating, single or repeating premature births, the single fetuses, twins or multiple pregnancies. I had studied a few cases of twins or multiple pregnancies natural or reproduced by artificial insemination or fertilization in vitro.

In the results obtained by analyzing the two groups we found the following:

Group I included a total of 440 pregnant women from a total of 1149 abortions in the first and second trimester representing a 38.29% percentage of cases hospitalized for maintaining pregnancy, abortion and imminent threat. In these cases during the four years I have led by at least three paraclinical harvesting beta HCG every patient and the plasma progesterone. The cases have been rigorously selected on both clinical and laboratory criteria to the exclusion from the study at the outset genital or other local general circumstances could possibly interfere with the etiopathogenesis of spontaneous abortion in the first two trimester turned out the light of a possible direct hipohormonal concurrent pregnancy.

Group II consisted of cases of premature birth (threat, imminent) between 29 and 37 gestational weeks. In the case report forms have been recorded all current episode data at
admission, and any history of infertility, habitual abortion or repeating, single or repeating premature births, the single fetuses, twins or multiple pregnancies. I had studied a few cases of twins or multiple pregnancies natural or reproduced by artificial insemination or fertilization in vitro.

Number of pregnant women investigated during 2006 - 2009 was 1957 out of a total of 5671 hospitalized premature births SJUC clinic II, representing a 34.50% share. Of the cases investigated for maintenance of pregnancy, respectively imminent threat of premature birth, we found a number of 319, 16.30%, Hipohormonală pregnancies. In these cases during the four years we have led by at least three harvests paraclinical every patient unconjugated estriol and progesterone levels. Cases were selected on both clinical and laboratory criteria for excluding from the study at the outset genital or other general local circumstances could interfere with a possible etiopathogenesis of premature births among 29-33 SG, group II A, and 34 - SG 37, group II B.

In conclusion of my dissertation on hipohormonal pregnancy I would like to mention that it exists and as such we have shown a both clinical – paraclinical first two trimesters of pregnancy (group I, 138 cases, 31.36% from a batch of 440 sent to investigate a total of 1149 hospitalized in the clinic abortion during the 4 years of study) and in the last trimester (group II, 319 cases, 16.30% of a batch of 1957 sent to investigate a total of 5671 births premature hospitalized during the four – year clinical study).

I mention that there are some really significant difference between the incidence of the first two hipohormonal pregnancy trimesters (31.36%) than in the third trimester of hipohormonal pregnancy (16.30%).

Without establishing a correlation between these percentages I must say that the difference is justified due to the fact that a number of obstetricians attaches great importance to the predominant hormone progesterone tokolitic treatment with other drugs mentioned during the trial, which effectively results in the maintenance of pregnancy for the third trimester, thus avoiding a series of failures of human reproduction. If the percentages were reversed there would be no hipohormonal pregnancy and mz hypothesis would not have been the subject of a dissertation thesis. The fact that we found these percentages correlated with other parameters studied, clinical and laboratory leads me to believe that the pregnancy is a complex hipohormonal entity present in everyday business practice and obstetrician that attaches much less importance compared with other pathologies type of preeclampsia / eclampsia, placenta or premature departure retroplacental hematoma – apoplexy, utero – cord, placenta inserted below and / or praevia, etc., situations where the mothers life and the fetus are endangered. I have not heard so far that a child or woman died because he was expelled from a hipohormonal pregnancy, but I must recognize that many of these diseases can or may accompany the hormonal categorical decisions, with insufficient or yellow body in placental trophoblast, the beta HCG, progesterone, unconjugated estriol factors that are determinant in leading, developing and maintaining a to term pregnancy.

Conclusions

I studied hipohormonal pregnancy over four years (2006-2009) in the Clinic II of Obstetrics - Gynecology, Emergency County Hospital Craiova.

The study focused on the detection of hipohormonal pregnancy both clinical and paraclinical (ultrasound, Blood and urine determinations usual,) and specific paraclinical hormone made in various laboratories (beta HCG plasmic, plasmic progesterone, unconjugated plasmic estrogens).
I divided my research, the study hipohormonal pregnancy in two groups: group I, the first two trimesters of pregnancy first trimester (0-12 S: G), second trimester (12-28 SG), group II (group II, 29 - SG 33, group II B, 34-3

In group I hipohormonal pregnancy incidence was in 138 cases of 440 cases explored from a total of 1149 abortions. The incidence of hipohormonal pregnancy I found it in 138 cases 31.36% respectively.

In group II hipohormonal pregnancy incidence was 319 cases in 1957 cases explored from a total of 5671 premature births. Hipohormonal pregnancy incidence was found in 16.30% of the cases explored. I mention at this point because we could not investigate all the various reasons, all the abortions, or the total of premature births cases in the clinic resuming only on the accessible cases to me that we have investigated complex clinical – paraclinical.

The hipohormonal pregnancy that we investigated it in group I (the first two trimesters) I showed a paraclinical determination by beta HCG and progesterone levels and they are much reduced in the 138 cases studied.

The hipohormonal pregnancy that we investigated in group II, I highlighted by paraclinical determinations of unconjugated estriol and progesterone, being much reduced in the 319 cases studied.

Hipohormonal pregnancy cases taken in the study were excluded from the start another preexistent pathology, concomitant or exacerbated of pregnancy (preeclampsia / eclampsia, uterus – placenta seizures, placenta praevia, diabetes, heart disease or hematologic, collagen, cromozomial aberrations, malformations) that could interfere with a possible hormone insufficiency in the pregnancy, by yellow body, or placental trophoblast or unit insufficiency fetal – placental shortages or fetal corticosuprarenal, fetal liver, placental trophoblast.

In the cases studied by me I took into account hipohormonal factors that determined discontinuation of normal course of the pregnancy in the first two trimesters, either in trimester 3 by excessive lowering of the synthesis and discharge of beta HCG, unconjugated progesterone and estriol. These are key factors for maintaining gestation to 40 SG in the context of the synthesis and reducing their discharge I noted in my study that maintaining that pregnancy is compromised, abortion with irreparably fetus abortion or premature birth.

An important aspect of my research has been the tokolitic treatment alternative given both in group I and group II. This tokolitic treatment is mentioned in detail in the paper was given by all colleges, without taking into account whether it is a hipohormonal pregnancy as a nosological entity or other maternal – fetal pathology that could lead to safer or less safe and another failure of synthesis and discharge of beta HCG, progesterone, unconjugated estriol likely to be present in other conditions excluding hipohormonal pregnancy. In my study, I insisted on hipohormonal pregnancy and I remembered that I often work mainly interested in its existence than any other pathologies identified maternal – fetal clinical - paraclinical.

In the analyzed hipohormonal pregnancy we have studied the parameters:

- Patient age.
- Place of origin.
- Socio – professional
- Gestational age at admission
- Gestation and parity.
- Personal obstetrical history
- Personal history various pathological

Analyzing these parameters we found that some of them might be risk factors for hipohormonal pregnancy: patient age, place of origin, gestation, parity, gestational age at admission, personal history of obstetrics. All these parameters were favoring influence on the
case studied by me on the incidence of hipohormonal pregnancy, they were widely reported throughout the paper.

Once hipohormonal pregnancy is diagnosed clinic – paraclinical requires dispensary, hospital possibly appropriate hospitalization, effective ultrasound monitoring and laboratory, aiming at its development with appropriate treatment both in and outside the hospital.

Treating the hipohormonal pregnancy is complex, having regard to the administration of progesterone preparations and / or progesterone derivatives (Aref, Utrogestan, Duphaston, Gravibinon, Gravibinan, Alilestrenol) associated with alternative therapy with beta mimetics (Gynipral, Salbutamol / Ventolin, Ritrodrină / Pre - Par, terbutaline / Brycanil), magnesium sulfate, common antispasmodics (Spasfon - lyoc, No – Spa Scobutil, Papaverine), antiprostaglandinics (Aspirin, Indomethacin), Nitroglycerin (sublingual or patches) receptor inhibitors ocitocici (Atosiban / TRACTOCILE).

Cases that we have had in clinical – paraclinical studies (group I, group II 138 and 319 457 cases in total) have completed 205 pregnancy rate of 45% . These cases are normally born or caesarean section removal of normal fetuses, without any complications, maternal – fetal development that could possibly be put into a hipohormonal pregnancy and / or alternative treatment carried out to maintain their pregnancy to term.

Hipohormonal pregnancy is a solitary obstetric pathological entity but may be coexistent with other feto – maternal pathology. In my study the incidence in group I was 31.36% and 16.30% in group II. On average adding the two lots and dividing to 2 shows an incidence of hipohormonal pregnancy studied by me of 23.83%. I can not comment on this percentage with other studies though I have looked in the past decade in the specialized literature on the incidence of hipohormonal pregnancy.

But I can say that there are studies in the world in which the decrease of beta HCG, plasmic progesterone and unconjugated estriol were found as other obstetrical pathologies unlabeled as hipohormonal pregnancy. They were shown as a double test, triple test, and associated abnormalities alpha 1 feto fetal protein as a prognostic for the trisomy 21 – Langdon syndrome – Down syndrome, trisomy 18 Edwards syndrome, trisomy 13 Patti, syndrome Crie-du-Chat chromosome aberration of the autosomal short arm of chromosome 5.

For me it was important to determine the clinical – paraclinical hipohormonal pregnancy outside all these etiopathogenic obstetrics contexts, the incidence observed by me being 23.83%. This incidence may be considered high compared with other obstetrical pathologies. It reflects the biological reality of my study being conducted excluding other severe obstetric pathologists. All these issues I have stated and supported by personal research on the cases studied in Clinic II of Obstetrics – Gynecology Clinic Emergency County Hospital Craiova is coordinated by Prof. D. Dr. Mihai B. Braila.

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