Liver Injury Due to Medications for Mental Health: An Analysis of the Drug-induced Liver Injury Network Prospective Study

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Background

- 1 in 6 adults in the United States are prescribed medications for their mental health[1,2]
- Antidepressants (AD) and antipsychotics (AP) are amongst the most commonly prescribed mental health agents
- The Drug Induced Liver Injury Network (DILIN) is a United States multi-center consortium that enrolls patients with DILI

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Aim

To describe and compare the patient demographics, clinical characteristics, and outcomes of DILI cases attributed to AD and AP medications

Methods

Patients: cases of acute DILI due to AD or AP medications from 2004 to 2025 enrolled in the DILIN Prospective Study

- Included only *high-confidence* causality cases (definite, highly likely, or probable)

Agents grouped by mechanism of action (MOA) where possible

Data:

- Patient demographics, clinical and lab characteristics, and outcomes collected

Statistics:

- Descriptive analysis of cases group by mechanism

Results

Table 1. List of Agents

Selective serotonin reuptake inhibitors (SSRI)	**8**
Escitalopram	4
Fluoxetine	1
Paroxetine	1
Vortioxetine	1
Serotonin-norepinephrine reuptake inhibitors (SNRI)	**14**
Duloxetine	11
Nefazodone	1
Trazadone	1
Venlafaxine	1
Atypical antipsychotics (AP)	**8**
Quetiapine	3
Olanzapine	3
Risperidone	1
Chlorpromazine	1
Other	**7**
Bupropion (Aminoketone)	6
Imipramine (TCA)	1

37 total cases, representing 1.5% of all cases enrolled in DILIN Prospective Study database as of January 2025

Table 2: Characteristics of Liver Injuries by MOA Class

	SSRI (n=8)	SNRI (n=14)	AP (n=8)	P-value
Causality score – n (%)				0.239
Definite	2 (25)	5 (36)	0 (0)	
Highly likely	4 (50)	8 (57)	5 (63)	
Probable	2 (25)	1 (7)	3 (37)	
Age, years – mean (SD)	30.2 (11.5)	48.2 (10.3)	37.7 (22.5)	**0.037**
Gender – n (%)				0.478
Male	3 (37)	3 (21)	4 (50)	
Female	5 (63)	11 (79)	4 (50)	
Race – n (%)				0.265
White/Caucasian	8 (100)	12 (86)	5 (63)	
Black/African American	0	1 (7)	0	
Other	0	1 (7)	3 (37)	
Days to DILI onset – median (IQR)	59.0 (38.5, 120.5)	54.0 (42.0, 62.0)	22.0 (17.0, 76.0)	0.353
Pattern of injury (at onset) – n (%)				0.186
Hepatocellular	5 (63)	7 (58)	3 (43)	
Cholestatic	1 (13)	5 (42)	4 (57)	
Mixed	2 (25)	0 (0)	0 (0)	
Peak liver enzyme values – median (IQR)				
AST (U/L)	335 (132, 699)	535 (467, 1882)	158 (124, 564)	0.09
ALT (U/L)	569 (328, 818)	1135 (511, 2116)	389 (239, 457)	**0.048**
ALP (U/L)	289 (214, 404)	328 (181, 477)	374 (111, 874)	0.981
Total bilirubin (mg/dL)	13.5 (4.3, 23.4)	11.3 (2.9, 17.4)	2.4 (0.6, 28.0)	0.512
INR	1.3 (1.1, 1.6)	1.6 (1.1, 1.9)	1.0 (1.0, 1.5)	0.190
Days from peak to ≥50% decrease – median				
AST (U/L)	9.0	3.0	4.0	0.818
ALT (U/L)	10.0	6.0	9.0	0.343
ALP (U/L)	22.5	17.0	43.0	0.315
Total bilirubin (mg/dL)	9.0	7.5	10.5	0.126
Treatment and outcomes – n (%)				
Corticosteroid use	2 (25)	4 (29)	2 (25)	0.99
Developed chronic DILI (≥6 months)	2 (25)	3 (21)	1 (12)	0.99
Transplant or Death	0	0	0	NA

Bupropion (n=6)

- Causality: highly likely (4), probable (2)
- Age, years (mean [SD]): 39.4 (18.5)
- Days to DILI onset (median [IQR]): 287 (121 – 476)
- Pattern of injury at onset:
  - *Hepatocellular:* 3 (50%)
  - *Cholestatic:* 2 (33%)
  - *Mixed*: 1 (17%)
- Peak liver enzymes (median [IQR])
  - *AST (U/L):* 706 (382, 2243)
  - *ALT (U/L):* 1318 (386, 1467)
  - *ALP (U/L):* 319 (137, 382)
  - *Total bilirubin (mg/dL):* 4.5 (2.3, 22.4)
  - *INR:* 2.3 (2.0)
- Days from peak to ≥50% improvement (median)
  - *AST (U/L):* 5
  - *ALT (U/L):* 11
  - *ALP (U/L):* 55
  - *Total bilirubin (mg/dL):* 7
- Treatment and outcomes:
  - Chronic DILI: 0
  - Death: 1 (17%)

Imipramine (n=1)

- Highly likely case, 35-year-old female
- 32 days to DILI onset
- Peak liver enzymes: AST 320 U/L, ALT 637 U/L, ALP 295 U/L, total bilirubin 4.1 mg/dL, INR 1.0
- Days from peak to ≥50% improvement: AST/ALT 4-6 days, ALP 14 days, bilirubin 2 days
- Outcome: no chronic DILI or death

Conclusion

- Despite frequent use of AD and AP medications in the United States, the frequency of reported DILI cases is low
- In the majority of cases, recovery is complete and rapid
- Rarely, severe cases leading to chronic DILI or death have been reported

References

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