Psychological, cognitive and maternal stress assessment in children with primary ciliary dyskinesia

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Original article

Background: **Primary ciliary dyskinesia (PCD) is a rare disorder due to structure and functional abnormalities of respiratory cilia. There are no reports on the behavioral and psychological aspects of children and adolescents with PCD. This study was undertaken to assess the cognitive and behavioural characteristics, and the parental stress of a population of school-aged children with PCD.**

Methods: **Ten PCD and 34 healthy school-aged children underwent Wechsler Intelligence Scale for Children-III edition, Child Behavior Check-List questionnaire (CBCL), Parenting Stress Index-Short Form tests in order to perform a behavioural and psychological evaluation.**

Results: **PCD children showed significant behavioral and social competent problems in CBCL scale than control children, in particular with regard to internalizing problems score (P<0.001). Parental distress, parent-child interaction and total stress in the mothers of PCD patients were higher than those in the controls' parents (P<0.001).**

Conclusion: **Our findings pinpoint the importance of specific psychological support in the clinical management of children with PCD.**

World J Pediatr 2013;9(4):312-317

Key words: **intelligent quotients; parental stress; primary ciliary dyskinesia; Wechsler Intelligence Scale for Children-III edition**

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doi: 10.1007/s12519-013-0441-1

Introduction

Primary ciliary dyskinesia (PCD) (MIM#242650) is a rare (1:15 000-30 000 live births) and predominantly autosomal recessive disorder due to structural and functional abnormalities of respiratory cilia.[1] Approximately 50% of the patients have mirror-image organ arrangement and other forms of heterotaxy (Kartagener syndrome).[2,3]

Early major clinical events in PCD are recurrent infections of the upper and lower respiratory tract that favour the development of progressive obstructive lung disease. Chronic respiratory symptoms have a significant impact on health, that may also result in possible restriction of life style.[4]

Since patients need frequent clinical evaluation and treatment including daily chest physiotherapy and inhalant therapies with bronchodilators plus antibiotics for recurrent respiratory infections, PCD is considered a disabling condition, highly stressful for the affected patients and their relatives.

In 2010, Pifferi et al[5] reported the importance in evaluation of psychological effects on both the family and patients and the decrease of life quality in the patients and their parents. In this study, a specialist team worked together with family physicians to evaluate whether the initial reaction of anger and denial is replaced by acceptance and coping with the proper management of the disease.[6]

Although the behavioral aspects and the parental stress of children and adolescents with several disabling genetic and/or chronic conditions were previously described,[7,8] there is no evidence for the impact in children affected by PCD and consequently no model studies are reported on the best psychological interventions to help patients or their carers manage the disease,[7] the role of mental health of patients[9] and the role of parent-child stress[8,10] on prognostic and therapeutic management of chronic disease.[7-10] Hence, we could borrow the management model from other chronic illnesses such as cystic fibrosis, asthma, diabetes, and headache.

Specifically, parenting stress levels in cystic fibrosis (CF) higher than those in healthy children were reported.[11] Moreover, parent-child stress and the lack of agreement between parents may be also associated with problems in compliance with treatment, with an adverse impact on the disease and health status of the children with CF.[10] On the other hand, although it was reported that chronic illnesses could impair the cognitive performances in developmental age, CF seems not to affect or impact the cognitive functioning,[12] and in asthmatic children the cognitive level may be involved only in the aspects of symptom monitoring, properly linked to the cognitive ability[13] even if no specific studies on the intelligence assessment were performed. The developing brains in children may present more sensitivity to the effects of diabetes than adults, and this may explain the neuropsychological impairment in this illness.[14]

In children affected by headache, no difference in full intelligence quotient was found even if the children with tension-type headache had a lower verbal intelligence quotient and a higher performance intelligence quotient than the healthy controls and children with migraine.[15]

To the best of our knowledge, there are no reports on the cognitive, behavioral and psychological aspects of children and adolescents with PCD. Moreover, no study in PCD assessed the degree of parental stress and the impact of chronic disease of the airways in the parent-child interaction. Thus, we hypothesized that PCD as other rare diseases could affect and impact the quality of family functioning and the psychological equilibrium of children.

Therefore, the present study was undertaken to assess the cognitive and behavioural characteristics, and the parental stress of school-aged children with PCD.

Methods

Population

Ten consecutive patients with PCD aged from 6 to 16 years (7 males, age range: 12.00±4.29 years) were studied over 9 months (December 2011 to September 2012).

The diagnosis of PCD, suspected on the basis of low nasal nitric oxide levels,[16,17] was made at a median age of 0.25 years (range: 0.08-10.3 years) and was based on the demonstration of abnormal motility and ultrastructural defects of cilia.[1] Nine patients had situs viscerum inversus, and no patient had heterotaxy.

Exclusion criteria included upper and lower respiratory tract infection and asthma exacerbation, heart disease, mental retardation [intelligent quotient (IQ) less than 70], epilepsy, and psychiatric disorders (i.e. attention deficit hyperactivity disorder, schizophrenia, depression and anxiety disorder).

We recruited 34 healthy children and adolescents aged from 8 to 16 years (24 males; mean age: 12.65±3.06 years). They were randomly selected from schools of Campania region.

Patients and controls were subjected to a psychological evaluation aimed to assessing the IQ level, behavioural aspects, and levels of maternal stress through standardized questionnaires. Only mothers without any neurological, psychiatric or chronic illnesses were enrolled in the study.

Informed consent was obtained from the parents of children and the Departmental Ethics Committee of the Second University of Naples approved the study design. All parents of the participating children gave written informed consent according to the *Declaration of Helsinki*.[18]

Intelligence assessment

The IQ of the subject was assessed by the Italian version of the Wechsler Intelligence Scale for Children-III edition (WISC-III),[19,20] applicable for children aged from 6 to 16 years. WISC-III is composed of 13 distinct subtests that include a verbal scale and a performance scale. Six verbal scales include language-based items, whereas the seven performance scales consist of visual-motor items that are less dependent on language. Five of the subtests in each scale produce scale-specific IQs as verbal IQ (VIQ) and performance IQ (PIQ), and the ten subtest scores produce a total scale IQ (Total-IQ).

Behavioural assessment

To assess the psychological and social competence of children, the Italian version of the Child Behavior Check-List questionnaire (CBCL) was used.[21] The CBCL is the most well-developed, empirically derived behaviour rating scale available for assessing psychopathology and social competence in children. It is a parent-completed survey assessing behaviour in children between the ages of 6 to 18 years. Parents/caregivers are instructed to answer questions about their child's behaviour during the past 6 months. Items are scored as follows: 0=not true (as far as you know), 1=somewhat or sometimes true, or 2=very true or often true. This questionnaire yields 8 factors: withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention-hyperactive, rule-breaking behaviour, and aggressive behaviour; as well as 3 global scores for externalizing and internalizing behaviours and total behaviour score.[21] In this study, the CBCL was administered only to the mother, as the parent who

usually spends more time with the children.

Parenting stress index-short form (PSI/SF)

To assess the perceived stress in the mothers of children with PCD, we used the Italian version of Parenting Stress Index-Short Form (PSI/SF).[22] The PSI-SF is a standardized tool, which yields scores of parental stress across four domains: parental distress, parent-child dysfunctional interaction, difficult child, and total stress. It has 36 items and provides both raw and percentile scores. Each item was graded on a 5-point likert scale. Higher scores indicated higher perceived stress in the parents.

The PSI/SF also produces a "defensive responding" score (DEF), which indicates likely response bias. A score at, or above, the 85th percentile indicates high stress levels.[22] The PSI/SF has been used widely, and psychometric evidence supports its reliability and validity.[23,24] The PSI/SF shows high internal consistency (Cronbach's *alpha*=0.92) and its validity has been established in parents of children with chronic medical conditions such as diabetes and asthma.[25-27] In this study, the PSI/SF was administered only to the mother, as the parent who usually spends more time with the children.

Statistical analysis

For all statistical analysis, the STATISTICA software (vers. 6, StatSoft, Inc, 2001) was used. The characteristics of population and the results of clinical evaluations of two samples (PCD and control) were compared with Student's *t* test and the Chi-square test, where appropriate. *P* values <0.01 were considered statistically significant.

Bonferroni correction was applied using for intelligence results 2 tests (VIQ and PIQ), for CBCL results 12 tests (activities, social, school, competence, withdrawn, somatic complaints, anxious/depressed, social, thought, attention, delinquent, aggressive) and for PSI results 4 tests (parental distress domain, parent-children dysfunctional interaction domain, difficult child subscale, DEF) because independent each others. Thus, we used an alpha level of 0.01/2=0.005 for intelligence evaluations, an alpha level of 0.01/12=0.0008 for CBCL results and an alpha level 0.01/4=0.0025 for PSI data. *F*-ratio test was applied for analysis of differences of variance between the groups.

Results

No significant differences between the two study groups were found for age (*P*=0.589), gender (*P*=0.720) and BMI (*P*=0.249). No significant variance differences were found (Table 1).

Mothers of both groups were not significantly different for age (37.18±3.18 *vs.* 38.02±3.71, *P*=0.520) and educational level (15.32±2.06 *vs.* 15.17±2.25, *P*=0.851).

There were no differences in WISC-III performance (PIQ), verbal (VIQ) and total scores (Total-IQ) in both PCD patients and healthy subjects (Table 2).

PCD subjects showed significantly higher scores in CBCL results, in particular with regard to withdrawn (*P*=0.002), somatic complaints (*P*<0.001), anxious/depressed items (*P*<0.001), attention (*P*=0.009) and internalizing problems items (*P*<0.001) (Table 3). However, no clinically relevant scores (≥70) were found in both groups of children, even if in the PCD group had a borderline clinical range found in 50% of the subjects for total score, 20% for withdrawn, 60% for somatic complaints, 50% for anxious/depressed, 10% for social, 10% for attention, 10% for delinquent and 60% for internalizing problems items. In the control group with CBCL results, no clinical range scores

Table 1. Population characteristics

Characteristics	PCD (*n*=10)	Controls (*n*=34)	*t* value	df	*P*	*F* ratio	*P* variances
Age	12.000±4.295	12.659±3.070	-0.543	42	0.590	1.957	0.155
Gender (M/F)	7/3	24/10	-	1	0.720	-	-
BMI	21.129±3.227	20.309±4.645	0.520	42	0.606	2.072	0.249

P<0.01 was considered statistical significant; Chi-square test was applied for Gender variable; *F*-ratio test was applied for differences of variance between groups calculation. BMI: body mass index; PCD: primary ciliary dyskinesia; M: male; F: female; df: degrees of freedom.

Table 2. Wechsler Intelligence Scale for Children-III scores

Variables	PCD (*n*=10)	Controls (*n*=34)	*t* value	df	*P*	*P**	*F* ratio	*P* variances
Total-IQ	107.200±12.381	105.441±8.099	0.532	42	0.597	1.195	2.337	0.073
VIQ	109.500±13.762	108.441±10.320	0.264	42	0.793	1.586	1.778	0.221
PIQ	103.200±10.891	101.324±10.164	0.505	42	0.616	1.232	1.148	0.718

P<0.01 was considered statistical significant; *F*-ratio test was applied for differences of variance between groups calculation. *: Bonferroni correction was applied (alpha level=0.005). PCD: primary ciliary dyskinesia; Total-IQ: total intelligence quotient; VIQ: verbal intelligence quotient; PIQ: performance intelligence quotient; df: degrees of freedom.

Table 3. Results of Child Behavior Check-List questionnaire in PCD patients and controls

Chracteristics	PCD (*n*=10)	Controls (*n*=34)	*t* value	df	*P*	*P**	*F* ratio	*P* variances
Total CBCL	56.200±12.682	44.353±9.293	3.256	42	0.002	0.027	1.863	0.187
Activities	33.300±4.596	37.118±7.109	-1.596	42	0.118	1.417	2.392	0.168
Social	40.600±4.502	45.176±5.786	-2.298	42	0.027	0.319	1.652	0.433
School	43.600±5.873	48.382±5.039	-2.542	42	0.015	0.177	1.358	0.493
Competence	34.100±2.132	40.294±6.590	-2.907	42	0.006	0.070	9.556	0.001
Withdrawn	58.000±7.972	51.235±2.475	4.380	42	0.000	0.001	10.377	0.000
Somatic complaints	64.900±10.005	52.882±4.388	5.523	42	0.000	<0.001	5.198	0.000
Anxious/depressed	62.200±9.438	51.912±2.734	5.724	42	0.000	<0.001	11.912	0.000
Social	55.700±6.567	52.559±3.940	1.886	42	0.066	0.795	2.777	0.031
Thought	54.900±5.646	50.676±2.879	3.214	42	0.003	0.030	3.847	0.004
Attention	57.500±6.737	51.941±3.265	3.632	42	0.001	0.009	4.257	0.002
Delinquent	54.300±6.750	50.765±1.860	2.782	42	0.008	0.097	13.177	0.000
Aggressive	53.000±3.197	50.882±2.157	2.435	42	0.019	0.231	2.197	0.096
Internalizing	62.900±11.995	45.971±8.126	5.175	42	0.000	<0.001	2.179	0.100
Externalizing	46.800±10.942	44.000±7.080	0.965	42	0.340	4.080	2.389	0.066

T-scores of ≥70 (≥98th percentile) are in the clinical range, less than 65 (<93rd percentile) are in the normal range, and between 65 and 70 (93rd-98th percentile) are in the borderline clinical range. *P*<0.01 was considered statistically significant; *F*-ratio test was applied for differences of variance between groups calculation. *: Bonferroni correction was applied (alpha level=0.0008). PCD: primary ciliary dyskinesia; df: degrees of freedom.

Table 4. Results of Parenting Stress Index-Short Form in PCD patients and healthy subjects

Variables	PCD (*n*=10)	Controls (*n*=34)	*t*-value	df	*P*	*P**	*F* ratio	*P* variances
PD	43.800±6.303	22.706±5.818	9.896	42	0.000	<0.001	1.174	0.686
P-CDI	35.300±4.523	19.147±1.987	16.412	42	0.000	<0.001	5.182	0.000
DC	23.400±3.098	21.412±3.627	1.570	42	0.124	0.496	1.371	0.642
DEF	24.800±4.237	13.029±3.503	8.909	42	0.000	<0.001	1.463	0.405
Stress Tot	102.500±6.536	63.265±5.236	19.686	42	0.000	<0.001	1.558	0.338

*: Bonferroni correction was applied (alpha level=0.0025); *P*<0.01 was considered statistical significant; *F* ratio test was applied for differences of variance between groups calculation. PD: parental distress domain; P-CDI: parent-children dysfunctional interaction domain; DC: difficult child subscale; DEF: defensive responding; df: degrees of freedom.

were found except 2.94% of children with a borderline clinical range in somatic complaint, social and thought items.

PSI-SF mean scores related to parental distress, parent-child interaction and total stress in the mothers of PCD patients were higher than those of mothers of the controls (*P*<0.001; Table 4). Moreover, the DEF score was significantly higher (*P*<0.001) in PCD (Table 4). All PCD mothers had high scores of stress (at, or above, the 85th percentile), but no clinically relevant PSI scores were found in mothers of the control group.

Discussion

The effect of chronic lung diseases on the quality of life of patients and their family has been well understood.

To interpret correctly the presence of internalizing problems in our PCD patients, we could consider a double perspective. The first one could be identified in the idea of impending death that the chronic lung disorders bring with them, as yet identified in cystic fibrosis.[6,7] The second one consists of that in general each chronic disease impacts the quality of life of family and children affected, as shown in patients with asthma,[13,26] cystic fibrosis,[6,7,28,29] diabetes,[14,27] and headache.[8] We could assume that PCD may cause a stressful condition in developmental age with psychological effects also on intra-familiar relationships. Alternatively, we could imagine that the internalizing problems in our children could be related firstly to the frequent hospitalizations, secondly to the own perception of the sickness status, and thirdly to the effect of denial and rejection parents' for the sons' pathology, as in other chronic illnesses.[6-8,13,14,26-29]

Hence, the higher scores in internalizing problems scale of the CBCL test, such as withdrawn (*P*=0.002), somatic complaints (*P*<0.001) and anxious/depressed (*P*<0.001) sub-items, could be related to the awareness of being different from other children. Also, the attention level alteration in the PCD group compared with the controls (*P*=0.009) could be interpreted as a sort of vicarious symptoms of internalizing problems as shown in other illnesses.[30-33]

In fact, this perception may be due not only to repeated medicalization but also to the consciousness of situs viscerum inversus that in developmental age

could lead to the growth of unresolved conflicts that could represent the appearance of emotional disorders. The findings about the parental stress level could be explained as a sort of general refusal response to PCD.

In fact, parents of children affected by genetic chronic illnesses experienced greater stress and burdens than parents of healthy children, yet parenting behavior and family functioning were quite similar to the healthy control group. Therefore, the higher levels of distress, an avoidant coping style, and low levels of family support were associated with poor psychological adjustment in affected children.[28,29]

In general, we can assume that when a child is diagnosed with a chronic, life-threatening illness, there is a significant effect on the healthy family, and the parenting stress tends to reflect the level of stress/difficulty present in the parent-child relationship, including stress attributable to parental distress, difficult child characteristics, and dysfunctional parent-child interactions. Notably, a research conducted by Hung et al[34] in 2004 suggested that different illnesses may result in different levels of parenting stress, even if we may assume that the illness tends to stress the parents.

For example, caring for a child with CF is stressful and this has implications for the main carer, the parental relationship, well siblings, family functioning as well as the affected child. On the other hand, conflict over childcare responsibilities and decision-making are the most commonly reported stresses experienced by parents caring for children with a chronic illness.[35-37] Similarly, children with asthma whose parents experienced higher levels of parenting stress have been shown to have poorer pulmonary function, more asthma attacks, and more subsequent hospitalizations than those whose parents had less stress and more family cohesion and support.[38,39]

Conversely, Hullmann et al[40]reported that parents of children with asthma who experience strained interactions with them or are highly critical of them are less likely to engage in effective disease management. Therefore, these studies suggested that children's health outcomes are related to how well their parents function and adhere to the prescribed regimen. This is particularly important for parents of children with cystic fibrosis, diabetes, and asthma as most of the daily treatments are performed by parents.[40]

However, we should take into account limitations of this study. First, our data were derived from a small group affected by PCD from a specific region of Southern Italy. Second, the parental stress levels were assessed only in mothers. Third, WISC-III was used instead of the recent version for the evaluation of cognitive level. But we consider the present study is the first one on psychological aspects of subjects with PCD and their families, indicating the importance of specific psychological support in the clinical management of this condition.

Funding: None.

Ethical approval: This study was approved by the Ethics Committee of Federico II University.

Competing interest: None of the authors has conflict of interest.

Contributors: Carotenuto M designed the study and drafted the article. Esposito M performed data collection and analysis. Di Pasquale F revised the manuscript. De Stefano S also contributed to data collection and analysis. Santamaria F approved the final version for publication.

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Received November 27, 2012
Accepted after revision June 5, 2013