



The Overlooked Childhood Problems in Pediatric Cerebral Palsy Subjects

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Abstract: This is one of the first studies delineating some characteristic features of certain common childhood problems of pediatric cerebral palsy (CP) subjects that might have been overlooked in previous medical visits. We collected data on immunization and also blood, urine and stool specimens of 89 CP subjects and 80 control patients. The CP subjects had significantly higher ratios of anemia, urinary tract infections and missed shots of immunization than patients presenting with first seizure as control group ($p < 0.05$ for each). There was no difference in ratio of intestinal parasites but was quite high in both groups (18%). It will afford a good opportunity for CP subjects if pediatric neurologists, who regularly follow up these patients, focus on some non-neurological but common childhood problems as well.

Key Words: Cerebral Palsy; Urinary Tract Infection; Anemia; Missed Immunization Shots; Intestinal Parasites.

Pediyatrik Serebral Palsi Vakalarında Yaygın Çocukluk Problemleri

Özet: Bu çalışma bir eğitim hastanesinde ayaktan takip edilen pediyatrik serebral palsi (SP) vakalarında daha önce yapılmış muayenelerinde gözden kaçırılmış olabilecek yaygın çocukluk problemlerinin sıklığını belirleyen ilk çalışmalardan biridir. Aynı pediyatrik nöroloji polikliniğinde takip edilen SP hastaları ile kontrol grubu olarak alınan ilk nöbet şikayetiyle başvuran vakalar karşılaştırıldı. Vakaların aşı verileri toplandı. Ayrıca 89 SP ile 80 kontrol hastasında kan, idrar ve gaitada parazit tetkikleri incelendi. Serebral palsi grubunda kontrol grubuna göre anlamlı derecede daha yüksek anemi, idrar yolu enfeksiyonu ve eksik aşılama oranları tespit edildi (her sonuç için $p < 0.05$). Bağırsak paraziti oranı açısından farklılık tespit edilmedi ancak bu oran her iki grupta da hafif yüksek (%18) bulundu. Serebral palsi vakalarını düzenli takip eden pediyatrik nöroloji poliklinik hekimlerinin nörolojik olmayan yaygın çocukluk problemlerine de zaman ayırması, bu hastalar için iyi bir fırsat olacaktır.

Anahtar Kelimeler: Serebral Palsi; İdrar Yolu Enfeksiyonu; Anemi; Unutulmuş Aşı Dozları; İntestinal Parazitler.

Introduction

Cerebral palsy (CP) of the childhood is the term used to describe a group of disorders of the development of movement and posture that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain.¹ The majority of CP patients (70%) are presumed to result from brain injury during intra-uterine life.² An additional 20% are believed to result from brain injury during the birthing process and prematurity problems.² The incidence of cerebral palsy has remained virtually unchanged over the past 40 years at approximately 2.5 per 1000 live births.¹ Ironically, advances in medicine have decreased

the incidence from some causes (Rh disease and congenital infections etc.), but have increased its incidence from other causes-notably, prematurity and multiple pregnancies.¹

Cerebral palsy causes significant limitations in the activities of daily living (ADL), particularly self-care, in children of all ages.² Upon hearing the probable diagnosis, most parents ask: "Will my child walk or eat alone?" An often unspoken question is "Will my child be able to have a long life?" The presumption of a bleak future for a child sometimes causes parents to withdraw from the child and this can have a significant negative effect on the well-being of child.

Primary-care physicians or pediatricians generally concentrate on the referral complain and occasionally overlook the general well-being of the CP subjects. This may lead under-diagnosis of more common problems

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in childhood period i.e. anemia, intestinal parasites, urinary tract infections, missed shots of local immunization programs. This is more frequent in pediatric subspecialty outpatient clinics, in teaching hospitals, dealing with very specific disorders in certain organ systems.

We, therefore, aimed to investigate the CP patients visiting a teaching hospital who might have been overlooked in previous medical visits in terms of general medical problems.

Material and Method

The University Hospital of Inonu University serves children in eastern part of Turkey. The CP patients visiting pediatric neurology outpatient clinic were recruited for the study. The control group consisted of subjects visiting the same pediatric neurology outpatient clinic with the complaint of seizure for the first time. The study designed as prospectively and carried out between September 2004 and September 2006.

After obtaining oral informed consent, the parents were requested to obtain 3 samples of fresh stool for examination in the laboratory of Medical Parasitology Department. They were examined as soon after collection as possible for intestinal parasites using the modified formol ethyl acetate concentration method and native-lugol, trichrome and Kinyoun acid-fast staining. Each sample was evaluated by two experienced investigators.

We also obtained a clean-catch midstream urine sample collected into a plastic urine bag. Urine samples (0.001 mL) were cultured on blood and MacConkey agars and incubated at 37°C. The following day, bacterial colonies were identified and quantified by use of Remel Rapid NF Plus System (Remel Inc., Lenexa, KS) and Analytical Profile Index (API) strips (bioMerieux, Lyon, France). A positive urine culture was defined as more than 10⁵ colony-forming units/mL of a single microorganism.³

The venous blood samples (2 ml) were obtained to assess complete blood count parameters [hemoglobin (Hb), hematocrit (htc), mean corpuscular volume (MCV)] were determined by a Coulter Counter-S model (Coulter®; STKS, Coulter Corp., Hialeah, FL, USA). The subjects with Hb levels lower than age-related cut-off reference values were named as anemic.⁴

The parents were asked to display their immunization charts. If the charts were missing, the parents were kindly requested to bring them in the following visit.

Exclusion criterias in the study.

1. Patients younger than 18 months old; diagnosing cerebral palsy usually involves a period of waiting for the definite and permanent appearance of specific motor problems.⁵
2. Patients younger than 18 months old; this age is the upper limit for Turkish children for completing primary series of infancy immunization.
3. The subjects with known urological or nephrological anomalies like neurogenic bladder, recurrent urinary tract infections etc.
4. The subjects using intermittent catheterization.
5. The subjects using ferrous supplementation for diagnosed anemia.
6. The subjects missing immunization charts.

After the study period, the expanded programme of immunization (EPI) in Turkey included: Hepatitis B vaccine at birth, 2, 6 months or at 2, 3 and 9 months, four shots of diphtheria, tetanus, whole-cell pertussis (DTP) and oral polio at 2, 3, 4 and 15-18 months, single BCG at 2-3 months and single measles at 9 months. The booster doses were being applied at the first year of primary school as measles, BCG and attenuated diphtheria, tetanus without pertussis (dT).

Turkish Ministry of Health modified some vaccines in the EPI programme in 2007 (after the study period); a pentacellular vaccine (DTaP-Hib-IPV) with acellular pertussis, inactivated polio and Haemophilus influenza type B (Hib) replaced the scheme at 2, 4, 6 and 18-24 months. Also measles was substituted with mumps, measles and rubella (MMR) at 12 months of age. The second BCG and measles doses at primary school were canceled and MMR was replaced.

During the study period; 7-valent conjugate pneumococcal vaccine (which is also introduced into Turkish EPI in August 2008), combined vaccines with acellular pertussis (aP), Hib, MMR, hepatitis A and varicella were available on the market for extra vaccination (no insurance paid).

The data obtained by this prospective study was analyzed by SPSS for Windows Release 13, SPSS Inc, USA and EPI Info 6.0, CDC-Atlanta, USA, with the help of the Department of Biostatistics in Inonu University Medical Faculty. The difference between the two groups was studied by unpaired t-test, chi-square and Fischer's exact chi-square test. Statistical significance was considered when *p* values <0.05 for all tests.

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Table 1. Demographic data of the groups and the mean values of complete blood count parameters.

Group	No n (%)	Gender (F/M)	Mean Age (year±SD)	Mean Hb (g/dl±SD)	Mean Htc (%±SD)	Mean MCV (fl.±SD)	Mean WBC (10 ³ /ml±SD)
1	89 (52)	38/51	5.25±3.71	11.05±1.36	34.08±3.63	75.14±7.30	8.75±3.60
2	80 (48)	42/38	7.39±4.00	12.41±1.09	37.25±3.20	81.46±5.23	8.20±4.33
p	> 0.05	> 0.05	0.0001	0.0001	0.0001	0.0001	> 0.05

Results

Patient characteristics

The subjects were between 18 months and 16 years old. A total of 89 CP subjects and 80 subjects with the complaint of seizure for the first time were enrolled in the study. There were no statistical difference in terms of number of study subjects and gender ratio. However CP subjects were markedly younger than control group (Table 1). We believe that this age discrepancy is due to loss of elderly chronic CP subjects from routine follow-up visits with the misbelief that no benefit can furthermore be obtained by medical terms for their neurological problems.

Vaccination status

Patients with CP had substantially more missed shots of immunization (p: 0.0015) when compared to control group (Table 2). There were 31 missed shots vs. 11 in control group. The detailed list of vaccination status is shown on Table 2. There was only 1 subject (MMR vaccine) in CP group and 5 in the control group (3 Hib, 1 MMR, 1 varicella vaccines) who had their children vaccinated with extra vaccines and the difference was statistically insignificant.

Table 2. The detailed list of immunization charts.

Immunization status	CP group (n=89)	Control group (n=80)	P
Complete	58	69	
1 missing	16	9	
2 missing	9	1	
3 missing	6	1	
Total missing	31	11	0.0015
1 extra vaccine	0	5	
2 extra vaccines	1	0	
Total extra	1	5	0.102

Hematological parameters

Mean Hb, mean Htc and mean MCV values of CP group were substantially lower than control group (all p< 0.0001). When Hb and Htc levels of the subjects were evaluated according to their age-related reference

values, there were 38 anemic patients in CP group (42.6%) and 17 in control group (21.2%), which was significantly different (χ^2 :11.003, p<0.05).

Urinary tract infection

There was statistically significant difference between groups in terms of urinary tract infection (Table 3). The CP subjects (14%) have increased number of UTI when compared with control group (5%). The major organism infecting the urinary tract in both groups was *E. coli* with the same percentage (62%). The list of pathogens was detailed on Table 3.

Table 3. The detailed list of urinary tract and intestinal pathogens.

Pathogen	Cerebral Palsy (n=89)	Control group (n=80)	p
Urinary tract infection	<i>E. coli</i>	8	3
	<i>P. vulgaris</i>	1	1
	<i>K. oxytoca</i>	2	0
	<i>P. aeruginosa</i>	2	0
Total	13 (14%)	4 (5%)	0.038
Intestinal parasites	<i>G. lamblia</i>	10	9
	<i>E. vermicularis</i>	4	5
	<i>B. hominis</i>	2	0
	<i>Entamoeba coli</i>	0	2
Total	16 (18%)	15 (19%)	>0.05

Intestinal parasites

There was no difference between the groups in terms of intestinal parasitic infestation (Table 3). Both groups had the same percent of intestinal pathogens (18% vs 19%). The most common pathogens were similar in groups, *G. lamblia* and *E. vermicularis*.

Discussion

Diagnosing CP usually involves a period of waiting for the definite and permanent appearance of specific motor problems. Making the diagnosis of cerebral palsy is only the beginning since it is a condition that originates in early childhood but affects individuals throughout their life span. The role of the pediatric health care provider is to help families manage the ongoing health issues that may arise, and to give the

families the confidence they are doing all that they can. In this study, we wanted to find out certain common pediatric problems, but of non-neurological origin, of CP patients visiting pediatric neurology outpatient clinic that might have been overlooked in previous medical visits.

There are no special recommendations for standard vaccination of patients with chronic neurological deficits in Turkey. These disabled children undergo nationwide implemented EPI. The neglect or reluctance to immunize children with neurological diseases has not been sufficiently documented yet. To our knowledge, there are only 2 studies in the literature. The first study⁶ dates back 25 years ago which is a retrospective review of the file records. The 25% of handicapped children in a Rehabilitation Centre had incomplete vaccination. In a recent study,⁷ Tillmann et al. showed that CP patients (n=66) received less immunization shots available and also vaccinated later than the scheduled time in Switzerland than age-matched healthy controls (n=132). Similarly, we found out that more than one-third of CP group (35%) in this study had one or more missed shots and this ratio was more than the double of the control epilepsy group (13%). Unfortunately, handicapped children are still at an increased risk for preventable infections. Therefore, asking for immunization records might afford a good opportunity for CP subjects during the pediatric neurology visit.

It is well-known that infections cause more complications in children with chronic neurologic disorders because of feeding difficulties, lacking of personal hygiene, immobilization and etc. In our study, only one CP subject had received MMR vaccine as an extra shot which means, unfortunately, the whole CP subjects were lacking MMR, varicella, Hib, hepatitis A and 7-valent pneumococcal vaccines. There is only one article clearly delineating a vaccine preventable disease course in physically handicapped children. Enright F and et al. summarized a varicella outbreak in a rehabilitation center⁸ where 55% had complications. However, the risk of hospitalization in general population in USA is 10 hospitalizations per 10.000 cases for children aged less than 14 years.⁹ That's why, the parents of CP subjects should be encouraged to undergo extra vaccination if any.

Children with cerebral palsy face multiple challenges to nutrition¹⁰ and are accepted as underweight due to their chronic disease. Previous studies in different cohorts showed that malnutrition is correlated with anemia^{11,12} and this is plausible since calorie deficient children are also very likely to be deficient in other micronutrients, notably iron. In the present study, the high anemia ratio of CP patients (42.5%) which is the double of the

control group highlights the importance of the topic. In a recent study, Ohwada H et al. found out anemia in 25.0% for males and 33.3% for females in elderly CP subjects.¹³ The higher anemia ratio in this study is presumed to depend on the fact that children need more calories and nutrients for growth. It is of great value not to overlook anemia in pediatric CP subjects because it is well-known that anemia affects cognitive function and physical work performance.¹¹

Nutrient loss and anemia can result from many of the common parasitic infections. Several studies provided quite convincing evidence of an important mechanism by which parasites can impair children's nutrition and growth.¹⁴ In this study, the incidence of intestinal parasites (18%) was equal in both groups. The search for keywords "CP and intestinal parasites" yields no article but one published 55 years ago in Polish. That's why we can't compare our results with the literature. We initially presumed that CP patients might have a higher incidence of intestinal parasites since the majority of subjects lacking personal hygiene. On the other hand, the limitations in ADL might have yielded less exposure to pathogens by environmental factors.

As a result of undernutrition and diminished mobility, constipation for these individuals is more than a nuisance which is a major predisposing factor to urinary tract infections.¹⁵ In addition, neurogenic bladder, intermittent catheterization and vesicoureteral reflux are major contributors to urinary tract infections for CP patients.¹⁶ Karaman MI et al. showed that neurogenic detrusor overactivity or dyssynergia (involuntary contractions during bladder filling) with a low bladder capacity was present in 21 CP children (58%). Having listed the major causes for UTI in CP patients, we should emphasize the importance of personal hygiene in preventing UTI which is surely lacking in the majority of CP patient.

Urinary tract infections in CP subjects have been investigated less thoroughly although it is expected to be a common problem in pediatric CP subjects. Ozturk M et al.¹⁶ showed that 13/40 pediatric CP patients (32.5%) had UTIs whereas their 21 siblings, in the control group, had only one infection. In our study, 13 of the CP patients (14%) and 4 of the epilepsy group (5%) had UTIs and it was statistically higher (p:0.038). The reason why we had a lower ratio of UTIs than the previous study surely depends on excluding the subjects with known underlying nephrological/urological problems. Even if, the CP subjects have no history or symptoms of UTI, obtaining urine culture in regular visits might have helped early treatment of infection and early diagnosis of underlying pathology for proper management, as well.

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The most common pathogen was *E. coli* in both groups with similar ratio (62%). This result is similar to many latest published articles in pediatrics.¹⁷ On the other hand, we had 2 isolations of *P. aeruginosa* in CP patients which is quite rare in otherwise healthy subjects. In a very recent study, Tabibian JH et al. studied associations between uropathogen species and host characteristics with 319 samples at a university hospital clinical microbiology laboratory.¹⁸ The patients with *P. aeruginosa* UTI were more likely to have undergone urinary tract procedures (43% vs. 15% overall), have a neurogenic bladder (29% vs. 12% overall), received recent antibiotic therapy (52% vs. 24% overall). Two subjects in our study didn't have urinary tract procedure or catheterization but an urological consultation surprisingly revealed that they both were suffering neurogenic bladder.

This study has some limitations since we wanted to search the overlooked medical problems of CP subjects pertaining to their non-neurological medical conditions. To achieve this goal, we used many exclusion criteria. That's why, these results do not reflect the actual prevalence of aforementioned problems in this cohort. We believe that, the actual ratios of these common problems are much higher than this study if all the patients were included. As the literature on this epidemiological aspect in CP subjects is very limited, we expect that the present study will prompt similar studies in this field.

Finally, this prospective study highlights that the physicians, particularly in subspecialty outpatient clinics, should not only take care of specific referral complaints of their patients but also should be cautious about their general well-being.

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