

doi: 10.13241/j.cnki.pmb.2017.02.042

血清抑制素 B 评估成年隐睾患者术后睾丸功能恢复的临床价值*

董 莉 陶 惠[△] 王淑珍 许 英 张美春

(兰州军区兰州总医院体检中心 甘肃 兰州 730050)

摘要 目的:探讨血清抑制素 B(InhB)用于评价成年隐睾患者术后睾丸功能恢复的临床价值。**方法:**收集 2011 年 10 月~2015 年 9 月于我科就诊的 138 例成年隐睾患者作为观察组,另收集 100 例健康志愿者作为正常对照组。用双抗体夹心酶联免疫吸附法检测观察组患者术前、术后 30 天和 90 天及正常对照组的血清 InhB 水平,并参照 WHO 人类精液检查与处理实验室手册(第五版)方法进行精液常规检查。**结果:**与正常对照组比较,观察组患者术前、术后 30 天和 90 天血清 InhB 水平、精子活率、精子密度均明显降低,差异均有统计学意义($P < 0.05$)。观察组术后 30 天血清 InhB 水平、精子活率、精子密度与术前比较差异均无统计学意义($P > 0.05$),观察组术后 90 天血清 InhB 水平、精子活率、精子密度明显高于术前,差异均有统计学意义($P < 0.05$)。观察组术前、术后 30 天和 90 天的精液量与正常对照组对比差异均无统计学意义($P > 0.05$)。观察组术前、术后 30 天和 90 天及正常对照组血清 InhB 水平与精子浓度均呈正相关(观察组术前: $r=0.81, P < 0.05$, 观察组术后 30 天: $r=0.78, P < 0.05$, 观察组术后 90 天: $r=0.84, P < 0.05$, 正常对照组: $r=0.77, P < 0.05$)。**结论:**血清 InhB 用于评估成年隐睾患者术后睾丸功能恢复具有一定的临床应用价值。

关键词:血清抑制素 B; 隐睾; 睾丸; 功能

中图分类号:R697.22 文献标识码:A 文章编号:1673-6273(2017)02-363-03

The Clinical Value of Serum Inhibin B in the Evaluation of Testicular Function Recovery of Adult Patients after Cryptorchidism Surgery*

DONG Li, TAO Hu[△], WANG Shu-zhen, XU Ying, ZHANG Mei-chun

(The Department of Medical center, Lanzhou General Hospital of Lanzhou Military Area Command, Lanzhou, Gansu, 730050, China)

ABSTRACT Objective: To investigate the clinical value of serum InhB in the evaluation of testicular function recovery of adult patients after cryptorchidism surgery. **Methods:** A retrospective study was performed on 138 patients with cryptorchidism (observation group) and 100 healthy persons (control group). Double-antibody sandwich enzyme-linked immunosorbent assay was used to detect the levels of InhB in serum of patients (preoperation and 30, 90 d postoperation) and healthy persons. Semen parameter according to WHO laboratory manual for the examination and processing of human semen was detected. **Results:** The levels of serum InhB, sperm motility and sperm density preoperation and on the 30th, 90th day postoperation of observation group were obviously lower than those of the control group ($P < 0.05$). The levels of serum InhB, sperm motility and sperm density on the 30th day postoperation and preoperation of observation group showed no significant difference ($P > 0.05$). The levels of serum InhB, sperm motility and sperm density on the 90th day postoperation of observation group were obviously higher than those of observation group preoperation ($P < 0.05$). The levels of ejaculation sperm volume of observation group (preoperation and 30, 90 d postoperation) and control group showed no statistical significance ($P > 0.05$). The levels of serum InhB was positively correlated with the sperm density of observation group (preoperation and 30, 90 d postoperation) and control group (observation group preoperation: $r=0.81, P < 0.05$, observation group 30 d postoperation: $r=0.78, P < 0.05$, observation group 90 d postoperation: $r=0.84, P < 0.05$, control group: $r=0.77, P < 0.05$). **Conclusion:** InhB level could be helpful to evaluate the recovery of testicular function after cryptorchidism surgery of adult patients.

Key words: InhB; Cryptorchidism; Testicle; Function recovery

Chinese Library Classification(CLC): R697.22 **Document code:** A

Article ID: 1673-2673(2017)02-363-03

前言

隐睾是泌尿外科常见的先天性生殖系统畸形疾病之一,成人约占 0.3%^[1,2],是引起男性不育的主要因素之一,治疗方法为睾丸下降固定术^[3,4],但目前缺乏评估成年患者术后睾丸功能恢

复的有效指标。抑制素 B(InhibinB, InhB)是睾丸支持细胞直接分泌的产物,具有调控精子发生的作用,其在血清中表达水平可以反映和评价睾丸的功能^[5,6]。本次临床研究通过检测成年隐睾患者术前及术后血清 InhB 水平,探讨血清 InhB 检测在评估成年隐睾患者术后睾丸功能恢复中的临床意义及价值。

* 基金项目:国家自然科学基金项目(81170400)

作者简介:董莉(1981-),女,护师,从事临床专科护理研究,电话:13919938104, E-mail: 3225679824@qq.com

△ 通讯作者:陶惠(1981-),女,主管护师,主要从事临床医学检验研究,电话:0931-8995191, E-mail: 1511457694@qq.com

(收稿日期:2016-03-15 接受日期:2016-03-31)

1 资料与方法

1.1 一般资料

收集 2011 年 10 月~2015 年 9 月于我科就诊的 138 例成年隐睾患者作为观察组,以《中国泌尿外科疾病诊断治疗指南(2014 版)》为诊断标准^[1],年龄范围 22~26 岁,平均年龄(23.87±2.36)岁。其中,单侧隐睾 122 例(左侧隐睾 36 例、右侧隐睾 86 例),双侧隐睾 16 例;睾丸位于腹股沟管外环口位置 97 例,位于腹股沟管内位置 21 例,位于腹股沟管内环口位置 17 例,腹腔内 3 例。正常对照组 100 例,系健康志愿者,均已签署临床研究知情同意书。

1.2 研究方法

1.2.1 主要试剂和仪器 选购兰州科美特生物有限公司人血清 InhB ELISA 试剂盒,使用美国 Bio-tek 公司 ELx800 酶标仪进行检测。精液常规检查使用北京伟力新世纪科技发展有限公司 WLJY-9000 精子分析仪、低速离心机、37℃ 恒温水浴箱、医用冰箱。

1.2.2 标本采集 于清晨 7:00 抽取健康志愿者空腹禁食静脉血 3 mL,观察组患者于入院后 1、术后 30、90 d 清晨 7:00 抽取空腹禁食静脉血 3 mL,室温自然凝固 10~20 min,以 3000 r/min 离心 20 min 后留取上清液(置于-4℃ 医用冰箱保存),于 24 h 内将当天留取所有标本测定完毕。精液收集:禁欲 3~7 d

后,于每日 16:00,采取手淫方式收集精液,精液采集后,于 37℃ 恒温水浴箱温育精液标本 30 min,完全液化后进行精液常规检查。

1.2.3 标本检测 使用双抗体夹心酶联免疫吸附法检测观察组及正常对照组中血清 InhB 水平,试验过程严格按照说明书进行,将血清标本加样完毕后,测定 450 nm 波长处吸光度值,根据该值计算出各组中血清 InhB 水平。精液常规检查参照 WHO 人类精液检查与处理实验室手册(第五版)的标准及方法进行。

1.3 统计学方法

采用 SPSS15.0 软件进行统计分析,计量资料用均数±标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验,相关性分析采用 Pearson 相关分析,以 P<0.05 为差异有统计学意义。

2 结果

2.1 正常对照组及观察组患者手术前后血清 InhB 水平的比较

与正常对照组比较,观察组患者术前、术后 30 天和 90 天血清 InhB 水平均明显降低,差异均有统计学意义(P<0.05)。观察组术后 30 天血清 InhB 水平与术前比较差异无统计学意义(P>0.05),观察组术后 90 天血清 InhB 水平明显高于术前,差异有统计学意义(P<0.05)。

表 1 正常对照组及观察组患者手术前后血清 InhB 水平的比较($\bar{x} \pm s$)

Table 1 Comparison of the serum levels of InhB between the normal control group and the observation group at different time points($\bar{x} \pm s$)

Groups	Time point	n	InhB (ng/mL)
Observation group	Before operation	138	80.32±19.55 ^{▲#}
	At 30 days after operation	138	91.22±17.21 [▲]
	At 90 days after operation	138	115.66±10.86 ^{▲#}
Control group	Control group		201.07±38.16 [▲]

Note: [▲]P<0.05 compared with the normal control group; [●]P>0.05 compared with the observation group at 30 days after operation; [#]P<0.05 compared with the observation group at 90 days after operation.

2.2 正常对照组及观察组患者手术前后精液量、精子活率、精子密度水平的比较

观察组术前、术后 30 天和 90 天的精液量对比差异均无统计学意义(P>0.05),与正常对照组对比差异均无统计学意义(P>0.05)。观察组术前、术后 30 天和 90 天的精子活率、精子密

度均较正常对照组降低,差异均有统计学意义(P<0.05),观察组术后 30 天精子活率、精子密度与术前比较差异无统计学意义(P>0.05),观察组术后 90 天精子活率、精子密度明显高于术前,差异有统计学意义(P<0.05)。

表 2 正常对照组及观察组患者手术前后精液量、精子活率、精子密度水平比较($\bar{x} \pm s$)

Table 2 Comparison of the levels of ejaculation sperm volume, sperm motility and sperm density between the normal control group and the observation group at different time points($\bar{x} \pm s$)

Groups	Time point	n	Sperm volume (mL)	Sperm motility (a+b grade sperm ratio, %)	Sperm motility(10 ⁶ /mL)
Observation group	Before operation	138	2.16±1.05 [*]	12.32±3.15 ^{▲#}	9.34±3.23 ^{▲#}
	At 30 days after operation	138	2.07±0.98 [*]	14.19±3.24 [▲]	10.29±2.96 [▲]
	At 90 days after operation	138	2.21±0.87 [*]	29.16±10.12 ^{▲#}	20.21±13.45 ^{▲#}
Control group		100	2.27±0.91 [*]	40.23±11.35 [▲]	30.21±15.21 [▲]

Note: ^{*}P>0.05 compared with the normal control group. [▲]P<0.05 compared with the normal control group; [●]P>0.05 compared with the observation group at 30 days after operation; [#]P<0.05 compared with the observation group at 90 days after operation.

2.3 血清 Inhb 表达水平与精子浓度的关系

观察组术前、术后 30 天和 90 天及正常对照组血清 Inhb 水平与精子浓度均呈正相关(观察组术前: $r=0.81$, $P<0.05$, 观察组术后 30 天: $r=0.78$, $P<0.05$, 观察组术后 90 天: $r=0.84$, $P<0.05$, 正常对照组: $r=0.77$, $P<0.05$)。

3 讨论

因男科科普教育落后,尤其在某些偏僻落后地区,通常因不育而就诊的成人隐睾患者并不少见^[7,8],尽早手术治疗的目的是保护和改善患者的生育能力。临床常用评价睾丸生精能力的指标主要有促卵泡激素、黄体生成素、睾酮、精液常规、睾丸体积等,其特异性一般。由于缺乏评估隐睾术后睾丸功能恢复的检测指标,部分患者反复多次化验精液,并再次接受睾丸活检等有创检查,给患者带去一定的痛苦^[9]。因此,一旦隐睾诊断明确并接受手术后,了解睾丸功能恢复情况就显得尤为迫切。

Inhb 是一类分子量为 32kD 的糖蛋白激素,由睾丸支持细胞合成分泌,在血清中的表达水平与精子的发生、发育具有密切关联性,为曲细精管的发育提供支持作用。与血清 FSH 表达水平受到 GnRH、E₂、T 等激素的综合影响不同,Inhb 能够直接反映曲细精管生精上皮功能状态和睾丸整体功能,是评估精子发生、发育的血清学标志物之一,也是反映输精管功能的重要标志物^[10-15]。因此,本次临床研究采用血清 Inhb 作为检测和评估成年隐睾患者术后睾丸功能恢复的临床内分泌学指标。在睾丸支持细胞发育较差的患者中,如先天性性腺发育迟缓和隐睾的患者血清 Inhb 水平较低,提示睾丸功能不全,且血清 Inhb 水平越低,睾丸功能越差^[16-18]。本次临床研究发现成年隐睾患者血清 Inhb 水平、精子活率、精子密度均较健康人明显降低,而在术后 30 天,患者血清 Inhb 水平、精子活率、精子密度均有所上升,术后 90 d 血清 Inhb 水平、精子活率、精子密度均较术后 30 d 明显上升,提示随着术后睾丸功能的逐渐恢复,患者血清 Inhb 水平逐渐上升。进一步行相关性分析发现隐睾患者术前、术后 30 d 和 90 d 及正常对照人群血清 Inhb 水平与精子浓度均呈显著正相关,提示血清 Inhb 水平用于评估睾丸功能恢复具有一定的参考价值,而且可以降低甚至避免患者再次接受睾丸活检等有创检查的可能^[19-21],减轻患者的痛苦和经济负担。

综上所述,血清 Inhb 用于评估成年隐睾患者术后睾丸功能恢复具有一定的临床应用价值,进一步的研究将加大临床研究样本,密切监测 Inhb 水平、精子活率、精子密度等指标以明确隐睾术后睾丸功能恢复的时限和程度。

参考文献(References)

- [1] 中华医学会男科学分会.《男科疾病诊断与治疗指南(手册)》[M]. 人民卫生出版社, 2014: 122-161
Chinese Medical Association Andrology Branch. The guidelines of andrology disease diagnosis and treatment (manual) [M]. People's Health Publishing House, 2014: 122-161
- [2] Komarowska MD, Hermanowicz A, Czyzewska U, et al. Serum Bisphenol A Level in Boys with Cryptorchidism: A Step to Male Infertility[J]. Int J Endocrinol, 2015, 28: 973154
- [3] 中华医学会泌尿外科学分会.《中国泌尿外科疾病诊断治疗指南(2014 版)》[M]. 人民卫生出版社, 2014: 410-412
Chinese Medical Association Urology Branch. The guidelines of Chinese diagnosis and treatment of urological diseases (2014 edition) [M]. People's Health Publishing House, 2014: 410-412
- [4] Kempisty B, Jackowska M, Wozna M, et al. Expression and cellular distribution of INHA and INHB before and after in vitro cultivation of porcine oocytes isolated from follicles of different size [J]. J Biomed Biotechnol, 2012: 742829
- [5] Walton KL, Kelly EK, Chan KL, et al. Inhibin Biosynthesis and Activity Are Limited by a Prodomain-Derived Peptide [J]. Endocrinology, 2015, 156(8): 3047-3057
- [6] Breslin WJ, Paulman A, Sun-Lin D, et al. The inhibin B (Inhb) response to the testicular toxicants mono-2-ethylhexyl phthalate (MEHP), 1,3 dinitrobenzene (DNB), or carbendazim (CBZ) following short-term repeat dosing in the male rat [J]. Birth Defects Res B Dev Reprod Toxicol, 2013, 98(1): 72-81
- [7] 赵玉农, 方向明, 肖明, 等. 成人隐睾症治疗体会 [J]. 现代医药卫生, 2012, 24(28): 3781-3782
Zhao Yu-nong, Fang Xiang-ming, Xiao Ming, et al. Treatment of adult cryptorchidism[J]. Journal of Modern Medicine & Health, 2012, 24(28): 3781-3782
- [8] Hauser R, Skakkebaek NE, Hass U, et al. Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union[J]. J Clin Endocrinol Metab, 2015, 100(4): 1267-1277
- [9] 习明, 程璐, 万跃平, 等. 隐睾患者术后抑郁情况及抑郁相关因素分析[J]. 中华男科学杂志, 2015, 21(1): 57-60
Xi Ming, Cheng Lu, Wan Yue-ping, et al. Incidence of depression and its related factors in cryptorchidism patients after surgical treatment [J]. National Journal of Andrology, 2015, 21(1): 57-60
- [10] Maknaji Y, Harrison CA, Robertson DM. Feedback regulation by inhibins A and B of the pituitary secretion of follicle-stimulating hormone[J]. Vitam Horm, 2011, 85: 299-321
- [11] Smit M, Dohle GR, Wildhagen MF, et al. Can inhibin-B predict the outcome of microsurgical epididymal sperm aspiration in patients with suspected primary obstructive azoospermia [J]. Asia j Androl, 2007, 9(3): 382-387
- [12] Tsametsi C, Mintziori G, Lliadou P K, et al. Dynamic endocrine test of inhibin B and anti-Mullerian hormone in men with non-obstructive azoospermia [J]. Gynecol Endocrinol, 2011, 27(9): 661-665
- [13] Lambert, Messerlian GM, Harlow BL. The influence of depression, body mass index, and smoking on serum inhibin B levels in late reproductive-aged women [J]. J Clin Endocrinol Metab, 2006, 91(4): 1496-1500
- [14] 柴成伟, 刘国昌, 覃道锐, 等. 血清抑制素 b 评估儿童睾丸发育状况的作用[J]. 现代医院, 2015, 15(8): 20-21
Chai Cheng-wei, Liu Guo-chang, Qin Dao-rui, et al. Effect of serum inhibin B on the development of testis in children [J]. Modern Hospital, 2015, 15(8): 20-21
- [15] Cortes D, Clasen-Linde E, Hutson JM, et al. The Sertoli cell hormones inhibin-B and anti Mullerian hormone have different patterns of secretion in prepubertal cryptorchid boys [J]. J Pediatr Surg, 2015, 8[Epub ahead of print] (下转第 392 页)

- Cardiovasc Diabetol, 2013, 12: 69
- [19] Weiss JN, Korge P, Honda HM, et al. Role of the mitochondrial permeability transition in myocardial disease [J]. *Circ Res*, 2003, 93(4): 292-301
- [20] 薛亮, 尹长城. 线粒体 - 内质网结构偶联的研究进展[J]. *中国细胞生物学学报*, 2013, 12: 1791-1796
- Xue Liang, Yin Chang-cheng. Research progress of mitochondria endoplasmic reticulum physical coupling [J]. *Chinese Journal of Cell Biology*, 2013, 12: 1791-1796
- [21] Zheng H, Whitman SA, Wu W, et al. Therapeutic potential of Nrf2 activators in streptozotocin-induced diabetic nephropathy [J]. *Diabetes*, 2011, 60(11): 3055-3066
- [22] Cullinan SB, Diehl JA. Perk-dependent activation of nrf2 contributes to redox homeostasis and cell survival following endoplasmic reticulum stress[J]. *J Biol Chem*, 2004, 279: 20108-20117
- [23] Albená T, Dinkova-Kostova, Andrey Y. Abramov. The emerging role of Nrf2 in mitochondrial function [J]. *Free Radical Biology and Medicine*, 2015, 88(ParB): 179-188
- [24] Stjepana Kovac, Plamena R. Angelova, Kira M. Holmström, et al. Abramova. Nrf2 regulates ROS production by mitochondria and NADPH oxidase[J]. *Biochim Biophys Acta*, 2015, 1850(4): 794-801
- [25] Luciano Cominacini, Chiara Mozzini, Ulisse Garbin, et al. Endoplasmic reticulum stress and Nrf2 signaling in cardiovascular diseases [J]. *Free Radical Biology and Medicine*, 2015, 88 (11): 233-242
- [26] Palsamy P, Bidasee KR, Shinohara T. Selenite cataracts: activation of endoplasmic reticulum stress and loss of Nrf2/Keap1-dependent stress protection[J]. *Biochim Biophys Acta*, 2014, 1842(9): 1794-805
- [27] Fang Wang, Chunhua Pu, Peng Zhou, et al. Cinnamaldehyde Prevents Endothelial Dysfunction Induced by High Glucose by Activating Nrf2 [J]. *Cell Physiol Biochem*, 2015, 36(1): 315-324
- [28] Dromparis P, Paulin R, Sutendra G, et al. Uncoupling protein 2 deficiency mimics the effects of hypoxia and endoplasmic reticulum stress on mitochondria and triggers pseudohypoxic pulmonary vascular remodeling and pulmonary hypertension [J]. *Circ Res*, 2013, 113(2): 126-36
- [29] Ming Lu, Xiu-Lan Sun, Chen Qiao, et al. Uncoupling protein 2 deficiency aggravates astrocytic endoplasmic reticulum stress and nod-like receptor protein 3 inflammasome activation [J]. *Neurobiology of Aging*, 2014, 35(2): 421-430
- [30] Tian X Y, Wong W T, Xu A, et al. Uncoupling protein-2 protects endothelial function in diet-induced obese mice [J]. *Circ Res*, 2012, 110(9): 1211-1216

(上接第 365 页)

- [16] Mitchell V, Boitrelle F, Pigny P, et al. Seminal plasma levels of anti-Müllerian hormone and inhibin B are not predictive of testicular sperm retrieval in nonobstructive azoospermia: a study of 139 men[J]. *Fertil Steril*, 2010, 94(6): 2147-2150
- [17] Boitrelle F, Robin G, Marcelli F, et al. A predictive score for testicular sperm extraction quality and surgical ICSI outcome in non-obstructive azoospermia: a retrospective study [J]. *Hum Reprod*, 2011, 26(12): 3215-3221
- [18] Huang X, Bai Q, Yan LY, et al. Combination of serum inhibin B and follicle-stimulating hormone levels can not improve the diagnostic accuracy on testicular sperm extraction outcomes in Chinese non-obstructive azoospermic men[J]. *Chinese Medical Journal*, 2012, 125(16): 2885-2889
- [19] 邓伟, 杨杰, 陕文生, 等. 血清抑制素 b 与卵泡刺激素对非阻塞性无精子症睾丸精子抽吸成功的预测价值的 Meta 分析[J]. *中国优生与遗传杂志*, 2015, 8: 115-117
- Deng Wei, Yang Jie, Shan Wen-sheng, et al. A Meta analysis of predictive value of serum inhibin B and follicle-stimulating hormone on sperm testicular extraction in non-obstructive azoospermia [J]. *Chinese Journal of Birth Health & Heredity*, 2015, 8: 115-117
- [20] 王鸿祥, 陈斌, 胡凯, 等. 抑制素 b 用于预测少弱精症患者精索静脉曲张术后预后研究[J]. *中国计划生育和妇产科*, 2015, 7(1): 14-17
- Wang Hong-xiang, Chen Bin, Hu Kai, et al. The prediction for prognosis of asthenozoospermia patient after varicocele surgery by serum InhB [J]. *China's Journal of family planning & gynecology*, 2015, 7(1): 14-17
- [21] 廖森成, 王君龙, 张玉勤, 等. 超声联合血清抑制素 b 在无精子症分型诊断中的应用价值 [J]. *影像诊断与介入放射学*, 2014, 5: 371-375
- Liao Sen-cheng, Wang Jun-long, Zhang Yu-qin, et al. Value of ultrasound combined with serum INHB in classification of azoospermia [J]. *Journal of Diagnostic Imaging & Interventional Radiology*, 2014, 5: 371-375