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An Insight Into Irisin Role In Gynecology and Obstetrics, A Review Article

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ABSTRACT

A transmembrane protein known as FNDC5 was identified in skeletal muscle, the heart, and the brain in 2002. A paper in 2012 described a cleaved protein called irisin is generated in response to exercise and may mediate some of exercise's positive benefits. Many articles have been published since then that have looked at the roles of irisin. Adipose tissue and metabolism have piqued researchers' attention because of their roles in the browning of white adipose tissue, which improves glucose homeostasis, obesity, type 2 diabetes, and atherosclerosis. Irisin's possible functions in bone remodelling and the brain have recently been discovered, including consequences that might be linked to Alzheimer's disease. Using novel markers to define disease pathophysiology reveals essential areas of concern for earlier diagnosis. Resulting in better treatment approaches and preventative strategies for illnesses affecting humans. This review examines various yet-to-be-determined applications and inconsistencies. We critically analyze current information and outline alternative ways to overcome existing uncertainties.

نظرة ثاقبة لدور الايرسين في أمراض النساء والتوليد مقال مراجعة

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الكلمات المفتاحية:
اضطرابات النمو لدى الاجنه
ايرسين
تسمم الحمل
هشاشة العظام

الملخص

تم التعرف على بروتين عبر الغشاء يُعرف باسم FNDC5 في العضلات الهيكلية والقلب والدماغ في عام 2002. وصفت ورقة بحثية في عام 2012 بروتينًا مشقوقًا يسمى ايرسين يتم إفرازه استجابة للتمرين وقد يكون له الفضل في بعض الفوائد الإيجابية للتمرين. تم نشر العديد من المقالات منذ ذلك الحين والتي نظرت في أدوار الايرسين . جذبت الأنسجة الدهنية والتمثيل الغذائي انتباه الباحثين بسبب دورها في تحول الأنسجة الدهنية البيضاء إلى اللون البني ، مما يحسن توازن الجلوكوز والسمنة ومرض السكري من النوع الثاني وامراض تصلب الشرايين. لقد تم مؤخرا اكتشاف وظائف الايرسين المحتملة في إعادة تشكيل العظام والدماغ ، بما في ذلك العواقب التي قد تكون مرتبطة بمرض الزهايمر. ان استخدام كواشف جديدة لتحديد الفيزيولوجيا المرضية للامراض هو نقطة جوهرية للتشخيص المبكر. حيث يفضي إلى أساليب علاجية واستراتيجيات وقائية أفضل للأمراض التي تصيب الإنسان. يفحص مقال المراجعة هذا مختلف التطبيقات والتناقضات التي لم يتم تحديدها بعد لدور الايرسين في الامراض النسائية بشكل نقدي ونضع الخطوط العريضة للطرق البديلة التي يملكها هذا الهرمون لتطبيقات مستقبلية محتملة.

Introduction

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Irisin is a recently identified hormone; stored in a precursor form in muscles; fibronectin Type III Domain contains 5 (FNDC5) protein [1]. It is activated by cleavage into proteolytic protein (irisin) before its secretion into the bloodstream. It was first discovered in rodents by Boström and colleagues in 2012. Irisin promotes a healthy metabolic process, induces thermogenesis, browns white adipose tissue resulting in positive energy balance, reduces body weight, and improves glucose homeostasis [2-3].

Furthermore, it exhibits anti-inflammatory, anti-apoptotic and anti-oxidative properties, which forms the elementary steps in the beginning, progression of many metabolic-related diseases [4].

It was extensively studied as a promising therapeutic agent for Type II diabetes and obesity. The expression of plasma irisin in skeletal muscle is primarily regulated by exercise and physical activity, a point of interest in clinical practice. Irisin is not a myokine only but an adipokine as well; both muscles and fatty tissues produce, making it a plausible marker for the integrity of muscle-fat-bone units integrity in osteoporosis-related research [4-5].

Irisin was proposed to have a defensive action against vascular injuries caused by atherosclerosis, hypertension, and diabetes. Its effect on increasing energy expenditure and improvement of insulin resistance alleviates endothelial cell injury. Moreover, It enhances endothelial cell proliferation and modulates smooth muscle cell [6].

Irisin was also separated from the human placenta and implicated in the abnormality of fetal growth patterns and early childhood.

The remarkable associations of irisin to metabolic diseases and important metabolic health issues devastating modern society; can contribute to discovering novel markers. However, few are known concerning the regulatory actions of irisin. This review will discuss the extraordinary actions and correlation that this new adipocytokine has regarding important metabolic health problems that empathize with women's health. Thus, opening the window for irisin related approaches aimed to promote women health.

Irisin and osteoporosis

Osteoporosis (OP) is a metabolic disease described 200 years and still fascinate researchers until now [7]. It is characterized by reduced bone mineral density and a T-score <−2.5. Commonly affect the older populace yet has a particular impact on postmenopausal women. Menopause is an aetiological risk for OP. At this challenging time, women suffer climacteric changes and hormonal depletion. Other risk factors include ethnicity, age, associated medical diseases, family history and drugs that implicate bone metabolism [8]. Previously OP screening and diagnosis relied on radiological imaging via Dual-energy X-ray absorptiometry (DEXA) scanning. Aiming for earlier diagnosis, researchers suggested biochemical screening. Indeed OP was a disease that is better prevented than treated. Yan et al . declared that older women have lower concentrations of irisin than healthy controls [9]. Wu et al. study discussed simial results, although his analysis recruited both genders, not only older women [10]. Singhal V et al. reported lower irisin values for young amenorrheic women compared to menstruating control [11].

Irisin improvement to bone strength is portrayed through multiple pathways. First, Irisin positively stimulates bone-forming markers via enhancing Myoblast differentiation to osteoblast (bone-forming cells) [12]. Second, it reduces osteoclast (bone resorption cells). Thus it contributes to strengthing mineral bone density. Moreover, it increases vascularity of the periosteum among the long bones, one of which is the hip bone. A common site for osteoporotic fragility fractures in postmenopausal women [13]. The ageing process, hormonal changes associating with menopause, sedentary lifestyle in the older populace and the decrease in physical activity all afflict muscle mass into wastage. Weakening of muscle will consequently weaken bone. Irisin suggested linking bone-muscle cross-talk; experiments in rats' models suggest a similar correlation in humans [14]. The imbalance between anabolic and catabolic activity inside bony structures is another proposed OP hypothesis, that imbalance renders the scale to catabolism consequently manifested as osteoporosis. Roomi et al. study discussed lower plasma levels of irisin as a marker for oxidative stress that contributed to OP changes in postmenopausal women [15]. The influence of irisin in neuronal cell development and function is receiving more attention in neurodegenerative disorders such as Alzheimer's and Parkinson's. This might be the missing point defining the link between healthy brains and physical activity [16].

In summary, irisin was investigated not as a marker but as a therapeutic agent in the OP with promising results regarding neuronal and muscle disease.

Irisin and preeclampsia

Preeclampsia (PE) is a pregnancy-specific syndrome described in 400 BC by Hippocrates. Defined as new-onset hypertension and presence of proteinuria in previously normotensive pregnant females after completed 20 weeks of pregnancy. In the absence of proteinuria, new-onset hypertension associated with end-organ dysfunction can diagnose PE [17]. The global incidence of PE is 5% to 10 %. The syndrome is characterized by vasospasm, hemoconcentration, and ischemic changes in the placenta, brain, liver, and kidney [18].

It is primarily a placenta disease with a grave feto-maternal complication that extend far below the pregnancy period. Till now, the exact aetiology of preeclampsia remains vague. A better understanding of its pathophysiology can improve our prediction and enhance obstetric care [19]. FNDC5; irisin precursor was found in the placenta of normal pregnancies, and its levels scored low in preeclamptic women compared to healthy controls. It was presented as a possible marker in preeclampsia. Pregnancy is a state of anabolic condition where positive energy balance is noticed and the marked accumulation of adipose tissue [20]. As pregnancy advances, irisin levels increase, and it exhibits a linear relationship with increasing insulin resistance. Irisin rise in pregnancy was accredited to the placenta [21].

Other researchers speculated that increment is a compensatory reaction due to insulin resistance proved by other markers as leptin. Such an increase was the reason behind decreases in body temperature and fat gaining in pregnancy [22]. Studies addressed irisin role in preeclampsia and provided conflicting results. Some has found significant correlations with maternal blood pressure and proposed its role in regulating blood pressure [23] others gave opposing result [24].

A trend of low serum irisin was correlated to the incidence of PE. However, all studies agreed it fails to be statistically significant [22-24]. Zhang et al. evaluated the role of irisin in discriminating the severity of PE and declared that it was not a useful marker [23].

Foda et al. reported that irisin levels were lower in mild preeclamptic than normotensive controls, and it showed higher values among women who gave birth vaginally than those delivered by cesarean section [25].

The reason behind the conflicting result in reporting irisin correlation may be explained by many factors that affect its estimation; physical activity, body fat composition, type of food intake and time of sampling all were influential factors to its release. So patients should all be fasting, resting, and sampling should be done simultaneously for all [26].

In summary, serum irisin can serve as a potential marker for screening those destined to develop PE. However, its therapeutic role is yet to be discovered.

Irisin and fetal growth pattern

The control of fetal growth is complicated, influenced by maternal, placental, and fetal factors. The supply of nutrients and oxygen to the fetus through the placenta is critical for proper fetal development [27]. The inability of a fetus to develop according to its genetic potential is known as abnormal fetal growth. The fetus might be large or small for date [28]. Ultrasonic fetal measurements are used to determine the fetal growth trend. Fetal size is measured in terms of its size for gestational age and is shown on percentile charts based on both gestational ages as well as birth weight [29]. Recent studies have investigated irisin role as a regulator of fetal growth pattern for a possible association.

Al-Maini et al. conducted a prospective case-control study recruiting women in 37+0 to 40+6 weeks of a singleton pregnancy, divided into three sub-groups based on fetal growth milieu confirmed by ultrasound examination: Small, adequate, and large for a date. Serum level of irisin was evaluated for mothers and newly delivered babies [30]. The analysis revealed that small and growth-restricted

fetuses had significantly lower serum irisin levels than other groups. Although irisin scored high in large for date infants, it fails to show statistical significance versus adqueuant size infants, in accordance with other studies [31]. The gestational age was non-influential in regards to the serum irisin level; Keleş et al. study reported similar significant differences among gestational age of 34 weeks between small and adquent sized fetuses [32]. Maternal serum irisin showed no meaningful differences across the three subgroups, which imply that it has no role in the disturbed metabolic activity associating small and FGR [33]. Upon correlating serum irisin levels to the neonatal birth weight, it showed a positive correlation (weight, Ponderal and index customized centile) [30]. Moreover, serum irisin was accredited for controlling new bone thermal temperature regulation by browning adipose tissues through the non-shivering mechanism; mediated via irisin [34]. The growth of large for date fetuses in the neonatal period showed slower weight gain than adquent size, which may be attributed to the higher energy expenditure observed in those babies; function mediated by irisin [35].

In conclusion, irisin is linked to growth regulation for the fetus in utero and early infancy. It is recommended as a predictor marker for the abnormal fetal growth pattern.

Conclusion

This study has provided evidence of the possible application of the newly discovered adipocytokine in gynaecology and obstetrics. Although irisin's value has not explored in full, many of its application is still diagnostic. Remarkable therapeutic advancement has been made in OP related research and in diabetes. Many diagnostic markers exist the debut is exploring the best applied for clinical practice.

Abbreviations and Acronyms

OP=Osteoporosis

PE=Preeclampsia

DEXA= Dual-energy X-ray absorptiometry

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References

[1]- Martinez Munoz IY, Camarillo Romero ED, Garduno Garcia JD. Irisin a novel metabolic biomarker: present knowledge and future directions. International journal of endocrinology. 2018 Oct 9;2018.

[2]- Zhang Y, Li R, Meng Y, Li S, Donelan W, Zhao Y, et al. Irisin stimulates the browning of white adipocytes through mitogen-activated protein kinase p38 MAP kinase and ERK MAP kinase signaling. Diabetes 2014; 63: 514–525

[3]- Zhang J, Valverde P, Zhu X, Murray D, Wu Y, Yu L, Jiang H, Dard MM, Huang J, Xu Z, Tu Q. Exercise-induced irisin in bone and systemic irisin administration reveal new regulatory mechanisms of bone metabolism. Bone research. 2017 Feb 21;5(1):1-4.

[4]- Askari H, Rajani SF, Poorebrahim M, Haghi-Aminjan H, Raeis-Abdollahi E, Abdollahi M. A glance at the therapeutic potential of irisin against diseases involving inflammation, oxidative stress, and apoptosis: an introductory review. Pharmacological Research. 2018 Mar 1;129:44-55.

[5]- Roca-Rivada A, Castelao C, Senin LL, Landrove MO, Baltar J, Crujeiras AB, et al. FNDC5/Irisin is not only a myokine but also an adipokine. PLoS ONE 2013; 11 8: e60563

[6]- Zhang Y, Mu Q, Zhou Z, Song H, Zhang Y, Wu F, Jiang M, Wang F, Zhang W, Li L, Shao L. Protective effect of irisin on atherosclerosis via suppressing oxidized low density lipoprotein induced vascular inflammation and endothelial dysfunction. PloS one. 2016 Jun 29;11(6):e0158038.

[7]- Utian WH, Schiff I. NAMS-Gallup survey on women's knowledge, information sources, and attitudes to menopause and hormone replacement therapy. Menopause. 2018 Nov 1;25(11):1172-9.

[8]- Roomi AB, AL-Salih RM, Ali SA. The Effect of Insulin Therapy and Metformin on Osteoporosis in Diabetic Postmenopausal Iraqi Women. Indian Journal of Public Health Research & Development. 2019;10(4):1544-9.

[9]- Yan J, Liu HJ, Guo WC, Yang J. Low serum concentrations of Irisin are associated with increased risk of hip fracture in Chinese older women. Joint Bone Spine. 2018 May 1;85(3):353-8.

[10]- Wu LF, Zhu DC, Tang CH, Ge B, Shi J, Wang BH, Lu YH, He P, Wang WY, Lu SQ, Zhong J. Association of plasma irisin with bone mineral density in a large chinese population using an extreme sampling design. Calcified tissue international. 2018 Sep 1;103(3):246-51.

[11]- Singhal V, Lawson EA, Ackerman KE, Fazeli PK, Clarke H, Lee H, Eddy K, Marengi DA, Derrico NP, Bouxsein ML, Misra M. Irisin levels are lower in young amenorrheic athletes compared with eumenorrheic athletes and non-athletes and are associated with bone density and strength estimates. PloS one. 2014;9(6).

[12]- Qiao X, Nie Y, Ma Y, Chen Y, Cheng R, Yin W, Hu Y, Xu W, Xu L. Irisin promotes osteoblast proliferation and differentiation via activating the MAP kinase signaling pathways. Scientific reports. 2016 Jan 7;6(1):1-2.

[13]- Nygaard H, Slettaløkken G, Vegge G, Hollan I, Whist JE, Strand T, Rønnestad BR, Ellefsen S. Irisin in the blood increases transiently after single sessions of intense endurance exercise and heavy strength training. PloS one. 2015;10(3).

[14]- Colaianni G, Mongelli T, Colucci S, Cinti S, Grano M. Crosstalk between muscle and bone via the muscle-myokine irisin. Current osteoporosis reports. 2016 Aug 1;14(4):132-7.

[15]- Badr Roomi A, Nori W, Mokram Hamed R. Lower Serum Irisin Levels Are Associated with Increased Osteoporosis and Oxidative Stress in Postmenopausal. Reports of Biochemistry and Molecular Biology. 2021;10(1):13-9.

[16]- Dun SL, Lyu RM, Chen YH, Chang JK, Luo JJ, Dun NJ, Irisin-immunoreactivity in neural and non-neural cells of the rodent, Neuroscience. 2013 Jun 14; 240():155-62

[17]- Nori W, Roomi AB,.Akram W. Platelet indices as predictors of fetal growth restriction in Pre-eclamptic Women . Revista Latinoamericana de Hipertensión. 2020;15(4): 280-285

[18]- Tan MY, Wright D, Syngelaki A, Akolekar R, Cicero S, Janga D, Singh M, Greco E, Wright A, Maclagan K, Poon LC. Comparison of diagnostic accuracy of early screening for pre-eclampsia by NICE guidelines and a method combining maternal factors and biomarkers: results of SPREE. Ultrasound in Obstetrics & Gynecology. 2018 Jun;51(6):743-50.

[19]- Ukah UV, De Silva DA, Payne B, Magee LA, Hutcheon JA, Brown H, Ansermino JM, Lee T, von Dadelszen P. Prediction of adverse maternal outcomes from pre-eclampsia and other hypertensive disorders of pregnancy: A systematic review. Pregnancy Hypertension. 2018 Jan 1;11:115-23.

[20]- Moreno-Navarrete JM, Ortega F, Serrano M, Guerra E, Pardo G, Tinahones F, Ricart W, Fernández-Real JM. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. J Clin Endocrinol Metab. 2013;98: E769–E778.

[21]- Fu J, Han Y, Wang J, Liu Y, Zheng S, Zhou L, Jose PA, Zeng C. Irisin lowers blood pressure by improving endothelial dysfunction via AMPK-Akt-eNOS-NO pathway in the spontaneously hypertensive rat. Journal of the American heart association. 2016 Oct 26;5(11):e003433.

[22]- Garcés MF, Peralta JJ, Ruiz-Linares CE, Lozano AR, Poveda NE, Torres-Sierra AL, Eslava-Schmalbach JH, Alzate JP, Sánchez ÁY, Sanchez E, Angel-Müller E. Irisin levels during pregnancy and changes associated with the development of preeclampsia. The Journal of Clinical Endocrinology & Metabolism. 2014 Jun 1;99(6):2113-9.

[23]- Zhang LJ, Xie Q, Tang CS, Zhang AH. Expressions of irisin and urotensin II and their relationships with blood pressure in patients with pre-eclampsia. Clin Exp Hypertens 2017;39:460 7.

[24]- Farhan FS, Findakly SB, Sersam LW. Serum irisin levels in normotensive and preeclamptic pregnancies. Mustansiriya Medical Journal. 2018 Jul 1;17(2):80

[25]- Foda AA, Foda EA. Effect of delivery on maternal and neonatal irisin level in normal and preeclamptic pregnant women. Pregnancy Hypertens 2017;10:226 9

[26]- Winn NC, Grunewald ZI, Liu Y, Heden TD, Nyhoff LM, Kanaley JA,et al. Plasma irisin modestly increases during moderate and high intensity afternoon exercise in obese females. PLoS One 2017;12:e0170690.

[27]- Dimasuay KG, Boeuf P, Powell TL, Jansson T. Placental responses to changes in the maternal environment determine fetal growth. Frontiers in physiology. 2016 Jan 29;7:12.

[28]- Vedmedovska N, Rezeberga D, Teibe U, Melderis I, Donders GG. Placental pathology in fetal growth restriction. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2011 Mar 1;155(1):36-40.

[29]- Oken E, Kleinman KP, Rich-Edwards J, Gillman MW. A nearly continuous measure of birth weight for gestational age using a United States national reference. BMC pediatrics. 2003 Dec;3(1):1-0.

[30]- Al-Maini EH, Mizher MS, Shafi FF. The Correlation of Maternal and Fetal Blood Irisin with Fetal Growth Pattern and Birth Weight. Systematic Reviews in Pharmacy. 2021;12(1):359-66.

[31]- Baka S, Malamitsi-Puchner A, Boutsikou T, Boutsikou M, Marmarinos A, Hassiakos D, et al. Cord blood irisin at the extremes of fetal growth. Metabolism - Clinical and Experimental.2015;64(11):1515-20

[32]- Keles E, Turan FF. Evaluation of cord blood irisin levels in term newborns with small gestational age and appropriate gestational age. SpringerPlus. 2016;5(1):1757

[33]- Çağlar M, Göksu M, Isenlik BS, Yavuzcan A, Yılmaz M, Üstün Y, Aydin S, Kumru S. Irisin in idiopathic foetal growth restriction. Journal of endocrinological investigation. 2014 Jul 1;37(7):619-24

[34]- Asakura H. Fetal and Neonatal Thermoregulation Journal of Nippon Medical School. 2004;71(6):360 70 -

[35]- Symonds ME, Pope M, Budge H. Adipose tissue development during early life: novel insights into energy balance from small and large mammals. Proceedings of the Nutrition Society. 2012;71(3):363-70.