Understanding Abuse Risk Related to Immediate-Release Amphetamine

DISCLOSURE INFORMATION
Vallon Pharmaceuticals provided funding for this study.
David Siner is a full-time employee of Vallon Pharmaceuticals.
David Baker is a consultant to Vallon Pharmaceuticals.
Natasha Oyedele is a full-time employee of Inflexxion

Jonathan S. Rubin, MD, MBA[1], David Baker, MBA[2], David Siner, MSC[3], Natasha K. Oyedele, MPH[4]

[1]Jonathan Rubin Consulting, Newtown Square, PA, USA, [2]Vallon Pharmaceuticals, Philadelphia, PA, USA, [3]Vallon Pharmaceuticals, Tel Aviv, Israel, [4]Inflexxion Inc, Waltham, MA, USA

BACKGROUND

- While effective in the treatment of ADHD, CNS stimulants have been shown in multiple studies to have a high risk for abuse.[1-4] Published studies report that 40% or more of the people who misuse stimulants, particularly immediate release stimulants, do so by snorting or injecting them.[5] In order to further explore the incidence, as well as demographics and nature of amphetamine abuse in the US, data was analyzed from the National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO®) system. NAVIPPRO® is a national program that includes surveillance of substance abuse as well as prevention and intervention educational programs for substance abuse.
- NAVIPPRO® surveillance involves analyses of multiple data sources for indicators of prescription medication abuse. The various data sources are intended to complement each other; an indication of increased abuse of a particular product found in one data source can be examined and evaluated with other sources within NAVIPPRO®.

METHODS

- The analysis examined the past 30-day abuse of immediate-release (IR) amphetamine prescription stimulant products (Adderall® (brand and generic), Dexedrine® and DextroStat®), in comparison to extended-release (ER) amphetamine prescription stimulant products (Adderall XR®(brand and generic), Vyvanse®, and Dexedrine Spanules®). In addition, the analysis examined the past 30-day abuse of any amphetamine prescription stimulant product, including IR amphetamine and ER amphetamine. The analysis of the abuse of amphetamine products, categorized as IR amphetamine, ER amphetamine or all amphetamine, was conducted among a sentinel population of adult patients entering substance abuse treatment or assessed for substance abuse problems using the proprietary data stream from the NAVIPPRO® system: the Addiction Severity Index-Multimedia Version (ASI-MV®). The Addiction Severity Index (ASI) is a structured clinical interview used to measure the severity of a range of problem areas typically associated with alcohol and drug abuse: Medical Status, Employment Status, Drug Use, Alcohol Use, Legal Status, Family and Social Relationships, and Psychiatric Status.[6] The ASI- MV® is a self report version of the ASI.[6]
- The study examined data in the ASI-MV® obtained from self-report of adult patients during the period from January 1, 2010 to September 30, 2016 (Q1 2010 – Q3 2016). Data obtained included the rate of past 30 day abuse, the route of abuse, the source of procurement of the amphetamine product, and the drug severity score. Abuse rates were calculated by two methods: the number of abuse cases per 100 ASI reports as well as the number of abuse cases per 100,000 prescriptions dispensed of the drug category. The drug severity score is a rating based on a number of items measured during the interview assessment, including drug use in the past 30 days as well as duration of use. The drug severity score was sorted into the following categories: no real problem (0-1), slight problem (2-3), moderate problem (4-5), considerable problem (6-7), and extreme problem (8-9).

RESULTS

Demographics

A total of 452,077 ASI-MV® reports were evaluated in the period from January 1, 2010 to September 30, 2016. Of these reports, 7,837 patients reported past 30-day stimulant abuse. The demographics of the overall population and the stimulant abuse population were similar (Table 1). Both the overall population and the stimulant abuse population were predominantly male, white and the majority of subjects (63%) were between the ages of 21 and 39 years.

Table 1: Demographics of the ASI-MV total population and past Stimulant Abusers

		All ASI-MV assessments (n=452,077)		Stimulant Abusers (n=7,837)	
		n=	452,077	n=	7,837
		Frequency	Percent	Frequency	Percent
Gender	Male	286,770	63%	4,030	51%
	Female	165,263	37%	3,806	49%
	Missing	44	0%	1	0%
Age	Younger than 21	34,244	8%	903	12%
	21 to 25	86,536	19%	1,673	21%
	26 to 29	69,876	15%	1,544	20%
	30 to 39	126,860	28%	2,494	32%
	40 to 49	80,398	18%	877	11%
	50 to 59	44,714	10%	300	4%
	60 to 69	8,611	2%	42	1%
	70 to 79	779	0%	2	0%
	80 to 89	51	0%	1	0%
	90 and Older	8	0%	1	0%
	Missing	0	0%	0	0%
Race	White	275,397	61%	6,702	86%
	Black	80,341	18%	317	4%
	Hispanic	66,784	15%	477	6%
	Other	29,538	7%	341	4%
	Missing	17	0%	0	0%

Abuse rates

When the abuse rates were evaluated, either as cases per 100 ASI assessments, or as cases per 100,000 prescriptions dispensed, the abuse rate with amphetamine IR was higher than the abuse rate with amphetamine ER (Tables 2 and 3).

Table 2: Abuse rates per 100 ASI-MV® assessments

2010-Q3 2016			Cases/100 ASI Assessments
Category	Total Abuse Cases	Total ASIs	Rate per hundred	Standard Error*100
Any Amphetamine	5,923	452,077	1.31	0.03
Amphetamine ER	3,256	452,077	0.72	0.02
Amphetamine IR	3,902	452,077	0.86	0.03

Table 3: Abuse rates per 100,000 prescriptions (Rx) dispensed

2010-Q3 2016			Cases/100,000 Rx dispensed	
Category	Total Abuse Cases	Total Rx	Rate per 100,000	Standard Error*100,000
Any Amphetamine	5,923	182,507,369	3.25	0.08
Amphetamine ER	3,256	111,259,280	2.93	0.10
Amphetamine IR	3,902	71,248,089	5.48	0.17

Routes of abuse

An examination of routes of administration (ROA) of past 30-day abuse (Table 4) reveals that oral ingestion and/or chewing were the most commonly cited routes of abuse among the stimulant abusers, followed by insufflation and injection. The rate of abuse by insufflation was higher for IR amphetamines as compared with ER amphetamines (Table 5).

Table 4: Routes of administration of past 30 day abuse

2010-Q3 2016							
Category	Oral	Snort	Smoke	Inject	Other Routes	Chew	Total Abusers
Any Amphetamine	4,858 (82%)	2,206 (37%)	73 (1%)	477 (8%)	886 (15%)	733 (12%)	5,923
Amphetamine ER	2,621 (81%)	1,109 (34%)	37 (1%)	257 (8%)	482 (15%)	294 (9%)	3,256
Amphetamine IR	3,197 (82%)	1,578 (40%)	44 (1%)	320 (8%)	586 (15%)	559 14%)	3,902

When the cases of intranasal amphetamine abuse and intravenous amphetamine abuse are combined, IR amphetamines are more commonly used by abusers, with a rate of 0.38 per hundred for amphetamine IR and 0.28 for amphetamine ER (Table 5).

Table 5: Abuse cases via intravenous or intranasal route of administration

2010-Q3 2016			Cases/100 ASI Assessments	
Category	Total Abuse Cases via IV and intranasal ROA	Total ASIs	Rate per hundred	Standard Error*100
Any Amphetamine	2,453	452,077	0.54	0.02
Amphetamine ER	1,250	452,077	0.28	0.02
Amphetamine IR	1,736	452,077	0.38	0.02

Sources of procurement

The most frequently reported source for any amphetamine drug among cases was family/friend (57.1%), followed by dealer (25.9%), and abuse of the patient's own prescription (18.8%) (Table 6).

Table 6: Sources of procurement

2010-Q3 2016									
Category	Own Rx	Many MDs	Internet	Family/ Friend	Dealer	Rx Forgery	Stealing	Other	Total Abusers
Any Amphetamine	1,113 (18.8%)	97 (1.6%)	15 (0.3%)	3,383 (57.1%)	1,534 (25.9%)	20 (0.3%)	160 (2.7%)	886 (15.0%)	5,923
Amphetamine ER	474 (14.6%)	47 (1.4%)	9 (0.3%)	1,848 (56.8%)	925 (28.4%)	17 (0.5%)	104 (3.2%)	482 (14.8%)	3,256
Amphetamine IR	707 (18.1%)	63 (1.6%)	9 (0.2%)	2,212 (56.7%)	1,028 (26.4%)	6 (0.2%)	93 (2.4%)	586 (15.0%)	3,902

Abuse cases by age

The majority of amphetamine abusers were young adults between the ages of 21 and 39 (Table 7).

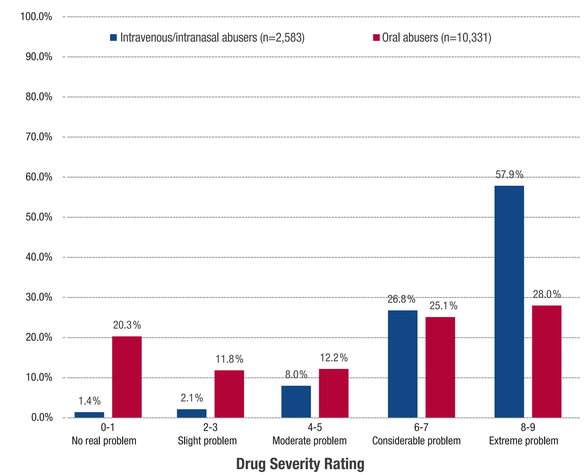
Table 7: Abuse cases by age

2010 - Q3 2016											
Category	Younger than 21	21-25 Years	26-29 Years	30-39 Years	40-49 Years	50-59 Years	60-69 Years	70-79 Years	80-89 Years	90 and Older	Total Abuse Cases
Any Amphetamine	743	1303	1201	1907	575	172	22	0	0	0	5,923
Amphetamine ER	525	765	638	980	267	71	10	0	0	0	3,256
Amphetamine IR	396	848	830	1308	388	119	13	0	0	0	3,902

Drug abuse severity

Overall, IV/IN abusers had more severe problems as measured by the drug abuse severity score. More than twice as many IN/IV abusers had extreme problems compared to oral abusers (57.9% vs 28%); The severity of drug abuse problems was shifted towards more considerable or extreme problems with IN/IV abusers compared to Oral abusers; 85% of IN/IV users report considerable or extreme problems compared with just over 50% of Oral abusers.

Figure 1: Drug severity among IV/IN abusers and Oral abusers



CONCLUSIONS

- A survey of self-reports of abuse cases demonstrated that the rate of amphetamine abuse is more common with IR amphetamine than with ER amphetamine.
- Consistent with previous reports[5, 7-11] intranasal abuse of amphetamine is quite common, seen in 34-40% of cases of amphetamine abuse.
- Procurement of amphetamine from family or a friend was the most commonly observed source for amphetamine in abuse cases, which has implications for prescribers of amphetamines when the prescriber is counseling patients and their families.
- Most abuse cases of amphetamines in this survey occurred in young adults.
- Patients who abuse amphetamines via the intranasal or intravenous route are more likely to have a considerable or extreme drug severity score than those who abuse amphetamines via the oral route.
- These analyses suggest that abuse of IR amphetamine products is common among prescription stimulant abusers, and the frequency of more dangerous ways of abuse (via the IV or intranasal routes) affirms the magnitude of the public health problem.

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