

杜氏肌营养不良(DMD)患儿营养状况与膳食营养摄入情况的横断面研究*

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【摘要】目的 调查杜氏肌营养不良症(Duchenne muscular dystrophy, DMD)患儿营养状况及膳食摄入情况,初步探索两者的相关关系,为制定DMD患儿合理营养治疗提供理论依据。**方法** 选择2017年7月-2021年4月于四川大学华西第二医院就诊并经基因检测法诊断为DMD的共223名2~14岁患儿作为研究对象,采用3天24小时膳食回顾法进行膳食调查,采用化学发光法测定血清维生素D水平。**结果** 营养状况正常DMD患儿仅占33.2%,生长迟缓、低体重、超重、肥胖发生率分别为13.5%、14.4%、14.3%、8.1%,血清维生素D缺乏和不足患儿分别占9.0%和89.7%;膳食调查DMD患儿每日碳水化合物、蛋白质和脂肪供能比分别为(47.40±6.64)%、(14.46±2.22)%和(38.17±5.30)%;每日膳食钙和维生素D摄入量分别为(433.32±164.39) mg/d、(155.73±89.30) IU/d;生长迟缓DMD患儿蛋白质摄入量/蛋白质平均需要量的比值($P=0.003$)和能量摄入量/能量需要量的比值($P=0.007$)低于营养状况正常DMD患儿。**结论** DMD患儿膳食结构明显不合理,且营养缺乏与营养过剩问题并存。DMD患儿合理的营养指导方案及规范的营养管理措施仍有待进一步研究。

【关键词】 杜氏肌营养不良 营养状况 膳食营养

Cross-Sectional Study of Nutritional Status and Dietary Nutrient Intake in Children with Duchenne Muscular Dystrophy (DMD) in China HE Miao^{1,2}, CAI Xiao-tang¹, PENG Wen-tao¹, SONG Jie¹, ZHOU Hong-min¹, LI Xing-rong¹, WU Xiao-na^{1,2△}. 1. Department of Clinical Nutrition, West China Second University Hospital, Sichuan University, Chengdu 610041, China; 2. Key Laboratory of Birth Defects and Related Diseases of Women and Children of the Ministry of Education, Sichuan University, Chengdu 610041, China

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【Abstract】 Objective To investigate the dietary nutrient intake and the nutritional status of children with Duchenne muscular dystrophy (DMD), and to explore the correlation between them, so as to provide theoretical basis for the formulation of proper nutritional treatment for children with DMD. **Methods** A total of 223 children aged 2 to 14 years who came to West China Second University Hospital, Sichuan University from July 2017 to April 2021, and who were diagnosed with DMD by genetic testing were enrolled as the subjects of the study. Dietary assessment was conducted with a 3-day 24-hour dietary recall, and serum vitamin D level was measured by chemiluminescence method. **Results** Only 33.2% of the children with DMD were found to be of normal nutritional status. The incidences of stunted growth, underweight, overweight and obesity were 13.5%, 14.4%, 14.3% and 8.1%, respectively. Among the children with DMD, those with serum vitamin D deficiency and insufficiency accounted for 9.0% and 89.7%, respectively. According to the dietary recall of the children with MDM, the daily energy ratio of carbohydrate, protein and fat were (47.40±6.64)%, (14.46±2.22)%, and (38.17±5.30)%, respectively. The daily intake of dietary calcium and vitamin D were (433.32±164.39) mg per day and (155.73±89.30) IU per day, respectively. The ratio of daily protein intake to the estimated average requirement for protein ($P=0.003$) and ratio of daily energy intake to the estimated energy requirement ($P=0.007$) were lower in children with stunted growth than those of DMD children of normal nutritional status. **Conclusion** The dietary structure of children with DMD is obviously not suited to their condition and nutritional deficiency coexists with overnutrition among them. Further research needs to be done for developing appropriate nutritional guidance programs and standardized nutritional management measures for children with DMD.

【Key words】 Duchenne muscular dystrophy Nutritional status Dietary nutrition intake

杜氏肌营养不良症(Duchenne muscular dystrophy, DMD)是一种严重的X连锁隐性遗传性退行性神经肌肉疾病,该病为男性患儿特发性遗传性疾病,发病率为1/3 500~1/5 000活产男婴^[1-2],临床特征包括进行性肌无

力、小腿腓肠肌肥大、血清肌酸激酶显著升高、Gowers征阳性等^[3-4]。随着年龄增长,DMD患儿脂肪组织增加、肌肉量减少、体活动减少、基础代谢率降低,营养相关并发症逐渐增加并恶化^[5-6],包括生长迟缓、超重肥胖、消瘦、骨密度降低、糖代谢异常等^[7]等营养相关症状。

良好的营养状况有利于改善延缓DMD患儿疾病进

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展,提高其生存质量。膳食结构不合理、宏量及微量营养素摄入过多或不足均会影响DMD患儿的营养状况。目前国内外对DMD患儿缺乏膳食摄入情况调查与分析,且没有相关的饮食营养指导。本研究旨在通过调查分析DMD患儿的营养状况及膳食营养摄入情况,了解DMD患儿存在的营养状况及膳食问题,并初步探索DMD患儿膳食营养摄入与营养状况的相关关系,为进一步制定DMD患儿合理营养指导方案提供理论基础。

1 对象和方法

1.1 研究对象

共选择2017年7月-2021年4月在四川大学华西第二医院小儿神经科就诊的223名DMD患儿进行现场调查,均为男性。纳入符合基因学检测确诊为DMD且配合治疗患儿作为研究对象,排除其他类型肌营养不良患儿。本研究通过四川大学华西第二医院医学伦理委员会审批,批准号:医学科研2018伦审批第(033)号。

1.2 研究方法

体格测量和膳食调查均由经统一培训合格后同一批专业人员进行。采用便携式身高测量仪测量儿童身高,精确到1 cm,体质量由电子体质量测量器测量,结果精确到0.1 kg,小腿围采用无弹性皮尺测量,所有仪器使用前均已进行校准。采用3天24小时膳食回顾法,通过《中国食物成分表》及美国农业部食品成分数据库(USDA food composition databases)计算膳食营养素摄入情况,与《中国居民膳食营养素推荐摄入量(DRIs)》同年龄同性别推荐量进行比较。

1.3 定义和判定标准

根据WHO推荐的年龄别身高(height-for-age z-score, HAZ)、年龄别体质量(weight-for-age z-score, WAZ)以及年龄别体质量指数(BMI-for-age z-score, BAZ)作为评价标准^[8]。体质量指数(body mass index, BMI)=体质量/身

高,单位为 kg/m^2 。HAZ <-2 为生长迟缓;5岁以下及5岁以上儿童分别以WAZ和BAZ作为近期营养评价标准,z值 <-1 为低体质量,z值 >1 为超重,z值 >2 为肥胖;HAZ ≥ -2 且WAZ/BAZ为 $-1 \sim 1$ 范围时为营养正常,否则为营养失衡。

1.4 统计学方法

定量资料采用 $\bar{x} \pm s$ 表示,采用单因素方差分析进行组间比较,LSD分析法和Kruskal-Wallis单因素分析进行两两比较;计数资料用百分比(%)表示,采用卡方检验进行两两比较。 $\alpha=0.05$ 。

2 结果

2.1 生长发育情况

本次调查DMD患儿均为2~14岁男性,平均年龄(6.64 ± 2.64)岁。DMD患儿基本情况及营养状况分布详见表1和图1,结果各年龄组HAZ、WAZ或BAZ无明显区别。DMD患儿营养问题较为明显,其中66.8%患儿存在营养失衡,营养不良与营养过剩问题并存,分别占14.4%和22.4%。DMD患儿营养问题随年龄增加趋于明显,分析结果显示,相较于4~<7岁患儿, ≥ 10 岁患儿BAZ值处于正常范围人数偏低且超重肥胖发生率偏高($P=0.000$)。DMD患儿血清维生素D平均为(17.84 ± 5.55) ng/mL,仅1.3%患儿水平处于正常范围(>30 ng/mL),9.0%(20人)存在维生素D缺乏(<10 ng/mL),存在维生素D不足($10 \sim 30$ ng/mL)占总人数89.7%,不同年龄段儿童维生素D水平没有显著差别。

2.2 每日各类食物及膳食营养素摄入情况

不同年龄患儿各类食物摄入情况详见图2。DMD患儿饮食习惯欠佳,尤其是奶蛋类摄入情况,7~<10岁患儿奶类摄入量明显低于7岁以下患儿($P=0.023$), ≥ 10 岁患儿蛋类摄入量显著低于4~<7岁患儿($P=0.012$)。无食用奶制品及蛋类习惯的患儿分别占22.4%、26.5%,79.4%患儿每日饮奶不足300 mL,全日奶量超过500仅2人。

表1 DMD患儿基本情况($\bar{x} \pm s$)

Table 1 The general data of children with DMD ($\bar{x} \pm s$)

Age/yr.	Height/cm	Body mass/kg	BMI/(kg/m^2)	Calf circumference/cm	HAZ	WAZ or BAZ
<4 ($n=29$)	96.5 $\pm$ 6.11	15.7 $\pm$ 2.17	16.7 $\pm$ 1.28	22.8 $\pm$ 1.79	-0.75 $\pm$ 1.17	0.04 $\pm$ 0.93
4-<7 ($n=101$)	106.5 $\pm$ 6.68	18.4 $\pm$ 2.88	16.1 $\pm$ 1.35	24.0 $\pm$ 2.21	-0.90 $\pm$ 0.98	0.16 $\pm$ 0.95
7-<10 ($n=65$)	122.4 $\pm$ 7.11	25.0 $\pm$ 5.64	16.5 $\pm$ 2.44	27.8 $\pm$ 3.31	-1.04 $\pm$ 0.91	0.18 $\pm$ 1.38
≥ 10 ($n=28$)	140.3 $\pm$ 12.49	38.2 $\pm$ 10.78	19.2 $\pm$ 3.28	33.2 $\pm$ 6.43	-0.93 $\pm$ 1.05	0.51 $\pm$ 1.52
F	214.526	121.271	16.495	61.253	0.591	0.914
P	0.000	0.000	0.000	0.000	0.621	0.435

BMI: Body mass index; HAZ: Height-for-age z-score; WAZ: Weight-for-height z-score; BAZ: BMI-for-age z-score. One-way ANOVA was done and LSD method was used for paired comparison between groups.

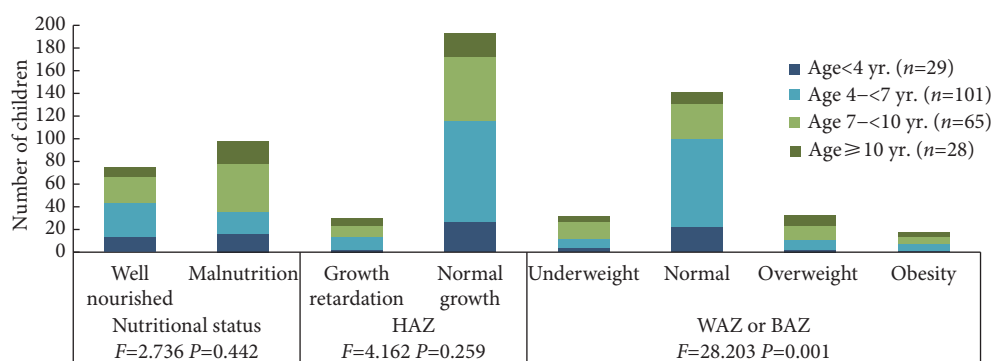


图 1 DMD 患儿营养状况评价

Fig 1 The evaluation of the nutritional status of children with DMD

R×C Chi-square test was used for measuring nutritional status, height-for-age z-score (HAZ), weight-for-height z-score (WAZ) and BMI-for-age z-score (BAZ).

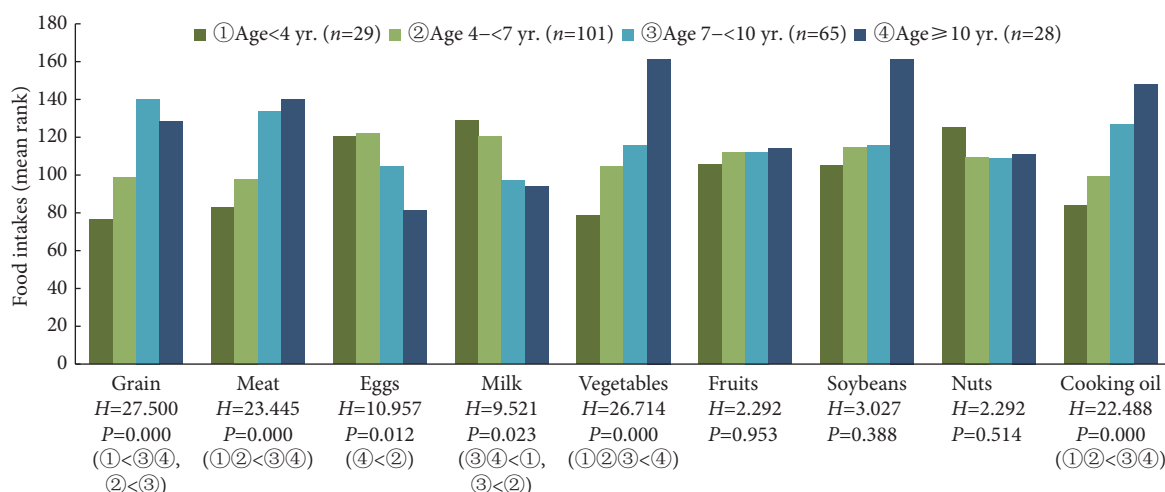


图 2 DMD 患儿每日各类食物摄入情况 (R)

Fig 2 The distribution of daily intake of varies kind of food in children with DMD (R)

Kruskal-Wallis univariate analysis was used.

不同年龄患儿每日主要膳食营养素摄入情况详见图3。DMD 患儿膳食营养素摄入不均衡,碳水化合物、蛋白质、脂肪供能比分别(47.40 ± 6.64)%、(14.46 ± 2.22)%、(38.17 ± 5.30)%,各年龄段三大产能营养素供能比无显著差别。DMD 患儿能量摄入量与DRIs同年龄同性别儿童能量需要量(estimated energy requirement, EER)比值平均为 0.91 ± 0.21 ,68.2%患儿能量摄入低于EER,其中 ≥ 10 岁患儿能量摄入量/EER的比值低于其他年龄组($P=0.001$)。DMD 患儿蛋白质摄入量普遍偏高,蛋白质摄入量与DRIs同年龄同性别蛋白质平均需要量(estimated average requirement, EAR)的比值平均为 1.70 ± 0.59 , ≥ 10 岁患儿比值最低($P=0.000$),88.8%患儿蛋白质摄入量高于蛋白质EAR,77.6%患儿高于蛋白质推荐摄入量(recommended nutrient intake, RNI)。不同年龄患儿膳食钙和膳食维生素D摄入量均偏低且各年龄段没有明显差异,平均分别为(433.32 ± 164.39) mg/d、(155.73 ± 89.30) IU/d。

2.3 DMD 患儿膳食营养摄入量与营养状况的关系

本研究结果仅显示,生长迟缓DMD 患儿蛋白质摄入量/EAR的比值($P=0.003$)和能量摄入量/EER的比值($P=0.007$)低于正常患儿,WAZ或BAZ正常患儿碳水化合物及能量摄入量低于超重和肥胖患儿,其他营养素摄入在不同DMD 患儿中无显著差别,详见表2、表3。

3 讨论

3.1 DMD 患儿营养问题突出

DMD 常隐匿发病于3~6岁,临床症状及营养相关并发症随年龄呈进行性加重^[5,9]。目前尚无有效治愈DMD 的方法,临床治疗以皮质类固醇治疗为主,辅助呼吸支持、营养治疗、康复训练等,改善肌肉功能和心肺功能,延长行走时间,提高生存质量。疾病进展及药物治疗副作用显著影响DMD 患儿营养状况^[10]。本研究采用HAZ及WAZ/BAZ评价DMD 患儿营养状况,结果显示

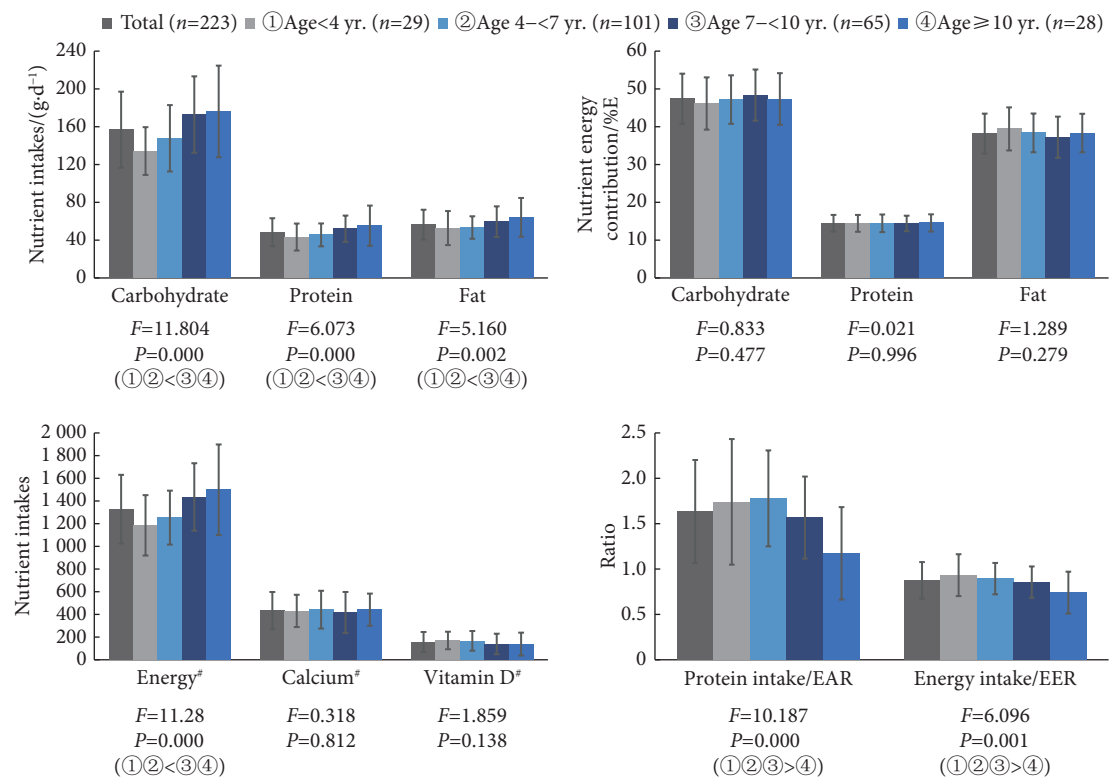


图 3 DMD 患儿每日主要膳食营养素摄入情况 ($\bar{x} \pm s$)

Fig 3 The distribution of daily intake of main dietary nutrients of children with DMD ($\bar{x} \pm s$)

One-way ANOVA was used for serum vitamin D comparison between the groups and LSD method was used for paired comparison between the groups. # Units of energy, calcium, and vitamin D intakes are kcal/d, mg/d, and IU/d, respectively. EER: Estimated energy requirement; EAR: Estimated average requirement.

表 2 生长迟缓与正常 DMD 患儿膳食营养素摄入量的比较 ($\bar{x} \pm s$)

Table 2 The comparison of main nutrient intake between DMD children with stunted growth and those with normal growth ($\bar{x} \pm s$)

Nutritional status	HAZ		t	P
	Growth retardation group (n=30)	Normal growth group (n=193)		
Age/yr.	7.71±2.98	6.47±2.55	2.414	0.017
Carbohydrate intake/(g/d)	150.65±41.05	157.88±40.26	-0.912	0.363
Protein intake/(g/d)	45.88±14.34	56.80±14.98	-0.588	0.557
Fat intake/(g/d)	54.07±16.39	56.80±15.70	-0.881	0.379
Energy intake/(kcal/d)	1 272.21±310.90	1 337.24±301.89	-1.092	0.276
Calcium intake/(mg/d)	413.75±187.78	435.97±161.09	-0.686	0.493
Vitamin D/(IU/d)	135.09±99.02	158.71±87.68	-1.347	0.179
Carbohydrate energy contribution/%	47.43±6.96	47.41±6.62	0.013	0.990
Protein energy contribution/%	14.69±2.08	14.42±2.25	0.607	0.544
Fat energy contribution/%	38.18±5.44	38.16±5.31	0.020	0.984
Protein intake/EAR	1.49±0.48	1.73±0.60	-2.142	0.003
Energy intake/EER	0.81±0.20	0.92±0.20	-2.713	0.007

EER: Estimated energy requirement; EAR: Estimated average requirement.

DMD 营养相关问题较为突出, 营养缺乏与营养过剩问题并存。本研究中仅 33.2% 患儿营养状况良好, 生长迟缓 (13.5%)、超重肥胖 (22.4%) 发病率远高于我国正常儿童

青少年发病率 (生长迟缓 0.8% ~ 3.2%)^[11]、超重肥胖 17.3%^[12] 及国外研究水平^[13-14]。

我国学龄儿童基线 25(OH)D 为 (35.4±12.0) nmol/L,

表 3 低体质量、超重、肥胖与正常DMD患儿膳食营养素摄入量的比较 ($\bar{x} \pm s$)Table 3 The comparison of dietary nutrient intake in underweight, overweight, obese and normal-weight children with DMD ($\bar{x} \pm s$)

Nutritional status	Underweight group (n=32)	Normal group (n=141)	Overweight group (n=32)	Obesity group (n=18)
Age/yr.	7.69±3.11*	5.98±2.32	8.31±2.53*	7.95±2.20*
Carbohydrate intake/(g/d)	163.08±38.13	149.95±36.81	173.66±44.01*	178.95±55.81*
Protein intake/(g/d)	49.77±15.42	47.17±14.33	53.74±17.17	49.95±14.35
Fat intake/(g/d)	57.84±18.17	54.96±15.43	60.64±15.68	61.15±14.93
Energy intake/(kcal/d)	1 371.95±315.90	1 283.11±283.65	1 450.37±329.36*	1 467.63±346.88*
Calcium intake/(mg/d)	415.46±173.42	428.67±152.87	463.59±177.84	443.68±207.29
Vitamin D/(IU/d)	134.56±85.54	158.79±81.38	157.42±112.29	152.65±102.65
Carbohydrate energy contribution/%	47.98±6.81	46.96±6.76	48.03±6.81	48.53±6.71
Protein energy contribution/%	14.40±2.05	14.59±2.23	14.68±2.22	13.59±2.40
Fat energy contribution/%	37.62±5.23	38.46±5.52	37.62±5.18	37.73±4.88
Protein intake/EAR	1.62±0.70	1.74±0.58	1.65±0.58	1.62±0.50
Energy intake/EER	0.88±0.25	0.91±0.20	0.90±0.22	0.94±0.22

* $P<0.05$, vs. normal group. EER: Estimated energy requirement; EAR: Estimated average requirement.

缺乏率为36.1%^[15]。本研究中DMD患儿血清维生素D平均仅为(17.84±5.55) ng/mL, 98.7%DMD患儿血清维生素D缺乏或不足, 远高于我国儿童维生素D缺乏率(21.4%)^[16]。多数国内外^[15, 16-19]研究结果显示, 儿童青少年血清维生素D水平约为(23.36~35.4) mmol/L, 均高于本研究结果。

3.2 DMD患儿膳食营养摄入不合理问题需得到重视

本研究发现DMD患儿膳食结构不合理, 碳水化合物供能比摄入量偏低, 而蛋白质、脂肪供能比偏高, 其中66.2%患儿碳水化合物供能比低于50%, 35.1%患儿脂肪供能比高于40%。国内相关研究表明我国正常儿童蛋白质、脂肪摄入量均低于本研究^[20]。此外, DMD患儿饮奶习惯差, 79.4%患儿每日饮奶不足300 mL, 且饮奶量随年龄增长显著降低。李子一等^[21]研究发现我国3~12岁儿童半年内不饮奶儿童比例为8.97%~22.45%, 且奶类摄入量随年龄呈下降趋势, 与本研究结果相似。

DMD患儿膳食维生素D平均摄入量为(155.73±89.30) IU/d, 且随年龄增长呈下降趋势, 低于我国男性学龄儿童均值(204 IU/d)^[22], 远低于美国1~18岁男性青少年摄入水平(236~240 IU/d)^[16]。由此可见, 加强管理DMD患儿维生素D摄入及补充有待进一步改善。

3.3 膳食营养摄入与DMD患儿营养状况的关系值得进一步探究

DMD属于慢性进展性疾病, 且营养状况受膳食结构的显著影响, 若在疾病进展过程中没有合理的干预措施, 其病情及营养状况将随年龄逐渐恶化, 降低患儿生存质量。本研究中68.2% DMD患儿每日能量摄入不能满足平

均需要量, 但营养过剩问题仍然较为显著, 其原因可能因为DMD患儿长期激素治疗以及病情进展导致肌肉组织消耗、脂肪组织增加、基础代谢量降低、能量需求改变等^[6, 23], 因此根据DMD患儿营养及生长发育情况制定个体化营养需求量尤为重要。生长迟缓DMD患儿蛋白质($P=0.003$)、能量摄入量($P=0.007$)与平均需要量之比均低于身高正常患儿, 由此可见, 为DMD患儿提供充足的能量和蛋白质对于DMD患儿更加重要。也有研究^[24-25]提出DMD患儿处于高代谢水平, 其蛋白质需求量应高于正常儿童, 但DMD患儿蛋白质推荐摄入量仍值得进一步探索。在未来研究中应进一步扩大样本量或者采用多元分析方法进一步探索营养摄入对DMD患儿营养状况的影响。

KINNETT等^[26]学者提出DMD患儿确诊后立即进行合理的营养管理十分必要, 膳食结构不合理、机体代谢水平改变以及缺乏规范化营养管理可能是导致其营养失衡的主要原因。相较于体脂率, 单纯通过BMI水平可能低估DMD患儿超重肥胖发病率^[22]。本研究对我国DMD患儿膳食营养摄入情况及营养状况进行了初探, 了解其营养状况及目前存在的膳食营养摄入的相关问题, 但缺乏相关体脂率和体成分测量数据。在未来研究中, 应结合DMD患儿体格测量指标及人体成分分析结果, 综合评价患儿营养状况, 并且进一步探索DMD患儿的膳食营养摄入情况, 为制定DMD患儿合理营养指导方案提供理论研究基础, 最终延缓患儿病程进展、改善营养状况、提高生活质量。

* * *

利益冲突 所有作者均声明不存在利益冲突

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