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An Electronic Decision Support Intervention Reduces Readmissions for Patients With Cirrhosis

Jeremy Louissaint, MD[1], **Katie Grzyb, MHSA**[2], **Linda Bashaw, BA**[2], **Rima A. Mohammad, PharmD**[3], **Neehar D. Parikh, MD, MS**[1], **Elliot B. Tapper, MD**[1]

[1]Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, Michigan, USA

[2]Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA

[3]Department of Clinical Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, Michigan, USA.

Abstract

INTRODUCTION: Rifaximin use in combination with lactulose is associated with a decreased risk of overt hepatic encephalopathy (HE).

METHODS: We prospectively evaluated the impact of an interruptive electronic medical record alert to indicate rifaximin for patients with cirrhosis and HE on lactulose.

RESULTS: The intervention was associated increased rifaximin utilization, particularly for nongastroenterology and hospitalist services odds ratio 1.20 95% confidence interval (1.09–1.31). For patients with HE, the intervention was associated with a lower readmission risk-adjusted subdistribution hazard ratio 0.63 95% confidence interval (0.48–0.82).

DISCUSSION: An interruptive alert in the electronic ordering system was associated with a lower risk of readmissions.

INTRODUCTION

Readmissions occur after roughly 3 of 10 hospital discharges for patients with cirrhosis (1,2). Comorbid hepatic encephalopathy (HE) is the most potent predictor of readmissions (3). Rifaximin is approved for the reduction of breakthrough episodes of HE on lactulose (4) and can therefore reduce the risk of readmissions (5,6). Although its effects are robust among real-world patients (5), as few as 50% of patients hospitalized with HE are discharged on rifaximin (7). We previously found that standardized lactulose dosing

Correspondence: Elliot B. Tapper, MD. etapper@umich.edu.

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CONFLICTS OF INTEREST

Potential competing interests: E.B.T. has served on advisory boards for Mallinckrodt, Kaleido, Rebiotix, Novo Nordisk, and Bausch Health; consulted for Ambys, Axcella, Allergan, and Novartis; and has received unrestricted research grants from Valeant/Bausch and Gilead. Bausch played no role in the funding, concept, design, analysis, or writing of this study. No other author has pertinent conflicts of interest.

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combined with prompts for rifaximin use were associated with significantly reduced readmissions (8). Herein, we evaluate the impact of an interruptive alert to indicate the use of rifaximin for patents with HE on lactulose.

METHODS

Design

We prospectively tracked 30-day readmissions for all live, non-hospice discharges for adults with cirrhosis from January 1, 2019, to December 30, 2020. We developed and deployed 2 one-time best-practice advisory alerts for persons with HE and active lactulose orders–1 fired on opening the record of a chart after lactulose was ordered (if rifaximin was not previously ordered) and the other during discharge planning. Orders for rifaximin were suggested only for patients on lactulose. Clinicians could easily silence the alert for patients they deemed not meeting criteria–for example, if they felt the patient's HE was not an active problem or it was a first episode. The alert also provided a telephone number to a transitional care pharmacist to encourage seeking insurance coverage for the medication (see Supplementary Figure, http://links.lww.com/AJG/C382). The intervention was deployed in a stepped fashion: a preintervention period, intervention for gastroenterology (GI) and (nonteaching) hospitalist services, and subsequently for the remainder of hospital services (e.g., internal medicine with house staff, family medicine, and cardiology). This study was approved as quality improvement by the University of Michigan Institutional Review Board.

Outcomes

We first assessed the difference in readmissions overall and for those with HE after the intervention in a pre-post fashion using multivariable logistic regression. We also conducted a multivariable analysis using a Fine-Gray competing risk model for the time to readmission. We adjusted for factors with *a priori* associations with readmissions (age, model for end-stage liver disease–sodium, ascites, albumin, and transjugular intrahepatic portosystemic shunt placement).

RESULTS

Cohort characteristics are described in Table 1. Inhospital rifaximin use was stable on the GI and hospitalist services throughout the study period from 73.5% before the intervention to 74.5% after the intervention, adjusted odds ratio (OR) 1.04 95% confidence interval (CI) (0.95–1.13). In contrast, rifaximin use increased from 52.6% before the intervention for the other services to 71.1% after the intervention, adjusted odds ratio (OR) 1.20 95% CI (1.09–1.31). Rifaximin ordered after the alert included 80% (label concordant) new prescriptions and 15% continued home prescriptions, and 5% potentially inappropriate prescriptions. When rifaximin was not ordered, it was because lactulose was deemed sufficient by the clinician (or used for constipation).

Beginning at 17.4%, 30-day readmissions on the GI and hospitalist services fell to 9.3% during the intervention period, adjusted OR 0.92 95% CI (0.87–0.96). For other services, the readmission rate fell from 9.7% to 8.5%, adjusted OR 0.97 95% CI (0.94–1.00) (Table 2). Although the number of readmissions decreased, the proportion primarily attributable

to HE remained stable. Overall, the intervention was associated with a significantly lower risk of readmission, adjusted subdistribution hazard ratio (sHR) 0.77 95% CI (0.65–0.91), and a lower mortality, adjusted sHR 0.80 95% CI (0.67–0.95). For patients with HE, the intervention was associated with a lower readmission risk–adjusted sHR 0.63 95% CI (0.48–0.82)–and, nonsignificantly, with lower mortality, adjusted sHR 0.82 95% CI (0.66–1.03; Table 3).

DISCUSSION

HE is the most important disease-specific driver of readmissions for hospitalized patients with cirrhosis. It is unique among cirrhosis complications in having a therapeutic strategy approved by the US FDA for the reduction of recurrent episodes and therefore readmissions. In this prospective study, we found an interruptive alert designed to increase rifaximin's uptake was associated with a reduced risk of readmissions.

Methods to increase uptake of rifaximin

Attention to human factors, making an action easy to accomplish within the clinician's workflow, improves the success of prescribing interventions (9). Some interventions can alert clinicians regarding best practice using posters, placards, or checklists. Unfortunately, our previous experience showed that checklists do not increase utilization, likely because they are physically separate from the electronic ordering system, outside of the order entry workflow, and require efforts to maintain adherence (8). Interruptive alerts deliver information at the point-of-care amidst the appropriate workflow for clinicians who are using the electronic ordering system. A noninterruptive alert–e.g., a banner at the top of the screen or text on the side of the page can be missed. Default orders might enhance uptake but may also increase overuse and limit clinician discretion. Our alert provided education and informed the clinician of the target population.

One of the barriers to rifaximin uptake that was not explored in this study is its cost. Cost controls may be helpful in expanding access. For now, rifaximin's insurance coverage requires additional work. We previously found that rifaximin dispensing after a discharge for HE on lactulose was higher for patients under the care of an advanced practice provider (6), suggesting that there are provider-level factors that mediate rifaximin utilization. Our intervention provided the contact information for a transitional care pharmacist who could facilitate prior authorizations. The availability and expertise of pharmacists may be important for the overall impact of the intervention on rifaximin uptake.

Contextual factors

These data must be interpreted in the context of the study design. First, as a single-center quality improvement intervention, our findings may not generalize to other settings. Any intervention must be tailored to the specific center's needs and context of care delivery and evaluated carefully after implementation. Second, it is unknown how many readmissions occurred at other centers. Third, we lack data on outpatient drug dispensing and the success of prior authorizations. Fourth, although we find a slight decrease in mortality, our data cannot confirm a true survival benefit. However, readmissions were not lower as a function

of higher mortality. Finally, our stepped design only partially accounts for the impact of secular trends on readmission risk, such as rising rates of alcohol use disorder and its liver complications.

We observed a significant reduction in 30-day readmissions after introducing an interruptive alert in the electronic ordering system. These data also highlight the role of focused interruptive alerts that we plan to explore for a variety of conditions in multicenter studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Baseline Details of each hospitalization by study phase and hospital service

	Gastroenterology/hospitalist service			Other services		
	Preintervention N = 184	Postintervention N = 950	*P* value	Preintervention N = 914	Postintervention N = 739	*P* value
Age (median yr, IQR)	58 (51–65)	58 (48–65)	0.41	61 (53–68)	61 (50–69)	0.22
Sex (female)	105 (57%)	478 (50%)	0.11	539 (59%)	437 (59%)	0.99
Private insurance	90 (49%)	501 (53%)	0.40	443 (48%)	382 (52%)	0.17
Alcohol-related cirrhosis	74 (40%)	471 (50%)	0.02	351 (38%)	335 (45%)	<0.01
Hepatitis C	17 (9.2%)	87 (9.2%)	1.00	118 (13%)	94 (13%)	0.97
Ascites	113 (61%)	475 (50%)	<0.01	286 (31%)	255 (35%)	0.18
Hepatic encephalopathy	129 (70%)	499 (53%)	<0.001	267 (29%)	221 (30%)	0.80
Varices	86 (47%)	518 (55%)	0.06	300 (33%)	304 (41%)	<0.001
HCC	10 (5.4%)	82 (8.6%)	0.19	106 (12%)	72 (9.7%)	0.26
MELD-Na (median, IQR)	18 (13–25)	18 (13–25)	0.93	15 (11–20)	16 (12–22)	<0.01
Albumin (median g/dL, IQR)	3.2 (2.8–3.6)	3.2 (2.8–3.6)	0.58	3.5 (3.0–3.9)	3.3 (2.9–3.9)	0.02
Inhospital events						
Paracentesis	53 (29%)	209 (22%)	0.06	90 (9.8%)	99 (13%)	0.03
SBP	23 (13%)	130 (14%)	0.75	58 (6.3%)	45 (6.1%)	0.91
TIPS	3 (1.6%)	40 (4.2%)	0.14	22 (2.4%)	45 (6.1%)	<0.001
Dialysis	0	2 (0.2%)	1.00	1 (0.1%)	4 (0.5%)	0.25
Endoscopy	28 (15%)	201 (21%)	0.08	80 (8.8%)	83 (11%)	0.11
Colonoscopy	4 (2.2%)	37 (3.9%)	0.35	23 (2.5%)	15 (2.0%)	0.62

Other services include teaching services for internal medicine, surgery, cardiology, oncology, and others.

HCC, hepatocellular carcinoma; MELD-Na, model for end-stage liver disease–sodium; SBP, spontaneous bacterial peritonitis; TIPS, transjugular intrahepatic portosystemic shunt.

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Table 2.

30-day readmissions

Overall	Unadjusted readmissions by period			Adjusted[a] pre-post difference (OR)
	No intervention January 1, 2019–May 1, 2019	Intervention on GI/hospitalist services only May 2, 2019–January 27, 2020	Hospital-wide intervention January 28, 2020–December 31, 2020	
First wave of intervention (primary gastroenterology service and hospitalist service)	32/184 (17.4%)	88/950 (9.3%)	88/950 (9.3%)	0.92 95% CI (0.87–0.96)
Second wave of intervention (other services)	89/914 (9.7%)	89/914 (9.7%)	63/739 (8.5%)	0.97 95% CI (0.94–1.00)

The periods are specified in the middle 3 columns. There is an overlap between the preintervention period for the other services and the postintervention period of the GI/hospitalist services reflecting the stepped design.

[a]Adjusted for age, MELD-Na, albumin, TIPS, and ascites. Other services included internal medicine teaching service, family medicine, cardiology, oncology, surgery, and surgical subspecialties.

CI, confidence interval; GI, gastroenterology; MELD-Na, model for end-stage liver disease–sodium; OR, odds ratio; TIPS, transjugular intrahepatic portosystemic shunt.

Table 3.

Adjusted risk of readmission and mortality associated with the intervention

	Only patients with hepatic encephalopathy		Whole cohort	
	Readmission risk Adjusted sHR	**Morality risk Adjusted sHR**	**Readmission risk Adjusted sHR**	**Morality risk Adjusted sHR**
Intervention period	**0.63 (0.48–0.82)**	0.82 (0.66–1.03)	**0.77 (0.65–0.91)**	**0.80 (0.67–0.95)**
Ascites	0.89 (0.68–1.18)	1.25 (1.00–1.55)	0.98 (0.82–1.16)	**1.42 (1.19–1.69)**
MELD (per point)	1.01 (0.99–1.03)	**1.04 (1.03–1.06)**	1.01 (0.99–1.02)	**1.05 (1.04–1.07)**
Age (per yr)	1.01 (0.99–1.02)	**1.03 (1.02–1.04)**	1.00 (1.00–1.01)	**1.03 (1.03–1.04)**
TIPS	0.70 (0.33–1.49)	0.91 (0.51–1.62)	0.84 (0.53–1.32)	0.77 (0.47–1.28)
Albumin (per g/dL)	1.08 (0.84–1.38)	**0.61 (0.49–0.75)**	1.07 (0.93–1.22)	**0.55 (0.47–0.63)**

The risk of readmission and mortality are modeled using a Fine-Gray competing risk framework. Bolded values are statistically significant.

MELD, model for end-stage liver disease; sHR, subdistribution hazard ratio; TIPS, transjugular intrahepatic portosystemic shunt.