



ORIGINAL ARTICLE

Psychotropic Drug Use in Preschool and Toddler Age Groups: An Evaluation of Hospital Admissions

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ABSTRACT

Objective: This study is aimed to evaluate the frequency of psychotropic drug use in children under age 6, and determine the predictive variables of psychotropic drug use.

Methods: For six months, data of children aged up to 6 admitted to Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital, Child Psychiatry Department was evaluated. Statistical analyses were performed using SPSS version 17 for Windows. A value of $p < 0.05$ was accepted as significant.

Results: Total of 953 children under age 6 were recruited. Mean age was 3.5 years and 67.7% were male. 83.4% of all had at least one psychiatric disorder. The most common diagnosis was communication disorders (33.5%). Comorbid psychiatric disorder was found in 5.9% of all and the most comorbid diagnosis was an oppositional defiant disorder (3.3%). Psychotropic drug use was found in 7.3%. The most commonly used drug was risperidone (4%). Predictors of treatment were found as aged in 4-5 ($p = 0.002$); male gender ($p = 0.049$); anxiety ($p < 0.001$); attention-deficit/hyperactivity disorder (ADHD) ($p < 0.001$), and pervasive developmental disorder ($p < 0.001$).

Conclusions: Our results could be useful for preferences of clinicians in treatment of children under age 6, and predictions of scientists working on these age groups in pharmaceutical industry. Multi-centered, large clinic-based studies are needed to constitute a systematic approach for psychopharmacological treatment in these age groups.

Keywords: Psychotropic drug use, preschool, toddler

INTRODUCTION

Early childhood psychiatric disorders that cause impairment, reduce quality of life, and increase family burden could continue throughout adulthood in the absence of appropriate interventions (1). Timely identification and treatment of psychiatric conditions during early childhood would also improve social, academic, interpersonal and family functioning (2). It is

more difficult to detect psychiatric disorders in childhood compared to adulthood. This difficulty is particularly prominent in early childhood (3). Distinguishing between normal developmental features and symptoms of psychopathologies could be difficult in infants, toddlers and preschoolers (4). Besides, very young children are less likely to be able to report on their own experiences and feelings. Diagnostic classifications of psychopathologies used for psychiatric evaluation are also mostly relied on symptoms seen in adulthood. For these reasons, properly diagnosing psychiatric conditions in these age groups becomes rather challenging (5,6). In recent years, the use of psychotropic medication for the treatment of mental health problems in young children has increased, and drug choices

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have changed mostly (7). In other words, defining the prevalence, clinical presentations and treatment options of psychiatric diagnoses in young children are crucially important in terms of helping clinicians understand general trends in these age groups.

There is a very large amount of studies examining the prevalence of psychiatric disorders and treatment preferences in children and adolescents admitted to child psychiatry departments in the literature (8-19). However, there are only a few studies conducted on the use of psychotropic medications in toddlers and preschoolers (2,19,20). The prevalence of and indications for psychotropic medication were determined among preschool children in Medicaid Program from 36 states in USA (21). The cohort study showed that the rate of children received at least one psychotropic drug was 1.19%, and medications for attention-deficit disorder/attention-deficit/hyperactivity disorder treatment were most common, followed by depression or anxiety and psychotic illness or bipolar. The most commonly prescribed medications were found as antidepressants (sertraline), tranquilizers/antipsychotics (risperidone), amphetamine-type stimulants (amphetamine salt combination) and nonamphetamine stimulants (caffeine citrate), respectively (21). Psychotropic medications are used in preschoolers despite limited evidence supporting safety or efficacy. So, the difficulties experienced the in usage of psychotropic agents in young children lead clinicians to study on these age groups (3,20,22-24).

In this study, we aimed to examine demographic features, psychiatric diagnoses, use of psychotropic medications, and predictors of medication use in children under age 6 who presented to the Ankara Pediatric Hematology Oncology Training and Research Hospital, Child Psychiatry Department.

METHODS

Sample

The medical record of 12.320 children under age 18 admitted to Ankara Pediatric Hematology Oncology

Training and Research Hospital, Child Psychiatry Department between June 2013 and December 2013 were reviewed retrospectively. Electronic records of 953 children under age 6 were reached. The proportion of children under age 6 among 12.320 admissions was 7.7% (n=953). Of these whose demographics and clinical data were complete were included in this study. Psychiatric disorders were diagnosed with clinical interview according to DSM-IV-TR criteria by a child psychiatrist.

Statistical Analysis

All statistical analyses were performed by using SPSS version 17 for Windows (Statistical Package for Social Sciences, Version 17.0, Chicago: SPSS Inc., 2008) statistical software package. Categorical variables were analyzed with chi-square (χ^2) test and Fisher's exact test. Interval variables were analyzed with t-test. The predictors of psychotropic medication use were analyzed with binary logistic regression analysis. In all evaluations, $p < 0.05$ value was considered statistically significant.

RESULTS

Mean age of children under age 6 was 3.5 ± 1.2 (min-max=1-5 years), 67.7% of them (n=645) were male. The children were divided into two groups: toddlers (ages from 1 to 3) and preschoolers (ages from 4 to 5). 53.6% of children (n=511) were preschoolers and in this group there was significantly more males than females ($\chi^2(1)=5.674$, $p=0.017$) (Table 1).

As regards their psychiatric diagnoses, 83.4% of all children (n=795) had at least one psychiatric disorder. Communication disorders, the most common diagnosis (33.5%), were followed by mental retardation (MR; 19.6%), anxiety disorders (11%) and attention-deficit/hyperactivity disorder (ADHD; 10.6%). The comorbid psychiatric disorders were detected in 5.9% of children (n=56), and among them oppositional defiant disorder (ODD) was the most common comorbid diagnosis (3.3%, see Table 1).

Psychotropic agent use was found in 7.3% of children (n=70), whose mean age was 4.2 ± 0.7 years (aged 2-5

Table 1: Sociodemographic and clinical features of children aged under 6 years old in terms of medication use or not

	Total n=953	Medication none n=883	Medication yes n=70	Statistics t or χ^2	P
Variables					
Age (years) ^a	3.5 (1.2)	3.5 (1.2)	4.2 (0.7)	6.940	0.000
Gender, n (%)					
Males	645 (67.7)	595 (67.4)	50 (71.4)	0.485	0.486
Females	308 (32.3)	288 (32.6)	20 (28.6)		
Age groups, n (%)					
Ages 1-3 (toddler)	442 (46.4)	429 (48.6)	13 (18.6)	23.492	0.000
Ages 4-5 (preschooler)	511 (53.6)	454 (51.4)	57 (81.4)		
Psychiatric diagnosis, n (%)					
Normal	158 (16.6)	158 (17.9)	0	NA	
Communication dis.	319 (33.5)	319 (36.1)	0	NA	
MR (IQ \leq 69)	187 (19.6)	179 (20.3)	8 (11.4)	3.216	0.073
Anxiety disorders	105 (11.0)	77 (8.7)	28 (40.0)	64.728	0.000
ADHD	101 (10.6)	71 (8.0)	30 (42.9)	82.977	0.000
PDD	26 (2.7)	22 (2.5)	4 (5.7)	2.538*	0.117
BIF (IQ=70-79)	22 (2.3)	22 (2.4)	0	NA	
Depressive disorder	13 (1.4)	13 (1.4)	0	NA	
Enuresis	8 (0.8)	8 (0.9)	0	NA	
Adjustment disorder	8 (0.8)	8 (0.9)	0	NA	
Sleep disorders	4 (0.4)	4 (0.4)	0	NA	
Tic disorders	2 (0.2)	2 (0.2)	0	NA	
Comorbidity					
None	897 (94.1)	846 (95.8)	51 (72.9)	61.778*	0.000
Yes	56 (5.9)	37 (4.2)	19 (27.1)		
ODD	31 (3.3)	26 (2.9)	5 (7.1)	NA	
MR (IQ \leq 69)	7 (0.7)	6 (0.6)	1 (1.4)	NA	
Elimination disorders	7 (0.7)	0	7 (10.0)	NA	
ADHD	4 (0.4)	2 (0.2)	2 (2.8)	NA	
Conduct disorder-NOS	4 (0.4)	0	4 (5.7)	NA	
Tic disorders	3 (0.3)	3 (0.3)	0	NA	

a: Mean (standard deviation); *: Toddler; **: Preschooler; dis.: Disorder; NA: Not-applicable; BIF: Borderline intellectual functioning; MR: Mental retardation; NOS: Not otherwise specified; ADHD: Attention deficit hyperactivity disorder; PDD: Pervasive developmental disorder; ODD: Oppositional defiant disorder

years). The most frequently recommended psychotropic agent was risperidone (4%, n=38), followed by fluoxetine (1.8%, n=17) and hydroxyzine (1.2%, n=11). Children having either anxiety disorders, ADHD, PDD or MR were treated with medication. 26.7% of children diagnosed with ADHD (n=27) were treated with risperidone and 3% of them (n=3) were treated with methylphenidate (MPH). On the other hand, in children with anxiety disorders, 15.2% of them (n=16) were treated with fluoxetine, followed by

10.5% of them (n=11) with hydroxyzine and %1 of them (n=1) with sertraline. Risperidone was used in 15.4% of the children diagnosed with pervasive developmental disorders (PDD) (n=4), and 3.7% of the children diagnosed with mental retardation (n=7) (Table 2).

Mean age of children who used any psychotropic medication was significantly higher compared to children who did not use (t(98.9)=6.940, p<0.001). Also there was significantly higher proportion of medication use in

Table 2: The proportion of medications used in children aged under 6 years old based on diagnoses

		None (n=883)	RSP (n=38)	FLU (n=17)	HDX (n=11)	MPH (n=3)	SER (n=1)
	n	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ADHD	101	71 (70.3)	27 (26.7)	0	0	3 (3.0)	0
Anxiety	105	7 (73.3)	0	16 (15.2)	11 (10.5)	0	1 (1.0)
MR	187	179 (95.7)	7 (3.7)	1 (0.5)	0	0	0
PDD	26	22 (84.6)	4 (15.4)	0	0	0	0

RSP: Risperidone; FLU: Fluoxetine; HDX: Hydroxyzine; MPH: Methylphenidate; SER: Sertraline; ADHD: Attention deficit hyperactivity disorder; MR: Mental retardation; PDD: Pervasive developmental disorder

Table 3: The predictors of medication usage in children aged under 6 years old using with binary logistic regression

	B	SE	Wald	df	pvalue	Exp(B)	95% CI Exp(B)	
							Lower	Upper
Age (4-5 years)	-1.082	0.344	9.897	1	0.002	0.339	0.173	0.665
Gender (Male)	-0.625	0.317	3.881	1	0.049	0.535	0.288	0.997
Comorbidity	-0.489	0.419	1.363	1	0.243	0.613	0.270	1.393
Anxiety	-3.622	0.434	69.753	1	0.000	0.027	0.011	0.063
ADHD	-3.206	0.473	46.021	1	0.000	0.041	0.016	0.102
PDD	-2.682	0.703	14.573	1	0.000	0.068	0.017	0.271

SE: Standard error; ADHD: Attention deficit hyperactivity disorder; PDD: Pervasive developmental disorder

preschooler group compared to children in toddler group (81.4% vs. 18.6%, respectively, $\chi^2 (1)=23.492$, $p<0.001$). Children who had psychiatric comorbidity were found to have a significantly higher proportion of medication usage than that of children with no comorbidity (27.1% vs. 4.2%, respectively, $\chi^2 (1)=61.778$, $p<0.001$) (Table 1).

Since medication usage was significantly related to the variables of age, psychiatric disorder, and comorbidity, a binary logistic regression analysis was carried out and findings revealed that the predictors of psychotropic agent use were the following; aged 4-5 years ($p=0.002$ $\beta=-1.082$ 95%CI (0.173-0.665)), male sex ($p=0.049$ $\beta=-0.625$ 95%CI (0.288-0.997)), anxiety disorders [$p<0.001$ $\beta=-3.622$ 95%CI (0.011-0.063)], ADHD [$p<0.001$ $\beta=-3.206$ 95%CI (0.016-0.102)] and PDD [$p<0.001$ $\beta=-2.682$ 95%CI (0.017-0.271)] (see Table 3).

DISCUSSION

The admission rates of children aged 0-5 years to child psychiatry departments in Turkey were found to range between 21.4% and 32.9% (8,10-12). Harpaz-Rotem and Rosenheck (2004) reported a similar rate in their study

conducted in USA (14). In our cross-sectional study, the admission rate was relatively lower than previous studies, suggesting that Turkish parents consider that emotional and behavioral problems in these age groups are due to being younger rather than psychopathology of children. Potential other reasons are that socio-cultural features and/or economical levels of our sample could affect the rate of admissions in these age groups.

Zito et al. (2007) reported the percentage of children aged 1–3 years as 68% in their own study (22). Another study conducted by Fontanella et al. (2014) reported the proportions ranging from 50.2% to 52.1% for children aged 2-3 years (25). Similarly, the rate of 1-3 years old children in our study was found at 46.4%.

Similar to the cohort study of Garfield et al. (2015) (21), male gender was prominent in our sample (67.7%). Other studies conducted in Turkey have varying rates compared to our study in terms of gender. A retrospective study carried out in Ordu province revealed that 55.6% of the sample was male (8). Aras et al. (2007) showed that the rate of male gender in the sample of children aged 1–6 years who presented to the Dokuz Eylul University, Child and Adolescent Psychiatry Department was 72.5% (12). In another study, Akin (2013) pointed out that the

proportion of male gender among children aged 0–6 years admitted to the Batman State Hospital was 48.3% (9). Our findings were similar with these results for toddlers and preschoolers. In boys under aged 6 years, psychiatric disorders could be possible to be more common and symptomatic, or impair functionality much more compared to girls aged same years.

In our study, 83.4% of all children had at least one psychiatric diagnosis. Similarly, in a preschool aged group (0–6 aged), the rates of having any psychiatric diagnosis reported as 50.3% and 44.8% in previous studies (8,10). Another study carried out between 2002 and 2008 in the USA showed that the rate of psychiatric diagnosis increased from 9.9% to 14% in a preschool sample (22). In our study, 13.9% of all children had more than one psychiatric disorder. Fontanella et al. (2014) reported that this rate ranged from 0.9% to 1.7% (25). Our study was conducted in a multi-specialty children hospital that complicated patients are referred to by physicians in all around of Turkey. Therefore, participants of the study are more likely to be impaired. Our rate of having any psychiatric disorder that was higher than other studies could be explained by cross-sectional design of our study.

We found that communication disorders, mental retardation and anxiety disorders were common in children under age 6. These results are consistent with the other studies carried out on this field (8-10,14,19,25). In our sample, the rate of psychotropic medication use was 7.3%. Another study whose sample size of 274.518 reported this rate as 2.3% in the USA (22). An epidemiological study in Italy showed the rate of psychotropic medication use in children and adolescents as 1.7% (26). Similarly, a cohort study conducted in the USA between 2002 and 2008 in preschoolers revealed that the rate of psychotropic medication use increased from 1.7% to 1.9% (21, 25). A study that consisted of children aged 2–5 years in Thailand between 1994 and 2009 showed that the rate of psychotropic drug use was 1.07% (27). Another study in Turkey pointed out that 20.8% of children aged 0–5 years admitted to the child psychiatry department had used any psychotropic medication (19). A study that consisted of 1467 children under age 6 carried out in Dokuz Eylul University, Child

Psychiatry Department revealed that 6.3% of them were treated with a psychotropic agent (28). Our findings are consistent with the other studies conducted in Turkey in terms of the proportion of medication use but higher than in the other countries because of our sample's characteristics. Due to the socio-cultural features and/or economical levels of our sample, clinicians and parents seem to prefer psychopharmacological treatments instead of behavioural therapies. Further studies consisting of community samples will enlighten to these findings are needed.

Mean age of children whom we recommended psychotropic medication use was 4.2 ± 0.7 years (2–5 aged). This result was significantly higher than children who did not use any medication. Consistently with our findings, Garfield et al. (2015) reported that psychotropic medication use increased with age among preschool children (21).

In our study, mostly prescribed medication agents were risperidone, fluoxetine, hydroxyzine and methylphenidate (MPH), respectively. There is a very large amount of studies pointing out that these medication agents were commonly used in children under age 6 (19,24,27). Risperidone is one of the approved agents for use of children under age 6 by FDA. It is easy to use in children who cannot swallow any pills due to its liquid form and a great number of studies showed risperidone as effective and safe in children with disruptive behavior disorders, autism-related behavioral problems, bipolar disorder and acute stress disorder (29–32). Consequently, it is not surprising that the most prescribed agent in our sample was risperidone. Fluoxetine and hydroxyzine were the most preferable agents to treat children under age 6 with anxiety in our hospital. There are some case series studies pointing out that selective serotonin reuptake inhibitors (SSRI) like fluoxetine, sertraline and escitalopram are effective and tolerable in preschoolers (33,34). In our study, fluoxetine was mostly prescribed SSRI due to its liquid form. Hydroxyzine is one of the antihistaminic agents having mild sedation effect and lesser side effects compared the others and it can be used as anxiolytic. It could also be used in sleep disorders (28). For these reasons, this agent

could often be preferable in children under age 6. Although clinically-significant improvements in PDD symptoms were found in very young children receiving Omega-3-6-9 daily (35), there was no usage of Omega-3-6-9 in children with PDD in our sample.

In contrast to our findings, some studies revealed that amphetamines are mostly used agents in preschoolers in the USA (22,25). Amphetamines which were approved for young children by FDA in the USA are not available in our country. Therefore, we could not use these agents in young children. In addition, there is a large number of convincing reports that methylphenidate is safe and tolerable in preschoolers (36-38). However, all ADHD drugs prescribed for young children are off-label in Turkey.

The predictors of medication use were an age in 4–5 years, male sex, anxiety, attention deficit hyperactivity disorder, and pervasive developmental disorder. Being preschooler and male were related to increased medication use (21,22,26,27). Fontanella et al. (2014) revealed that being 4 to 5 aged and male in preschoolers between 2002 and 2008, and having ADHD, bipolar disorders, and disruptive behavior disorders were related with medication use (25). Another study conducted in Turkish preschoolers between 1997 and 2002 showed that 73.9% of all children were 4 to 6 aged and 66.3% of them were male. These findings are consistent with our results.

Limitations of our study are the following; its design was cross-sectional and retrospective. Our study focused on only medication use of children under age 6 not complaints of them admitted to the child psychiatry department. Besides, the evaluation of psychotropic drug use based on electronic data is likely to be inefficient. Finally, our findings cannot be generalized to all children under age 6 in the community.

In conclusion; this cross-sectional study examining predictors of receiving psychopharmacologic interventions in children under age 6 has shown that medication use is recommended in case of an age in 4–5 years, male gender, anxiety, ADHD and pervasive developmental disorders. Our results could be useful for preferences of clinicians in the treatment of children under age 6, and the predictions of neuroscientists

working on these age groups in pharmaceutical industry. Future multi-centered, large clinic-based studies should focus on trends of treatment in early childhood psychiatric disorders, and constitute a systematic approach for psychopharmacological treatment in these age groups.

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