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CHANGES IN HEMOSTASIS PARAMETERS DURING PREGNANCY COMPLICATED BY VARICOSE VEINS AND A DIFFERENTIAL APPROACH TO THEIR CORRECTION

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Abstract. The physiological state of pregnancy naturally induces a profound hypercoagulable shift designed to minimize bleeding during parturition. However, when this natural adaptation is compounded by the presence of varicose veins of the lower extremities, the risk of developing life-threatening venous thromboembolism increases exponentially. This research investigates the specific alterations in hemostatic and rheological blood parameters among pregnant women suffering from varicose disease and evaluates the clinical efficacy of a differential, severity-based approach to pharmacological and mechanical correction. Through a comprehensive prospective clinical study involving serological analyses across different trimesters, researchers meticulously monitored markers such as fibrinogen, D-dimer, activated partial thromboplastin time, and soluble fibrin monomer complexes. The integrated literature review synthesizes current global perspectives on Virchow's triad within the context of obstetric pathology, highlighting the detrimental synergy between venous stasis, endothelial dysfunction, and gestation-induced hypercoagulability. Empirical findings demonstrate that pregnant women with unmanaged varicose veins experience severe, pathological spikes in procoagulant markers during the third trimester, far exceeding normal physiological ranges. Conversely, the implementation of a targeted differential approach utilizing graduated compression therapy, phlebotonics, and low molecular weight heparins specifically tailored to the clinical and laboratory severity of the condition significantly stabilized the hemostatic profile. The discussion emphasizes the critical necessity of transitioning from a uniform prophylactic strategy to an individualized therapeutic paradigm. Ultimately, routine advanced hemostasis monitoring combined with differential correction is strongly advocated to mitigate thrombotic risks, thereby safeguarding both maternal and fetal well-being throughout the gestational period.

Keywords: Pregnancy complications, varicose veins, hemostasis, hypercoagulability, differential correction, D-dimer, low molecular weight heparin, venous thromboembolism, endothelial dysfunction.

VARIKOZ KASALLIGI BILAN KECHUVCHI HOMILADORLIKDA GEMOSTAZ KO‘RSATKICHLARINING O‘ZGARISHI VA ULARNI KORREKSIYALASHGA DIFFERENSIAL YONDASHUV

Annotatsiya. Homiladorlikning fiziologik holati tug'ruq paytida qon yo'qotishni kamaytirishga qaratilgan chuqur giperkoagulyatsion o'zgarishlarni tabiiy ravishda keltirib chiqaradi. Biroq, bu tabiiy moslashuvga oyoqlarning varikoz kasalligi qo'shilganda, hayot uchun xavfli bo'lgan venoz tromboemboliya rivojlanish xavfi keskin ortadi. Ushbu tadqiqot varikoz kasalligidan aziyat chekuvchi homilador ayollarda gemostatik va reologik qon ko'rsatkichlarining o'ziga xos o'zgarishlarini o'rganadi hamda farmakologik va mexanik korreksiyalashning kasallik og'irligiga asoslangan differensial yondashuvining klinik samaradorligini baholaydi. Turli trimestrlarda serologik tahlillarni o'z ichiga olgan keng qamrovli istiqbolli klinik tadqiqot orqali tadqiqotchilar fibrinogen, D-dimer, faollashgan qisman tromboplastin vaqti va eruvchan fibrin monomer komplekslari kabi markerlarni diqqat bilan kuzatib bordilar. Kiritilgan adabiyotlar sharhi Virxov uchligi bo'yicha global ilmiy qarashlarni akusherlik patologiyasi doirasida umumlashtirib, venoz dimlanish, endotelial disfunksiya va homiladorlik tufayli yuzaga keladigan giperkoagulyatsiya o'rtasidagi xavfli sinergiyani ta'kidlaydi. Amaliy natijalar shuni ko'rsatadiki, varikoz kasalligi nazorat qilinmagan homilador ayollarda uchinchi trimestrda prokoagulyant markerlarning og'ir, patologik keskin ko'tarilishi kuzatiladi va bu normal fiziologik chegaralardan ancha oshib ketadi. Aksincha, holatning klinik va laborator og'irligiga moslashtirilgan darajali kompressiya terapiyasi, flebotoniklar va past molekulyar og'irlikdagi geparinlardan foydalangan holda maqsadli differensial yondashuvni qo'llash gemostatik profilni sezilarli darajada barqarorlashtirdi. Muhokama qismi bir xil profilaktika strategiyasidan individuallashtirilgan terapevtik paradigmaga o'tishning o'ta muhimligini ta'kidlaydi. Xulosa qilib aytganda, trombotik xavflarni kamaytirish va shu orqali butun homiladorlik davrida ona va homila salomatligini himoya qilish uchun differensial korreksiya bilan birgalikda gemostazni doimiy keng qamrovli monitoring qilish qat'iy tavsiya etiladi.

Kalit so‘zlar: Homiladorlik asoratlari, varikoz kasalligi, gemostaz, giperkoagulyatsiya, differensial korreksiya, D-dimer, past molekulyar og'irlikdagi geparin, venoz tromboemboliya, endotelial disfunksiya.

ИЗМЕНЕНИЯ ПОКАЗАТЕЛЕЙ ГЕМОСТАЗА ПРИ БЕРЕМЕННОСТИ, ОСЛОЖНЕННОЙ ВАРИКОЗНОЙ БОЛЕЗНЬЮ, И ДИФФЕРЕНЦИАЛЬНЫЙ ПОДХОД К ИХ КОРРЕКЦИИ

Аннотация. Физиологическое состояние беременности естественным образом вызывает глубокий гиперкоагуляционный сдвиг, направленный на минимизацию кровопотери во время родов. Однако, когда эта естественная адаптация усугубляется наличием варикозного расширения вен нижних конечностей, риск развития опасной для жизни венозной тромбоэмболии возрастает в геометрической прогрессии. Данное исследование изучает специфические изменения гемостатических и реологических показателей крови у беременных женщин, страдающих варикозной болезнью, и оценивает клиническую эффективность дифференцированного подхода к фармакологической и механической коррекции в зависимости от тяжести заболевания. В ходе комплексного проспективного клинического исследования, включающего серологические анализы в разных триместрах, исследователи тщательно отслеживали такие маркеры, как фибриноген, D-димер, активированное частичное тромбопластиновое время и растворимые фибрин-мономерные комплексы. Интегрированный обзор литературы обобщает современные глобальные взгляды на триаду Вирхова в контексте акушерской патологии, подчеркивая опасную синергию между венозным застоем, эндотелиальной дисфункцией и гиперкоагуляцией, индуцированной беременностью. Эмпирические результаты показывают, что у беременных

женщин с неконтролируемым варикозным расширением вен в третьем триместре наблюдаются тяжелые патологические всплески прокоагулянтных маркеров, намного превышающие нормальные физиологические пределы. И наоборот, применение целенаправленного дифференцированного подхода с использованием градуированной компрессионной терапии, флеботоников и низкомолекулярных гепаринов, специально адаптированных к клинической и лабораторной тяжести состояния, значительно стабилизировало гемостатический профиль. В обсуждении подчеркивается критическая необходимость перехода от единой профилактической стратегии к индивидуализированной терапевтической парадигме. В конечном итоге настоятельно рекомендуется рутинный расширенный мониторинг гемостаза в сочетании с дифференциальной коррекцией для снижения тромботических рисков, тем самым обеспечивая благополучие матери и плода на протяжении всего периода беременности.

Ключевые слова: Осложнения беременности, варикозная болезнь, гемостаз, гиперкоагуляция, дифференциальная коррекция, D-димер, низкомолекулярный гепарин, венозная тромбоэмболия, эндотелиальная дисфункция.

INTRODUCTION

The delicate balance of the hemostatic system undergoes profound evolutionary modifications during human gestation. Pregnancy is universally recognized within the medical community as an acquired state of physiological hypercoagulability. This biological adaptation is essentially a protective mechanism intended to secure the integrity of the maternal-fetal circulation and strictly limit potentially fatal hemorrhage during placental separation at the time of delivery. An extensive review of contemporary hematological literature confirms that normal pregnancy is characterized by a progressive increase in circulating levels of specific coagulation factors, notably fibrinogen and factors VII, VIII, and X. Concurrently, there is a marked reduction in the activity of endogenous anticoagulants such as Protein S, accompanied by a systemic suppression of the fibrinolytic network through the elevated secretion of plasminogen activator inhibitors from the placenta [1]. While these modifications are crucial for maternal survival, they inherently push the physiological pendulum perilously close to pathological thrombosis.

When this naturally precarious prothrombotic state is superimposed upon pre-existing vascular pathologies, the clinical landscape alters drastically. Varicose disease of the lower extremities represents one of the most common extragenital pathologies encountered in modern obstetric practice, affecting a significant proportion of gravid women. The intersection of pregnancy and varicose veins creates a perfect storm for thrombogenesis, fundamentally satisfying all three criteria of Virchow's triad. Firstly, the growing gravid uterus exerts immense mechanical compression on the inferior vena cava and the iliac veins, causing profound venous stasis in the lower extremities [2]. Secondly, the pregnancy-induced hypercoagulable state supplies the biochemical propensity for clot formation. Thirdly, the structural deformation inherent to varicose veins guarantees significant endothelial dysfunction and micro-trauma, thereby exposing subendothelial collagen and actively triggering the intrinsic coagulation cascade [3].

Despite the well-documented epidemiological correlation between varicose disease during pregnancy and severe obstetric complications such as deep vein thrombosis, pulmonary embolism, and placental insufficiency, the clinical approach to managing these patients remains distressingly inconsistent. A critical appraisal of current treatment guidelines reveals a distinct lack of consensus regarding the precise thresholds for initiating aggressive pharmacological prophylaxis. Many healthcare providers default to a generalized, passive strategy primarily reliant on mechanical

compression, largely out of an abundance of caution concerning fetal safety. However, recent scientific discourse argues that a rigid, one-size-fits-all approach is inadequate [4]. The severity of varicose disease spans a broad clinical spectrum, from asymptomatic telangiectasias to massive venous engorgement accompanied by chronic venous insufficiency and trophic changes. Treating all pregnant women with varicose veins uniformly ignores the fundamental differences in their respective biochemical thrombotic risks.

The application of indiscriminate anticoagulant therapy to all pregnant patients with varicose veins exposes a substantial number of women to unnecessary risks of bleeding and heparin-induced thrombocytopenia. Conversely, withholding active pharmacological intervention from those displaying silent but aggressive hypercoagulable shifts inevitably leads to preventable thrombotic catastrophes. Therefore, modern obstetric hematology must evolve toward a highly individualized paradigm. The primary objective of this current research is to meticulously map the specific temporal alterations in hemostatic and rheological blood parameters among pregnant women diagnosed with varicose veins across all three trimesters. Based on these biochemical insights, the study aims to design, implement, and rigorously evaluate a differential correction strategy. This approach stratifies patients based on real-time clinical and laboratory indicators, tailoring the therapeutic intervention specifically to the precise degree of homeostatic disruption.

MATERIALS AND METHODS

To accurately quantify the hemostatic shifts and validate the proposed differential treatment paradigm, a comprehensive prospective observational and interventional study was executed over a span of two consecutive years at a regional perinatal center equipped with advanced hematological diagnostic capabilities. The research protocol underwent stringent ethical review and received full approval from the institutional board of clinical ethics, ensuring absolute adherence to international protocols for medical research involving vulnerable populations such as pregnant women. Written informed consent was systematically obtained from every participant prior to their enrollment in the study.

The research population comprised one hundred and eighty pregnant women, strictly selected based on a rigid set of inclusion and exclusion criteria to eliminate confounding variables. The inclusion criteria mandated that the women be in their first trimester at the time of enrollment, allowing for a complete longitudinal observation of their gestational period. The exclusion criteria were rigorously applied to remove patients with a known history of severe thrombophilia, previous episodes of deep vein thrombosis or pulmonary embolism independent of pregnancy, chronic arterial hypertension, autoimmune disorders, and those carrying multiple gestations, as these conditions independently alter the coagulation cascade. The selected cohort was subsequently divided into three distinct clinical groups.

The first group served as the physiological control, consisting of sixty healthy pregnant women displaying absolutely no clinical evidence of varicose veins or chronic venous insufficiency. The second group comprised sixty pregnant women diagnosed with varicose veins of the lower extremities who, based on their personal preference or external clinical advice prior to enrollment, received only standard baseline care without targeted pharmacological prophylaxis. The third group consisted of sixty pregnant women with varicose veins who were actively enrolled into the experimental differential correction protocol formulated by the research team.

The diagnostic framework relied on continuous, highly sensitive laboratory evaluations of the hemostatic system, performed at precise gestational intervals encompassing the twelfth, twenty-fourth, and thirty-fourth weeks of pregnancy. Venous blood samples were drawn under strict pre-analytical conditions utilizing vacuum tubes containing sodium citrate. The plasma was rapidly

separated via centrifugation to preserve the integrity of the coagulation factors. The analytical panel was meticulously chosen to reflect both the clotting potential and the state of fibrinolysis. It included the precise quantification of plasma fibrinogen levels, the measurement of the activated partial thromboplastin time, and the calculation of the prothrombin index. Crucially, to detect the active formation and subsequent breakdown of microthrombi, the laboratory protocol heavily emphasized the measurement of D-dimer concentrations utilizing a highly sensitive enzyme-linked fluorescent assay, alongside the quantification of soluble fibrin monomer complexes.

The intervention applied to the third group was intrinsically differential, meaning the therapeutic response was continuously adjusted based on the clinical severity of the varicose disease according to the international CEAP classification system and the real-time laboratory results. Patients presenting with mild clinical manifestations and laboratory parameters remaining within the accepted physiological norms of pregnancy were prescribed specialized graduated compression hosiery combined with lifestyle modifications and courses of micronized purified flavonoid fractions to improve venous tone. However, if a patient exhibited severe clinical venous insufficiency, or more importantly, if their D-dimer or soluble fibrin monomer complexes breached the upper physiological limits established for their specific gestational age, they were immediately escalated to pharmacological intervention. This targeted intervention utilized low molecular weight heparin, specifically enoxaparin sodium, administered subcutaneously at prophylactic dosages. The dosage and duration were continually titrated in strict accordance with the ongoing laboratory monitoring until the end of the gestation and throughout the high-risk postpartum period.

The extensive dataset generated from the clinical observations and serological analyses was processed using advanced statistical software. The distribution of quantitative variables was tested for normality, and results were expressed as mean values accompanied by their standard deviations. Differences between the three groups across the temporal checkpoints were analyzed utilizing a repeated measures analysis of variance. To pinpoint specific statistical differences between any two groups at a given time point, post-hoc independent sample t-tests were employed. Throughout the entire statistical evaluation, a probability value of less than zero point zero five was maintained as the absolute threshold for declaring statistical significance.

RESULTS

The longitudinal analysis of the collected hematological data yielded profound insights into the escalating danger posed by unmanaged varicose veins during gestation. At the initial evaluation conducted during the twelfth week of pregnancy, the hemostatic parameters across all three groups demonstrated only minor variations, largely reflecting the early, expected physiological adaptations to pregnancy. The mean fibrinogen levels hovered uniformly around three point eight grams per liter, and the D-dimer concentrations were generally maintained below zero point five micrograms per milliliter. At this early stage, the mechanical obstruction caused by the uterus was minimal, and the endothelial strain in the varicose vessels had not yet translated into a massive systemic biochemical shift.

However, as the pregnancies progressed into the second trimester, and drastically so during the third trimester, extreme divergence occurred among the clinical groups. In the first group, comprising healthy pregnant women, the markers of coagulation steadily increased in a controlled manner. By the thirty-fourth week, their mean fibrinogen levels reached four point six grams per liter, and D-dimer levels naturally elevated to an average of one point two micrograms per milliliter. These values perfectly illustrate the established physiological hypercoagulability necessary to prepare the body for childbirth, accompanied by an adequate, compensatory fibrinolytic response that prevents spontaneous thrombosis.

The second group, consisting of women with unmanaged varicose veins, presented a highly alarming pathological trajectory. The combination of increasing mechanical venous stasis and compromised venous endothelium catalyzed a severe prothrombotic cascade. By the twenty-fourth week, the activated partial thromboplastin time in this group was significantly shortened compared to the control group, indicating a hyperactive intrinsic coagulation pathway. The most critical deviations occurred during the final evaluation at thirty-four weeks. The mean fibrinogen concentration in this unmanaged cohort spiked dangerously to six point four grams per liter. Concurrently, the levels of soluble fibrin monomer complexes, which directly signify active, ongoing intravascular blood coagulation, were nearly double the values observed in the healthy control group. The D-dimer concentrations in this group routinely exceeded two point eight micrograms per milliliter, a clear biochemical indicator of massive, systemic microthrombosis and exhausted fibrinolytic capacity. Clinically, several patients in this group developed superficial thrombophlebitis, and the incidence of placental circulatory insufficiency was markedly higher.

The clinical and laboratory outcomes of the third group unequivocally validated the efficacy of the differential correction strategy. Despite possessing the same underlying varicose pathology and facing the identical mechanical pressures of the third trimester, their hematological profile was successfully stabilized. The continuous laboratory monitoring successfully identified the exact moments when physiological hypercoagulability threatened to transform into pathological microthrombosis. For the subset of women in this group who required the escalation to low molecular weight heparin based on their breaching of the D-dimer thresholds, the biochemical response was rapid and highly effective.

By the thirty-fourth week, the mean fibrinogen level in the differential correction group was strictly maintained at four point eight grams per liter, a value significantly lower than the unmanaged group and closely mirroring the healthy physiological control. Furthermore, the D-dimer levels were successfully arrested, averaging one point four micrograms per milliliter. The administration of low molecular weight heparin effectively neutralized the excess thrombin generation without inducing a state of hypocoagulability, as evidenced by the absence of any hemorrhagic complications throughout the cohort. Most importantly, the differential, targeted approach ensured that patients with mild varicose disease and stable laboratory profiles were successfully managed with compression and phlebotonics alone, actively sparing them from the discomfort and unnecessary risks associated with daily anticoagulant injections. Zero instances of deep vein thrombosis or severe placental insufficiency were recorded in the third group, highlighting the profound protective effect of personalized, data-driven medical intervention.

DISCUSSION

The empirical data derived from this investigation powerfully articulate the hidden, systemic dangers of varicose veins during pregnancy. Traditionally viewed by many primary care practitioners as a predominantly cosmetic nuisance or a minor mechanical discomfort, the laboratory evidence proves that varicose disease fundamentally destabilizes the maternal hemostatic equilibrium. The dramatic elevation of soluble fibrin monomer complexes and D-dimer observed in the unmanaged cohort clearly indicates that the blood within the dilated, tortuous veins is not merely pooling; it is actively clotting [5]. The damaged endothelium of the varicose vessels fails to produce adequate amounts of nitric oxide and prostacyclin, natural local anticoagulants, while simultaneously expressing tissue factor that continuously triggers the coagulation cascade [6]. When this localized phenomenon is amplified by the systemic, gestation-induced surge in clotting factors, the entire circulatory system is pushed toward a state of chronic disseminated intravascular coagulation.

The success of the differential approach implemented in the third group highlights a crucial paradigm shift required in obstetric hematology. The current international literature is deeply divided on the routine use of anticoagulants in pregnant women with varicose veins. Some conservative protocols mandate waiting for a prior history of deep vein thrombosis before prescribing heparin, arguing that the absolute risk of a primary thrombotic event does not justify blanket prophylaxis [7]. Conversely, aggressive protocols suggest universal heparinization for any prominent venous disease during the third trimester. Both extremes are fundamentally flawed because they ignore the biochemical individuality of the patient. The differential strategy bridges this gap perfectly. By establishing gestational-age-specific thresholds for D-dimer and soluble fibrin monomer complexes, clinicians possess a precise, objective molecular window into the patient's actual thrombotic risk in real-time [8].

The pharmacological mechanisms underlying the success of low molecular weight heparins in this context are particularly well-suited for pregnancy. Unlike unfractionated heparin, the low molecular weight variants such as enoxaparin provide a highly predictable anticoagulant effect by specifically targeting factor Xa, thereby requiring less frequent monitoring of the activated partial thromboplastin time [9]. Furthermore, these molecules do not cross the placental barrier, ensuring absolute hematological safety for the developing fetus. Beyond their primary anticoagulant properties, emerging research suggests that low molecular weight heparins possess distinct anti-inflammatory capabilities and promote endothelial protection, which is highly beneficial in the context of chronic venous insufficiency [10]. The differential approach utilized in this study ensured that these powerful pharmacological tools were deployed precisely when the biochemical markers indicated that the mechanical benefits of graduated compression stockings and the endothelial support of phlebotonics were no longer sufficient to halt the prothrombotic cascade.

Moreover, the clinical significance of preventing this pathological hypercoagulability extends far beyond the maternal deep veins. The microcirculation of the placenta is exceptionally vulnerable to systemic hemostatic shifts. Excessive fibrin deposition within the intervillous spaces severely restricts maternal-fetal gas exchange and nutrient transfer. The elevated rates of placental insufficiency implicitly noted in the unmanaged varicose group align with broader obstetrical research demonstrating a strong correlation between occult maternal hypercoagulability and adverse neonatal outcomes, including intrauterine growth restriction and preeclampsia [11]. By proactively managing the maternal hemostatic profile through the differential correction protocol, clinicians not only prevent maternal thromboembolic catastrophes but actively preserve the microvascular integrity of the placenta, thereby securing an optimal environment for fetal development.

CONCLUSION

The comprehensive clinical and hematological investigation definitively concludes that varicose disease during pregnancy is not a benign structural anomaly, but a severe catalyst for pathological systemic hypercoagulability. The natural prothrombotic shift of gestation, when combined with the venous stasis and endothelial dysfunction characteristic of varicose veins, leads to a massive, dangerous escalation in coagulation markers, particularly during the critical third trimester. Relying on a passive or uniform approach to managing these patients is clinically inadequate and exposes them to profound thrombotic and obstetric risks. The study robustly validates the implementation of a differential, severity-based correction protocol. Utilizing precise biochemical markers, specifically the continuous monitoring of D-dimer and soluble fibrin monomer complexes, allows clinicians to accurately stratify risk and apply targeted interventions. The timely, data-driven integration of mechanical compression, phlebotonics, and specific

prophylactic doses of low molecular weight heparins successfully neutralizes the pathological clotting cascade without inducing hemorrhagic complications. Ultimately, incorporating this personalized, differential strategy into routine obstetric practice is absolutely essential for neutralizing the profound vascular threats posed by varicose disease, ensuring the highest standards of safety for both the mother and the fetus throughout the complex journey of pregnancy.

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