·综述·

# Prader-Willi 综合征研究现状

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Prader-Willi 综合征(PWS)因最早(1956 年)由 Prader 报道而得名，是一种临床诊断的遗传障碍性疾病，通常与 15 号染色体上的 q11－13 片段印迹的缺失有关[1~3]，对于诊断 PWS 的主要临床标准包括：摄食过量和威胁生命的病态肥胖，智力缺陷，行为异常和生长激素缺乏导致的身材矮小以及性腺机能减退[4]。

## 1　PWS 病人的身体组成及相关代谢特点

PWS 多发于儿童，成年人也可发病。其患者的一个突出特点就是摄食过量，如不加以控制，会导致显著的中心性肥胖[5,6]，这种肥胖称为症状性肥胖，而 PWS 被认为是遗传性疾病中导致症状性肥胖的最常见原因[7]。研究表明：肥胖或身体脂肪组织的增加，尤其是内脏性肥胖，与胰岛素抵抗、糖耐量异常以及心血管疾病相关[8]，对健康有不利的影响[9]。那么 PWS 患者是否存在同单纯肥胖患者相同的身体组成以及肥胖相关的代谢问题就成为对 PWS 研究的热点问题之一。

Schoeller 等[10]研究显示：同单纯肥胖对照组比，PWS 患者存在特殊身体组成，即体内脂肪组织比例增高而瘦体组织比例降低，以后的研究也有相同的发现[11~14]。Theodoro 等[15]把 48 例 PWS 患者和 24 例单纯肥胖患者进行对照研究发现：PWS 组的四肢和躯干的瘦体组织显著低于肥胖对照组，其中下肢更为突出。同时数据还显示出 PWS 患者不同身体部位的脂肪组织与瘦体组织的比率要高于对照组，与 Goldstone 等[16]的报道相符。长期以来，导致 PWS 患者肥胖的病因仍未确定，还处于讨论中，大多数人把它归因于饱腹感异常而导致热量摄入的增加。DelParigi 等[17]把 PWS 患者能量摄入的增加归因于循环中 ghrelin 的升高。ghrelin 是一种内源性的促生长激素分泌受体的配体[18]并且是强有力的增加人食欲的物质[19]，它参与胃口、体重和生长激素分泌的短期和长期的调节[20]。已经有研究显示在 PWS 的儿童和成人患者中，ghrelin 水平比年龄及体质指数相匹配的对照组的受试者高 3～5 倍[17,21]。

肥胖会增加糖耐量异常、血脂异常等一些代谢并发症发生的危险[22]，而且是导致胰岛素抵抗的主要因素[23]。但 Bray 等[24]研究显示：PWS 患者一些肥胖相关的代谢并发症(如胰岛素抵抗和肝胰岛素输出减少等)的程度很轻，与其肥胖的程度不相符，Schuster 等[25]和 Eiholzer 等[26]的研究中也有相同的发现。Goldstone 等[27]对 13 例 PWS 患者和 44 例非 PWS 患者(其中肥胖 14 例，非肥胖 30 例)进行对照研究显示：PWS 组的绝对内脏脂肪量、内脏脂肪量占总体脂肪的百分数、内脏脂肪量占总体重的百分数均显著低于肥胖对照组，而与非肥胖对照组相似。同时 PWS 组胰岛素抵抗显著低于肥胖对照组，肝胰岛素输出显著高于肥胖对照组，作者认为这与选择性的低水平的内脏脂肪量有关，这是与单纯肥胖患者存在的突出不同点。之后对一些成人 PWS 的研究也同样发现 PWS 患者存在选择性的低水平的内脏脂肪量[28]。而 Talebizadeh 等[29]的研究则显示：PWS 组的内脏脂肪量有一个总体的下降趋势，和对照组(单纯肥胖)相比并无显著差别；但 PWS 组的胰岛素抵抗显著低于对照组，胰岛素敏感性显著高于对照组。

## 2　PWS 病人的能量消耗

已经有很多研究测量 PWS 患者的能量消耗，Schoeller 等[10]的研究发现：PWS 患者同肥胖对照组相比，其每日总能量消耗显著降低，之后的研究也有

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类似的发现[30]。

总的能量消耗与身体组成,代谢率以及体力活动三者相关。瘦体组织主要由肌肉组成,是体内主要的代谢活跃的组织,大多数的能量消耗都发生在肌肉组织。在一般人群中脂肪组织约占身体组成的 15% ~25%,但只有 2% ~5% 参与新陈代谢[31],因此,PWS 患者较低的瘦体组织和较高的脂肪比率被认为是显著的低能量消耗的一个原因[32],但不是唯一的原因;在一般人群大约有 20% ~40% 的能量消耗发生在体力活动中,食物热效应能量消耗的 10% ~15%,静息能量消耗占 60% 左右[33],在 Davies 等[34]的研究中发现 PWS 患者的自发体力活动显著低于对照组,而体力活动的能量消耗与活动的时间、强度、类型以及个体的能量消耗率有关[32]。因此,另一个导致 PWS 患者低能量消耗的可能原因为低水平的体力活动;此外,van Mil 等[35]研究发现 PWS 患者活动相关的能量消耗以及平均每日代谢率均显著低于对照组,Butler 等[32]报道,PWS 患者的个体能量消耗率显著低于对照组,同时,其静息能量消耗也显著低于对照组,与以前的研究[10,13,16]相符并且是低能量消耗的又一原因。van Mil 等[13]和 Goldstone 等[16]认为这与低瘦体组织的异常身体组成相关,而导致 PWS 患者的低水平瘦体组织的确切病因还不清楚[13]。综上所述,身体组成、体力活动以及代谢率这三个因素均与 PWS 患者低的能量消耗相关。据报道[36],在儿童和成人 PWS 患者使用生长激素治疗,能增加其瘦体组织、能量消耗以及体力活动,但远期效果还有待进一步研究。

## 3 行为治疗效果

对于 PWS 患者,如果能避免肥胖,其寿命可以接近正常[37],因此对 PWS 患者除了药物治疗以外,控制饮食、减轻体重和体育锻炼等行为治疗也是十分重要的。行为治疗的主要目的是控制体重增长和防止行为问题(如偷食),基于这两个主要目的,Descheemaeker 等[38]提出了行为治疗的四个原则:低能量饮食;行为的改变;提高其运动的技巧;父母参与对其的治疗及教育。

PWS 患者每日热量的摄入要根据其生长发育的曲线而定[39],对于刚学走步及年幼的儿童,每日摄入热量推荐为 800 ~900 千卡,并且随着患者生长发育缓慢增加热量的摄入。但同时要注意到由于总体能量摄入的减少,长期坚持可能会造成某些营养素的缺乏。因此,推荐给患者额外补充铁、钙和维生素。同时,运动也是非常重要的治疗手段,合理运动能有效地减轻体重。此外,对患者进行严密的监测和改变其周围环境以防止其偷食等行为对于控制患者体重也是非常有意义的[40]。

在 Deschildre 等[41]的报道中,1 例存在肥胖相关的呼吸道梗阻的 PWS 患者,其实际体重为理想体重的 3 倍,血气检查提示有呼吸衰竭,给予患者低能量饮食(600 千卡/d)结合面罩吸氧 4 个月后,患者体重减至理想体重的 2 倍,血气恢复至正常范围。Harris 等[42]的研究中显示 PWS 患者睡眠相关的呼吸障碍的发生与体重有很密切的关系,体重的减轻可以降低呼吸障碍的程度。之后,Nishida 等[43]通过行为治疗使 2 例女性 PWS 患者体重显著降低并改善了与病态肥胖相关的呼吸衰竭症状。

合理的体育运动不仅可以使体重减轻,还可以使肌肉量增加。在 Eiholzer 等[44]报道中把 PWS 患者作为试验组,单纯肥胖患者作为对照组,两组都进行相同的体育运动,把小腿围和小腿皮褶厚度作为监测指标,结果发现:同对照组基线数据相比,试验组的小腿皮褶厚度显著降低而小腿围显著增加,显示出肌肉量的增加;同时发现试验组的自发运动以及运动能力显著增加,从而说明了合理的体育运动可以改善局部的身体组成。在 Schlumpf 等[45]的前瞻性对照研究中:把 PWS 分为试验组和对照组,通过 6 个月的肌肉训练计划,试验组瘦体组织及运动能力显著增加。Silverthorn 等[46]的研究也有类似的发现。

总之,研究 PWS 患者的身体组成和能量消耗既可以反映疾病的特点,又可以作为评价疾病治疗效果的指标,因此,对于疾病的研究以及指导疾病的治疗尤其是行为治疗是非常有意义的。

虽然 PWS 的病因已经清楚,但导致其患者异常身体组成和能量代谢的确切机制还未完全研究清楚,对于本病还未有特异的治疗方法,因此还需对这些问题进行更深一步的研究以指导对本病的治疗,此外,还应提高对本病的诊疗水平,以达到早期发现早期治疗,从而改善此病患者的生活质量和预后。

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