Clinical Features of Sulfonamide Hepatotoxicity vary Significantly by Patient age: Results from the US DILIN studies

Robert J. Fontana [1], Naga Chalasani [2], Sherry Gu [3], David E. Kleiner [4], Herbert L. Bonkovsky [5], Huiman Barnhart [3] , Jay H. Hoofnagle [6] for the Drug Induced Liver Injury Network [1] Michigan Medicine, Ann Arbor, MI; [2] Indiana University School of Medicine, Indianapolis, IN; [3] DCRI, Durham, NC; [4] National Cancer Institute, NIH, Bethesda, MD; [5] Wake Forest University/ NC Baptist Medical Center, Winston- Salem, NC; [6] NIDDK, Bethesda, MD.

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DIGITAL EXPERIENCE

INTRODUCTION

Sulfonamides including the commonly used antibiotic trimethoprim-sulfamethoxazole (TMP/SMZ) can cause immunoallergic skin reactions and cholestatic hepatitis

The clinical features and outcomes with sulfonamide DILI are not well described

AIM

To describe the clinical features, liver histology and outcomes of 105 consecutive patients with sulfonamide hepatotoxicity

METHODS & RESULTS

The clinical features and outcomes of high causality (scored as definite/ highly likely/ probable) sulfonamide cases enrolled into the DILIN Prospective or Retrospective studies between 2004 and 2021 were reviewed.

Fatal = Liver transplant or death

Among 105 cases, 93 were due to TMP/SMZ and 9 to sulfasalazine, 2 dapsone, and 1 sulfadiazine.

Available liver histology was reviewed centrally (DEK)

TMP/SMZ cases treated with corticosteroids were compared to severity matched- untreated cases with onset T bili of +/- 6 mg/dl

Data reported as median or %

RESULTS

93 TMP/SMZ DILI cases

	HC n=33	Mix N=30	Chol N=30	P
Age (yrs)	28.0	50.1	61.7	< 0.001
Female	58%	53%	43%	0.51
Cau AA Other	64% 21% 15%	87% 13% 0	80% 20% 0	0.14
Latency (d)	18	26	21	0.58
Rash	54%	40%	43%	0.47
Eos > 500/ul	23%	28%	21%	0.86
Peak bili Peak INR	4.9 1.4	7.5 1.1	6.9 1.1	0.19 0.03
Steroids	30%	21%	7%	0.06
Fatal	12%	3%	0%	0.12
Chronic	10%	19%	29%	0.23

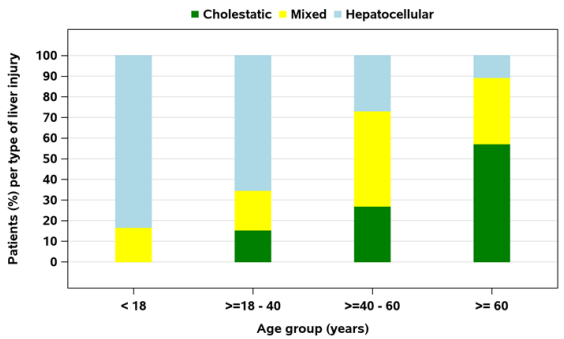

Figure 1: Liver injury pattern by age

Steroid treated vs untreated TMP/SMZ cases

	Steroids N=18	No steroid n=54	p
Age (yrs)	38.1	42.5	0.38
Female	78%	48%	0.03
Cau AA Other	89% 11% 0	67% 24% 9%	0.40
Rash	72%	44%	0.04
Eos > 500/ul	28%	21%	0.52
Initial ALT Initial INR	590 1.8	340 1.1	0.10 0.05
Peak ALT Peak INR	1018 1.5	508 1.1	0.002 0.06
Fatal	22%	0	0.003
To bili < ULN* To Alk< ULN* To AST<ULN*	15 28 13	22 78 22	0.06 0.43 0.09

* days from peak

The 12 cases due to other sulfonamides had a median latency of 37 days, 75% were HC, and 41% received steroids. None required LT or died.

In 16 liver biopsies, 88% had cholestasis and 57% had granulomas

CONCLUSION

TMP/SMZ hepatotoxicity is characterized by short latency, frequent immunoallergic features, and potentially severe outcomes

A hepatocellular injury pattern was seen in one-third of TMP/SMZ patients and was more frequent in younger patients and associated with more severe disease.

Corticosteroid therapy may hasten liver injury recovery in TMP/SMZ DILI patients but prospective, controlled studies are needed.

The 12 patients with DILI due to other sulfonamides were frequently hepatocellular and 41% received steroids but none died or underwent LT

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CONTACT INFORMATION

Robert J. Fontana, MD

3912 Taubman Center, Ann Arbo

rfontana@med.umich.edu