Adverse Events Associated with Risperidone Use in Pediatric Patients: A Retrospective Biobank Study

Kazeem A. Oshikoya[a], MD, PhD, Robert Carroll[b], PhD, Ida Aka[c], MPH, Dan M. Roden[a,b,d], MD, Sara L. Van Driest[a,c], MD, PhD

Affiliations: Departments of [a]Medicine, [b]Biomedical Informatics, [c]Pediatrics, and [d]Pharmacology, Vanderbilt University School of Medicine, Nashville, Tennessee, United States

'Drugs-Real World Outcomes'

ESM Table

156 adverse events reported in 110 individuals using risperidone and actions taken by the health care provider

Number of individuals with adverse event(s) (n=110)	Number of adverse events per patient	Adverse event(s)	Total adverse event(s) (n=156)	Time of onset of adverse event(s) relative to the time of risperidone commencement	Risperidone dose at time of adverse event(s)	Action taken by provider	Newly substituted antipsychotic drug (if applicable)
1	5	Heavy tongue, hypersalivation, droopy eyes, weight gain, and extrapyramidal symptom (akathisia)	5	10 days (heavy tongue, hypersalivation, and droopy eyes), and 6.8 months (akathisia and weight gain)	0.5 mg po q12h (heavy tongue, hypersalivation, and droopy eyes), 0.25 mg po every morning (akathisia and weight gain)	Risperidone dose was reduced to 0.25 mg po every morning when patient experienced heavy tongue, hypersalivation, and droopy eyes. The reduced dose of risperidone was continued	
1	4	Gynecomastia, hyperphagia, weight gain (obesity), and elevated blood sugar with diabetes	4	3 months (developed gynecomastia), 3 months later (hyperphagia and significant weight gain up to obesity), and 8 months later (developed diabetes)	2 mg po q6h (gynecomastia), 4 mg po qhs (hyperphagia and obesity), 2 mg po qhs (elevated blood sugar and diabetes)	Risperidone dose was reduced to 4 mg po qhs when patient developed gynecomastia; further reduced to 2 mg qhs when patient became hyperphagic and obese; and subsequently discontinued when patient developed diabetes. Risperidone was eventually replaced with new	

						antipsychotic drug	
1	4	Hyperphagia, weight gain, elevated blood sugar, and hyperlipidemia	4	3.4 months	0.25 mg po qhs	Risperidone dose discontinued	
1	3	Extrapyramidal symptom, daytime hypersomnia, and abnormal thyroid function test	3	9 months (dystonia), 16 days later (daytime hypersomnia), and elevated thyroid function occurred 11 months later	1 mg po every morning and 2 mg po qhs	Risperidone dose continued when patient developed dystonia (treated with beztropine). Risperidone discontinued following abnormal thyroid function test (treated with levothyroxine).	Paliperidone 6 mg po qhs
1	3	Daytime hypersomnia, worsening of constipation, and extrapyramidal symptom (akathisia)	3	6 months (started to experience daytime hypersomnia), 1.2 years later (started to experience worsening constipation), 1.2 years later (started to experience akathesia)	0.25 mg po qhs (daytime hypersomnia), 0.75 mg po every morning and 0.5 mg qhs (worsening of constipation), and 1.0 mg po every morning and mid-day, and 2.0 mg qhs (akathesia)	Risperidone dose was gradually reduced to 1.0 mg po q12h for 3 days, followed by 0.5 mg q12h until akathesia improved	
1	3	Hyperphagia, thirst, and extrapyramidal symptom	3	16 days (hyperphagia and thirst), and 23 days (extrapyramidal syndrome)	2.0 mg po q8h	Risperidone dose continued when patient experienced hyperphagia and thirst, but discontinued after experiencing abnormal body movement	Aripiprazole 5 mg po every morning
1	3	Nervousness, extrapyramidal symptom, and elevated blood	3	1 day after dose increase from 1.0 mg qhs to the current dose	0.5 mg p.o every morning and 1.0 mg qhs	Risperidone dose continued throughout the time AEs were	

		sugar (prediabetes)		(Nervousness), 4.8 year later (tremor), and 1 week later (prediabetes)		experienced by the patient. Tremor was treated with benztropine, while blood sugar was monitored regularly	
1	3	Weight gain, constipation, premature adrenarche	3	4.8 years	2.5mg po q12h	Risperidone dose discontinued	
1	3	Weight gain, hypotension, and prolonged QTc interval	3	2.3 months (weight gain), and 6.5 months (hypotension and prolonged QTc)	2 mg po qhs	Risperidone dose continued when patient experienced weight gain, but discontinued during hypotension and prolonged QTc	Aripiprazole 5 mg po qhs
1	3	Weight gain, hyperphagia, and elevated blood sugar with diabetes mellitus	3	4 weeks (hyperphagia), 5 months (weight gain), and 6.7 years (type 2 diabetes)	0.5 mg po qhs (hyperphagia and weight gain), 0.5 mg po q12h (diabetes mellitus)	Risperidone baseline dose continued when patient experienced hyperphagia and weight gain, but new dose discontinued when diabetes began	
1	3	Weight gain, elevated prolactin, and abnormal thyroid function test	3	4.2 years	1.0 mg po q12h	Risperidone dose discontinued. Abnormal thyroid thyroid function test manifested as Graves' disease treated with methimazole	Aripiprazole 2.5 mg po q12h
4	2	Weight gain and hyperphagia	8	2.4 months	0.25 mg po q12h	Risperidone dose continued	

				4.4 months	0.5 mg po qhs	Risperidone dose continued	
				6.8 months	0.5 mg po q24h	Risperidone dose discontinued	Aripiprazole 2 mg po qhs
				7.2 months	0.5 mg po qhs	Risperidone dose continued	
2	2	Day time hypersomnia and weight gain	4	4.0 months	0.25 mg po qhs	Risperidone dose continued	
				6.0 months	0.5 mg po q12h	Risperidone dose continued	
2	2	Daytime hypersomnia and fatigue	4	21 days	1.0 mg po qhs	Risperidone dose discontinued	
				3.5 months	0.375 mg po qhs	Risperidone dose continued	
1	2	Elevated blood sugar with diabetes mellitus, and hyperlipidemia	2	22.6 months	0.5 mg po every morning and 1.0 mg qhs	Risperidone dose continued	Clozapine 75 mg po qhs
1	2	Extrapyramidal symptom (akathisia) and worsened behavioral problems	2	2 months	0.5 mg po q12h	Risperidone dose discontinued	
1	2	Daytime hypersomnia and elevated thyroid function (TSH)	2	2 months (daytime hypersomnia), and 9 months later (elevated TSH)	0.5 mg po q12h (daytime hypersomnia), and 0.5 mg po qhs (elevated TSH)	Following daytime hypersomnia, risperidone dose reduced to 0.5 mg po qhs. Following elevated TSH, risperidone was discontinued	
1	2	Weight gain and extrapyramidal symptom	2	1 year	0.5 mg po qhs	Risperidone dose discontinued	Aripiprazole 2.5 mg po qhs
1	2	Weight gain and abnormal thyroid function (TSH)	2	1.5 years	0.5 mg po every morning	Risperidone dose continued	

1	2	Weight gain and elevated blood sugar	2	5 months	0.25 mg po q12h	Risperidone dose continued	
1	2	Weight gain and elevated prolactin	2	2.8 years (weight and hyperprolactinemia reported after several dose increase from 0.5 mg po q12h to 3.0 mg po qhs after year, followed by 4.0 mg po qhs after 2 years, and 5.0 mg po qhs after 3 days)	5.0 mg po qhs	Risperidone dose was reduced to 1.0 mg po q12h	
1	2	Weight gain and musculoskeletal pain	2	13.0 months	1.0 mg po every morning and afternoon, 1.5 mg qhs	Risperidone dose was tapered off over a month and replaced with Aripiprazole	Aripiprazole 5 mg po qhs
1	2	Weight gain and QTc prolongation	2	4.4 months	0.5 mg po q12h	Risperidone dose continued	Ziprasidone mg po qhs
1	2	Elevated blood sugar and hyperlipidemia	2	6 days	0.5 mg po q8h	Risperidone dose continued	
1	2	Hot flashes and fainting spells	2	8 days	0.25 mg po q12h	Risperidone dose discontinued	
1	2	Hyperphagia and abnormal thyroid function elevated (TSH)	2	1.5 months (hyperphagia), and 21 months later (elevated TSH level)	1 mg po q12h	Risperidone baseline dose continued when patient experienced hyperphagia, but discontinued when serum TSH level was elevated	Olanzapine 2.5 mg po q6h
16	1	Extrapyramidal symptom	16	1 day (after tolerating 1 mg po qhs for 7.6 months)	1mg po q12h	Risperidone dose discontinued	

	1 day (after tolerating 0.2 mg po q12hs for 13 days)	0.4 mg po q12h	Risperidone dose continued	
	2 days	0.125 mg po q12h	Risperidone dose discontinued	
	3 days	0.5 mg po q8h	Risperidone dose continued	
	4 days	0.25 mg po q12h	Risperidone dose discontinued	Quetiapine 6 mg po qhs
	10 days	0.25 mg po q12h	Risperidone dose discontinued	
	15 days	1 mg po q12h	Risperidone dose continued	
	1.4 months	1.5 mg po every morning and 1.0 mg qhs	Risperidone dose discontinued	
	2 months	0.25 mg po every morning and 0.5 mg qhs	Risperidone dose continued, while tremor was treated with benztropine	
	3 months	0.25 mg po qhs	Risperidone dose discontinued	
	5.4 months	5 mg po qhs	Risperidone dose discontinued	
	8.6 months	0.25 mg po q6h	Risperidone dose continued	
	9.2 months	0.25 mg po q12h	Risperidone dose discontinued	
	1 year	0.25 mg po q12h	Risperidone dose continued	

				1.1 years	0.125 mg po q8h	Risperidone dose discontinued	Aripiprazole 15 mg po every morning
				1.1 years	0.25 mg po qhs	Risperidone dose continued	Olanzapine 2.5mg po q12h
12	1	Weight gain	12	1 month	0.25 mg po qhs	Risperidone dose continued	Aripiprazole 2.5 mg po qhs
				2.8 months	1.0 mg po qhs	Risperidone dose discontinued	Aripiprazole 5 mg po every morning
				3.3 months	0.25 mg po qhs	Risperidone dose discontinued	
				3.6 months	1.0 mg po q12h	Risperidone dose continued	
				3.8 months	0.5 mg po q8h	Risperidone dose continued	
				4.4 months	2.0 mg po q24h	Risperidone dose discontinued	Paliperidone 1.5 mg po
				5.1 months	1.0 mg po qhs	Risperidone dose discontinued	
				6 months	0.5 mg po qhs	Risperidone dose discontinued	Aripiprazole 5 mg po q12h
				6.3 months	1.0 mg po q12h	Risperidone dose reduced to 1.5 mg po qhs	
				9.1 months	1 mg po qhs	Risperidone dose discontinued	Olanzapine 5 mg po q12h
				10 months	0.25 mg po q12h	Risperidone dose continued	Aripiprazole 2.5 mg po qhs
				1.8 years (weight gain after 1.2 years of risperidone; progressed to	1.0 mg po q8h	Risperidone dose initially reduced to 1.0 mg po qhs and	Aripiprazole 5 mg po qhs

				obesity despite dose reduction)		discontinued after 7 months
13	1	Day time hypersomnia	13	2 days after dose increment from 0.5mg po qhs	0.5 mg po every morning and afternoon, and 1.5 mg qhs	Risperidone dose reduced to 0.5 mg po q12h
				2 days	0.5 mg po qhs	Risperidone dose continued
				3 days	0.5 mg po q12h	Risperidone dose discontinued
				19 days	0.25 mg po qhs	Risperidone dose discontinued
				2 months	0.5 mg po qhs	Risperidone dose discontinued
				2.7 months	2.5 mg po q12h	Risperidone dose discontinued
				2.8 months	0.5 mg po every morning	Risperidone continued with a split dose of 0.25 mg po q12h
				7.7 months (tolerated several dose increases from 0.25 mg po qhs to 0.5 mg po qhs after 3 months; developed AE after the dose was further increased)	0.75 mg po qhs	Risperidone dose was reduced to 0.5 mg po qhs
				8 months	0.5 mg po every morning and 0.25 mg qhs	Risperidone dose was reduced to 0.5 mg po qhs
				11 months	0.25 mg po every morning and afternoon, 0.5 mg qhs	Risperidone dose continued

				11 months	0.25 mg po q12h	Risperidone dose discontinued	Aripiprazole 5 mg po qhs
				1.3 years	0.5 mg po q12h	Risperidone dose continued	
				1.4 years	0.25 mg po q12h	Risperidone dose discontinued	Aripiprazole 5 mg po qhs
6	1	Hyperphagia	6	1 day	0.25 mg po q6h	Risperidone dose continued	
				1.1 months	0.5 mg po qhs	Risperidone dose continued	
				1.3 months	1.0 mg po q12h	Risperidone dose continued	
				3.8 months	1.0 mg po qhs	Risperidone dose continued	
				8.2 months (tolerated 0.5 mg po q12h for for 8 months; developed AE after the dose was increased)	0.75 mg po q12h	Risperidone dose continued	
				1 year	0.5 mg po q6h	Risperidone dose continued	
5	1	Hypersalivation (sialorrhea)	5	2 months	0.6 mg po q12h	Risperidone dose continued	
				4.8 months	0.5 mg p.o q12h	Risperidone dose continued	
				6.3 months	1.0 mg po qhs	Risperidone dose continued	
				3.5 years (tolerated 0.25 mg po every morning and 0.5 mg po qhs for 3.5 years; developed AE 12 days later after the dose was increased)	0.5mg po every morning and 1.0mg po qhs	Risperidone dose continued	
				7.2 years (tolerated 0.5 mg po q12h for a year; developed	0.75 mg po q12h	Risperidone dose reduced to 0.25 mg po q12h	

				AE after the dose was increased)			
2	1	Hyperlipidemia	2	3.5 years	0.125 mg po qhs	Risperidone dose continued	
				5.1 months	0.5 mg po qhs	Risperidone dose discontinued	Ziprasidone 20 mg po qhs
3	1	Worsened behavioral problems (aggression) or (Behavioral outburst)	3	4 months	1.0 mg po qhs	Risperidone dose discontinued	Aripiprazole 10 mg p.o qhs
				1.6 years	0.25 mg po q12h	Risperidone dose discontinued	Olanzapine 5 mg po q12h
				2.5 months	0.25 mg po qhs	Risperidone dose discontinued	
2	1	Poorly controlled diabetes mellitus	2	3 days	0.25mg po every morning and 0.5 mg qhs	Risperidone dose continued, but insulin dose increased	
				15 months	0.5 mg po qhs	Risperidone dose discontinued	Aripiprazole 5mg po qhs
2	1	Precocious puberty	2	6 months	0.25 mg po qhs	Risperidone dose discontinued	
				1.3 years	0.5 mg po qhs	Risperidone dose discontinued	
2	1	Prolonged QTc	2	20 days	1.0 mg po every morning	Risperidone dose continued	
				3 months	0.125 mg po q6h	Risperidone dose reduced to 0.125 mg po qhs	
1	1	Acute exacerbation of neuromyotonia (muscle cramp)	1	12 days	0.5 mg po qhs	Risperidone dose discontinued	
1	1	Anxiety	1	5 months	0.5 mg po q12h	Risperidone dose discontinued	

1	1	Daytime fatigue	1	28 days	2.0 mg po qhs	Risperidone dose continued	
	1	Elevated blood sugar with diabetes mellitus	1	20 months	0.5 mg po qhs	Risperidone dose discontinued	
1	1	Early or increased menstrual flow in a female	1	3.7 months	5 mg po q24h	Risperidone dose discontinued	Aripiprazole 10 mg po qhs
1	1	Elevated blood pressure	1	4 months	0.5 mg po q12h	Risperidone dose continued	
1	1	Hyperthermia	1	12 days	0.125 mg po q8h	Risperidone dose discontinued	
1	1	Abnormal thyroid function (Elevated TSH)	1	6.1 months	1.25 mg po every morning and 1.0 mg qhs	Risperidone dose continued	
1	1	Gynecomastia	1	3.8 years	0.5 mg po q12h	Risperidone dose discontinued	
1	1	Headache	1	4.4 months	0.75 mg po qhs	Risperidone dose discontinued	Olanzapine 5 mg po qhs
1	1	Worsened constipation	1	1.3 months	0.25 mg po qhs	Risperidone dose discontinued	
1	1	Oculogyric crisis	1	8 days	0.25 mg po qhs	Risperidone dose temporarily withheld, treat with benztropine until symptom stopped. Risperidone done continue a week later and used along with benztropine	
1	1	Orthostatic hypotension	1	24 days	0.5 mg po q6h	Risperidone dose discontinued	Quetiapine 25 mg po q12h

1	1	Multiple bruises	1	1.2 years	0.5 mg po q12h	Risperidone dose continued
1	1	Restlessness	1	26 days	0.5 mg po qhs	Risperidone dose discontinued
1	1	Tachycardia	1	7 days	0.75 mg po q12h	Risperidone dose discontinued

Footnotes: “po” refers to by mouth, orally; “qhs” refers to every bedtime; “q6h” refers to every six hours; “q8h” refers to every eight hours; “q12h” refers to every twelve hours; “q24h” refers to every twenty-four hours; TSH refers to thyroid stimulating hormone; AE refers to adverse event.