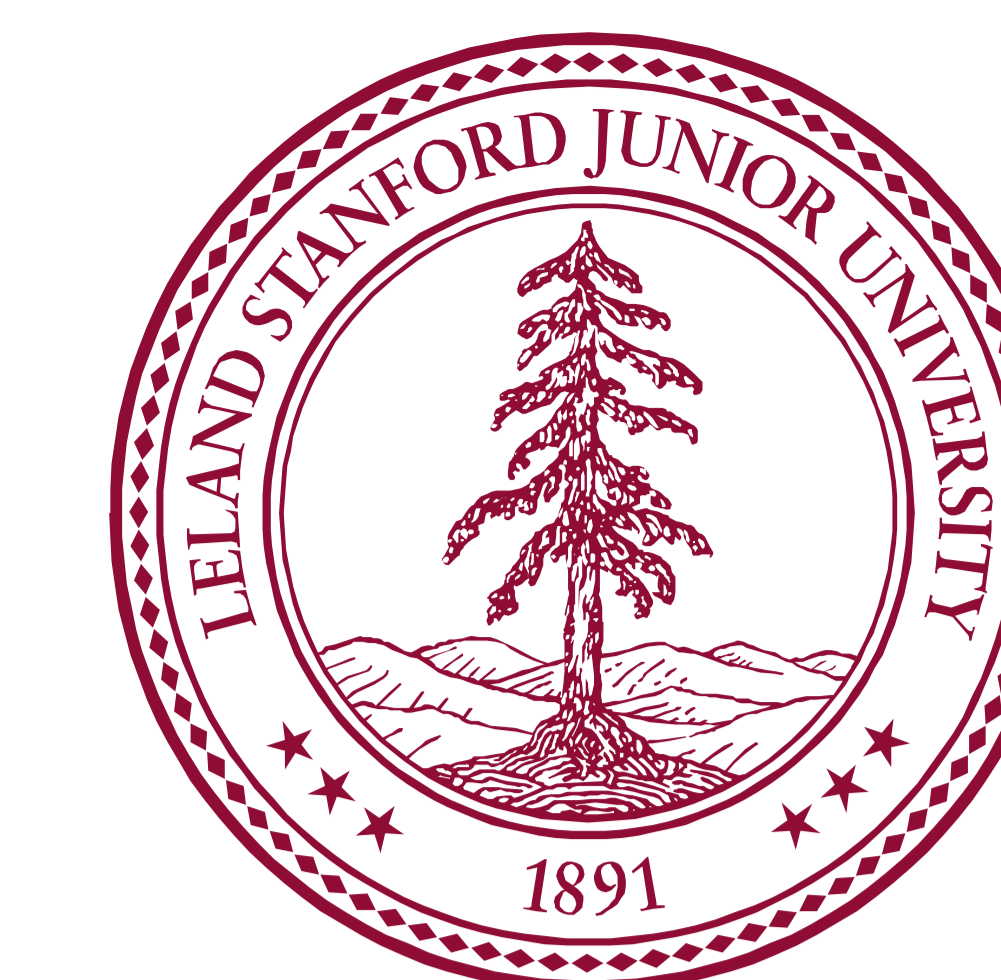




Differences in Antipsychotic Adverse Events among Adult, Pediatric, and Geriatric Populations - An Analysis of the FDA Adverse Events Reporting System



Narmadan A. Kumarasamy, Hersh Sagreiya, Yi-Ren Chen, Karthikeyan E. Ponnusamy, Amar Das
Stanford University Center for Biomedical Informatics Research, Stanford, CA

Introduction

In recent years, antipsychotic medications have been increasingly used in pediatric and geriatric populations. Many of these drugs were approved based on clinical trials in adult patients only. Preliminary studies have shown that the “off-label” use of these drugs in pediatric and geriatric populations may result in adverse events not found in adults. In this study, we utilized the large-scale FDA Adverse Events Reporting System (AERS) database to look at differences in adverse events from antipsychotics among adult, pediatric, and geriatric populations.

Methods

We performed a systematic analysis of the FDA AERS database using MySQL by standardizing the database using structured terminologies and ontologies. We compared adverse event profiles of atypical versus typical antipsychotic medications among adult (18-65), pediatric (age < 18), and geriatric (>65) populations. Data was analyzed using descriptive and comparative statistics.

Generic Name	Class	% of Adverse Events			p-value (vs. Adults)	
		Kids	Adults	Geriatrics	Kids	Adults
Aripiprazole	Atypicals	24.208	8.803	4.080	0.000	0.000
Chlorpromazine	Typicals	1.340	1.749	1.893	0.018	0.168
Clozapine	Atypicals	4.265	15.552	11.696	0.000	0.000
Fluphenazine	Typicals	0.020	0.526	0.370	0.000	0.026
Haloperidol	Typicals	4.285	5.768	11.381	0.000	0.000
Loxapine	Typicals	0.183	0.275	0.294	0.115	0.379
Mesoridazine	Typicals	0.000	0.023	0.022	0.146	0.480
Molindone	Typicals	0.061	0.027	0.098	0.093	0.001
Olanzapine	Atypicals	15.028	23.352	21.619	0.000	0.000
Paliperidone	Atypicals	0.589	0.547	0.207	0.351	0.000
Perphenazine	Typicals	0.020	0.279	0.359	0.000	0.097
Pimozide	Typicals	0.223	0.164	0.196	0.169	0.251
Promazine	Typicals	0.041	0.284	0.022	0.001	0.000
Quetiapine	Atypicals	22.827	24.431	22.011	0.006	0.000
Risperidone	Atypicals	21.730	12.915	23.197	0.000	0.000
Thioridazine	Typicals	0.366	0.399	0.533	0.362	0.034
Thiothixene	Typicals	0.000	0.458	0.141	0.000	0.000
Trifluoperazine	Typicals	0.061	0.300	0.316	0.001	0.402
Ziprasidone	Atypicals	4.752	4.149	1.567	0.022	0.000
All Atypicals		93.400	89.748	84.376	0.000	0.000
All Typicals		6.600	10.252	15.624	0.000	0.000

Table 1: Comparison of the Number of Adverse Events in Each Population: blue (significant kids vs adults), green (significant adult vs geriatrics), purple (significant for both comparisons)

Results

Drug Name	Event Kids	N	Event Adults	N	Event Geriatrics	N
Aripiprazole	WEIGHT INCREASED	102	DIABETES MELLITUS	288	TREMOR	27
Aripiprazole	TREMOR	86	WEIGHT INCREASED	235	NEUROLEPTIC MALIGNANT SYNDROME	22
Aripiprazole	DYSTONIA	82	INSOMNIA	227	PARKINSONISM	21
Aripiprazole	SOMNOLENCE	63	TREMOR	177	DEATH	18
Aripiprazole	EXTRAPYRAMIDAL DISORDER	62	ANXIETY	158	GAIT DISTURBANCE	15
Clozapine	TACHYCARDIA	37	GRANULOCYTOPENIA	611	DEATH	174
Clozapine	GRANULOCYTOPENIA	32	LEUKOPENIA	390	PNEUMONIA	100
Clozapine	SOMNOLENCE	31	PYREXIA	376	PYREXIA	63
Clozapine	WHITE BLOOD CELL COUNT DECREASED	26	DEATH	342	SOMNOLENCE	50
Clozapine	SEDATION	21	TACHYCARDIA	309	FALL	46
Haloperidol	SOMNOLENCE	35	DIABETES MELLITUS	205	AGITATION	78
Haloperidol	ACCIDENTAL EXPOSURE	26	DRUG INTERACTION	203	CONFUSIONAL STATE	75
Haloperidol	ACCIDENTAL DRUG INTAKE BY CHILD	24	NEUROLEPTIC MALIGNANT SYNDROME	196	DRUG INTERACTION	73
Haloperidol	TREMOR	23	SOMNOLENCE	148	FALL	68
Haloperidol	EXTRAPYRAMIDAL DISORDER	18	PYREXIA	147	PYREXIA	67
Olanzapine	WEIGHT INCREASED	106	DIABETES MELLITUS	2197	FALL	175
Olanzapine	DRUG EXPOSURE DURING PREGNANCY	92	WEIGHT INCREASED	1464	CONFUSIONAL STATE	142
Olanzapine	AGGRESSION	69	HYPERTENSION	906	DIABETES MELLITUS	138
Olanzapine	SUICIDAL IDEATION	58	PANCREATITIS	865	CEREBROVASCULAR ACCIDENT	107
Olanzapine	ABNORMAL BEHAVIOUR	46	DIABETES MELLITUS NON-INSULIN-DEPENDENT	720	PNEUMONIA	100
Quetiapine	WEIGHT INCREASED	121	DIABETES MELLITUS	2066	FALL	155
Quetiapine	SUICIDAL IDEATION	80	PANCREATITIS	871	DRUG INTERACTION	131
Quetiapine	TACHYCARDIA	74	WEIGHT INCREASED	662	DEATH	111
Quetiapine	CONVULSION	72	SOMNOLENCE	528	CONFUSIONAL STATE	107
Quetiapine	AGGRESSION	70	DIZZINESS	473	AGITATION	103
Risperidone	AGGRESSION	112	DIABETES MELLITUS	614	DRUG INTERACTION	161
Risperidone	WEIGHT INCREASED	69	WEIGHT INCREASED	390	SOMNOLENCE	161
Risperidone	CONVULSION	66	DRUG INTERACTION	341	DEATH	159
Risperidone	SUICIDAL IDEATION	65	DEPRESSION	327	CONFUSIONAL STATE	152
Risperidone	DRUG INTERACTION	55	SOMNOLENCE	292	FALL	135
Ziprasidone	DYSTONIA	26	DIABETES MELLITUS	243	MYOCARDIAL INFARCTION	15
Ziprasidone	SUICIDAL IDEATION	25	WEIGHT INCREASED	173	COMA	15
Ziprasidone	DEPRESSION	20	ANXIETY	116	LOSS OF CONSCIOUSNESS	11
Ziprasidone	SUICIDE ATTEMPT	20	DEPRESSION	105	SEDATION	11
Ziprasidone	WEIGHT INCREASED	19	INSOMNIA	104	AGITATION	11

Table 2: Number and Type of Events in Each Population for Major Drugs

Discussion

We found statistically significant differences between the number of adverse events in pediatric vs. adults with 7 antipsychotics, and between adults vs. geriatrics with 10 antipsychotics ($P < 0.05$). We also found statistically significant differences between the number of adverse events for atypical and typical antipsychotics within each population comparison ($P < 0.05$). Furthermore, the types of adverse events (e.g. metabolic or neurological) reported also varied statistically significantly between each population ($P < 0.05$).

Conclusions

Antipsychotic medications are commonly prescribed in the United States, and are increasingly used in pediatric and geriatric populations for which the drugs were never specifically tested. Our analysis of the FDA AERS database shows that there are significant differences in the number and type of adverse events among age groups and between atypical and typical antipsychotics for each age group. It is important for clinicians to be mindful of these differences when prescribing antipsychotics, especially if they are used off-label.

Contact Information

Narmadan A. Kumarasamy – narms@stanford.edu
Hersh Sagreiya - sagreiya@gmail.com
Yi-Ren Chen – yirenchen@stanford.edu
Karthikeyan E. Ponnusamy - k.e.ponnusamy@gmail.com
Amar Das – das@stanford.edu