Health Literacy and Heart Failure Care in Minority Communities

TO THE EDITOR: Sisk and colleagues (1) found that a nurse-led intervention reduced hospitalizations for patients with systolic heart failure who were recruited from ambulatory clinics in Harlem, New York. We recently reported similar findings with a self-management program in ambulatory patients with heart failure (both systolic and diastolic dysfunction) who were recruited from an academic internal medicine practice in North Carolina (2). Incidence of hospitalizations was reduced by 47%.

Our study sample included many patients with low education (an average of 9.5 years of schooling) and inadequate literacy (literacy rate, 41%). In our study, patients with low literacy seemed to derive similar or greater benefit from the intervention than patients with adequate literacy, although our sample size was too small to test formally for an interaction. Sisk and colleagues reported that 29.8% of participants had inadequate literacy. We’re interested to know whether they found a similar reduction in the risk for hospitalization of participants had inadequate literacy. We’re interested to know whether they found a similar reduction in the risk for hospitalization among participants with inadequate literacy compared with those with adequate literacy.

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References

IN RESPONSE: We appreciate Drs. Pignone and DeWalt’s comments. In our trial, we measured patients’ health literacy, however, not general literacy. These concepts differ considerably. In preliminary analyses, we found no evidence that low health literacy was correlated with the effectiveness of nurse management in terms of either of the primary outcomes of physical functioning or all-cause hospitalization. Specifically, we measured physical function by using the Short Form-12 (SF-12) physical component score, which we obtained at baseline and every 3 months through the end of the intervention at 12 months. We estimated a linear regression of the change in SF-12 physical component score on treatment assignment, an indicator for inadequate health literacy, and the interaction between inadequate health literacy and treatment assignment. Although the coefficient on treatment assignment was statistically significant, indicating a positive effect of nurse management, the coefficient on the interaction term between nurse management and inadequate health literacy (P > 0.20) provided little evidence that the intervention was more effective for patients with inadequate health literacy at baseline. Alternative specifications of this model, including models with additional control variables for sociodemographic factors and longitudinal models that used intervening data points at 3, 6, and 9 months, yielded similar null findings on health literacy. For all-cause hospitalizations, we estimated Poisson regression models with total hospitalizations over the 12-month study as a function of treatment assignment, inadequate health literacy at baseline, and the interaction between these 2 variables. The coefficient on the interaction term was not significant (P > 0.20).

These null findings on health literacy are particularly vexing because they tend to discount a potential reason why our intervention succeeded where similar interventions have not. Continued research on why disease management works in some patient populations but not in others is clearly needed and is a focus of our continuing efforts.

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The Promotion of Gabapentin

TO THE EDITOR: Steinman and colleagues (1) describe an explicit promotional campaign by gabapentin’s vendor that included efforts to inflate the literature on the drug “by contracting with medical education companies to develop review papers, original articles, and letters to the editor” that were favorable to gabapentin and then hiring physicians and pharmacists to be authors on these papers. Knowing that this was done makes the literature on gabapentin very difficult to interpret.

A PubMed search (performed on 25 August 2006) of gabapentin limited to randomized, controlled trials found 148 trials. Primary research literature includes several positive trials of gabapentin for hot flashes, bipolar disorder, alcohol withdrawal, pain syndromes, spasticity, the restless legs syndrome, chronic headache, and acquired nystagmus, among myriad other conditions. Limiting the search to clinical trials yielded 285 studies of gabapentin for conditions ranging from hiccups to priapism.

Either this drug has extremely broad (and biologically implausible) effectiveness for a variety of unrelated conditions or the literature is so corrupt that it is unsalvageable.

The unfortunate consequence is that we are unlikely to know for what conditions gabapentin is actually useful.

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Potential Financial Conflicts of Interest: None disclosed.
TO THE EDITOR: Steinman and colleagues (1) offered a purportedly “unique window for understanding the structure and methods of pharmaceutical promotion,” concluding that “[n]ew strategies are needed to ensure a clear separation between scientific and commercial activity.” The authors explored the well-documented abuses related to the off-label marketing of gabapentin. Unfortunately, they seem to imply that these actions are representative of current practice. Worse, the authors call for various reforms but seem unaware that many such reforms have already taken place. They state only that “a complex system has evolved” that has been “largely ineffective,” a claim that cannot be supported by the references cited because they predate most reforms.

The Pharmaceutical Research and Manufacturers of America (PhRMA) Code on Interactions with Healthcare Professionals (2), released 19 April 2002, has effectively stopped the abuse of advisory boards as described in the article. The recommendation that grant functions be separated from marketing functions, detailed in the 2003 U.S. Department of Health and Human Services Office of the Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers (3), has resulted in organizational changes within pharmaceutical companies that have removed marketing personnel from decisions related to continuing medical education (CME) grants. In addition, most pharmaceutical companies now generally prohibit medical education companies that receive CME grants from having any role in promotional or marketing activities. Most medical education and communications companies have also made organizational changes that separate independent education from promotion.

In September 2004, the Accreditation Council for Continuing Medical Education (ACCME) adopted new Standards for Commercial Support (4). These standards require providers to develop education that is independent from commercial influence and to identify and resolve conflicts of interest for faculty or authors who develop or contribute content. Finally, the International Committee of Medical Journal Editors undertook major revisions of their Uniform Requirements for Manuscripts Submitted to Biomedical Journals (5) in 2001, 2003, and 2006, aimed at preventing the abuses of the publication process described in the article.

While seemingly provocative, the findings of Steinman and colleagues are mostly of historical interest. To imply that these findings are indicative of current practices is both inaccurate and misleading. The North American Association of Medical Education and Communication Companies (NAAMECC), an association of more than 70 companies involved in CME, is deeply concerned about, and works to ensure, the integrity, quality, and educational value of CME. We assert that the CME of today has little in common with the actions described in Steinman and colleagues’ article.

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References

IN RESPONSE: Dr. Finucane’s enumeration of the large variety of controlled clinical trials of gabapentin is consistent with the company’s support of small research projects to promulgate messages about the drug in the medical literature. Although one might apply principles of evidence-based medicine to each of these studies, in practice

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References
it is difficult for physicians to critically evaluate the effectiveness of gabapentin for such a wide range of disorders.

We applaud the positive steps outlined by Mr. Peterson and colleagues to reduce commercial influence on educational activities. However, we remain skeptical of the claim that the practices we identified are only of historical interest. Current codes of conduct are largely self-administered and lack an enforcement mechanism, and we know of few systematic data on the extent to which those codes are being followed in letter and in spirit. Similar codes enacted by the pharmaceutical industry, the American Medical Association, and the ACCME, which were in force during the period we studied, were often ignored (1–3). Other research has shown frequent violations of self-regulation by the pharmaceutical industry (4). Thus, we affirm that self-regulation by all parties in these interactions has been insufficient to control undue commercial influence on the practice of medicine.

The risk for such influence persists because of a fundamental conflict of interest, whereby medical education and communications companies and other providers of CME face an incentive to cast a sponsor’s products in a favorable light to attract future funding from the sponsor. Despite recent efforts to strengthen guidelines on commercial support of CME, opportunities for abuse still exist (5). Current guidelines allow commercial supporters to raise concerns about content and permit CME providers to consult with commercial supporters about suggested speakers and topics. This creates a condition analogous to that identified by Dr. Sapers as the situation of individual physicians, balancing our ethical and professional obligations toward patients and the public, the private, for-profit status of medical education and communications companies raises special concern that financial interests may encroach on the scientific integrity of their educational programs.

Recent strengthening of codes of conduct, stimulated in part by the threat of federal prosecution, has been a welcome improvement in the management of direct and indirect forms of pharmaceutical promotion (6). However, major conflicts of interest and loopholes persist and must be addressed by vigorous regulation with independent oversight to separate commercial from scientific activities.

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Potential Financial Conflicts of Interest: Drs. Steinman, Chren, and Landefeld were unpaid expert witnesses in the litigation on which their manuscript was based, and Drs. Steinman and Landefeld participated in the creation of an online searchable archive of documents funded by the plaintiff’s lawyer in that litigation.

References
which the computer is attached; leave harmful software behind that could, for example, capture usernames and passwords and send them to the person on an ongoing basis; and copy financial or health data—all while the physician is viewing the patient’s health record on the device. Each of the devices we reviewed contains a program that must be used to view the patient record, and no reliable mechanism can verify the integrity of these programs. The only certain way for providers to avoid this type of attack is to avoid accepting such devices. Web-based personal health records, which are also available, are a safer alternative. Because they are viewed through a Web browser and require no special software to run, they are not subject to this type of attack.

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References

Hypothyroidism as a Mimic of Liver Failure in a Patient with Cirrhosis

Background: Hypothyroidism is an unusual cause of ascites. Hypothyroidism may also mimic hepatic encephalopathy in patients with cirrhosis. Reversible, hypothyroidism-induced ascites and encephalopathy simulating liver failure in a patient with cirrhosis awaiting liver transplantation has not been reported.

Objective: To describe the resolution of intractable ascites and encephalopathy with treatment of hypothyroidism in a patient with cirrhosis awaiting transplantation.

Case Report: A 40-year-old woman with cirrhosis secondary to chronic hepatitis C virus infection had intractable ascites and encephalopathy. She was listed for liver transplantation at another institution. She presented for a second opinion to determine whether additional evaluation and treatment might preclude the need for transplantation.

Her medical history included Hodgkin disease that was treated in the 1970s. Chronic hepatitis C virus infection was diagnosed in 1992 and was attributed to blood transfusion. Cirrhosis had been confirmed by liver biopsy. The patient had deteriorated clinically over time despite interferon monotherapy. She had encephalopathy that was unresponsive to lactulose, 120 mL daily, and ascites that did not respond to high-dose diuretics and was managed with large-volume paracentesis. Upper endoscopy showed portal gastropathy without varices. Tests at the referring institution revealed a serum albumin level of 29 g/L (normal range, 34 to 48 g/L), prothrombin time of 13.2 seconds (normal range, 12.3 to 14.6 seconds), alanine aminotransferase level of 60 U/L (normal range, 8.0 to 35.0 U/L), aspartate aminotransferase level of 63 U/L (normal range, 5.0 to 34.0 U/L), and positive hepatitis C virus RNA result.

At presentation, the patient had spider angiomata, ascites, and a mental status examination consistent with stage 3 hepatic encephalopathy. The serum–ascites albumin gradient, which was not calculated at the referring medical center, was 5 g/L, suggesting a high ascites protein content (the serum–ascites albumin gradient in ascites from portal hypertension is usually greater than 11 g/L). In addition, the patient’s ankle reflexes, which were tested as part of a routine neurologic evaluation, were markedly delayed in the relaxation phase, strongly suggesting hypothyroidism. These tests and the patient’s resistance to lactulose led us to question the diagnosis of liver failure and to test for thyroid function. The patient’s thyroid-stimulating hormone level was 155 mU/L (normal range, 0.35 to 5.50 mU/L).

The patient was treated with L-thyroxine, 50 µg daily increasing to 100 µg daily. The patient’s ascites, encephalopathy, and laboratory abnormalities normalized over 2 months. Liver transplantation was canceled.

Discussion: The patient’s clinical course and response to L-thyroxine supplementation suggest that, against the background of hepatitis C virus–induced cirrhosis, hypothyroidism was the cause of encephalopathy and ascites (myxedema ascites). We speculate that the lack of effect of lactulose was attributable to gastrointestinal hypomotility associated with hypothyroidism.

The literature on hypothyroidism simulating liver failure is limited. Yamamoto and colleagues (1) reported a case of cirrhosis with hyperammonemia that presented with dementia due to hypothyroidism. One report of a patient with encephalopathy and hypothalamic hypothyroidism showed improvement in symptoms of hypothyroidism and consciousness disturbance, suggesting that hypothyroidism may aggravate hyperammonemia and encephalopathy (2). In another patient with hepatitis C and hyperammonemic coma who did not clinically improve with encephalopathy treatment, L-thyroxine therapy normalized mental status and hyperammonemia (3). The patient we describe is similar to these cases but may have the atypical feature of a low serum–ascites albumin gradient. The limited literature on serum–ascites albumin gradient in myxedema ascites reports a high gradient (4, 5), the mechanism of which is unknown.

Conclusions: In summary, the case illustrates that hypothyroidism can simulate liver failure in a patient with hepatitis C virus–related cirrhosis. On the basis of this experience and others reported in the medical literature, we believe that clinicians should suspect hypothyroidism and evaluate thyroid function in patients with well-compensated cirrhosis, normal synthetic function as measured by normal prothrombin time, and apparent hepatic encephalopathy that is refractory to treatment.

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**Letters**

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**References**


**Correction**

**Correction: Estimated Glomerular Filtration Rate**

A recent letter on estimated glomerular filtration rate (GFR) (1) contained some errors. The equation for calculating the critical difference is reported incorrectly. The calculation is as follows:

\[
\frac{1.414}{1.1} \times 1.96 \times (\text{analytic CV}^2 + \text{intra-individual CV}^2)^{0.5}
\]

Also, in the author’s example of a white 60-year-old man with a creatinine level of 70.7 μmol/L (0.8 mg/dL), the estimated GFR is 98.6 mL/min per 1.73 m². The last sentence should have been: “It is perhaps more cautious to still give MDRD Study equation results as more than 60 mL/min per 1.73 m² and 90 mL/min per 1.73 m² without giving precise absolute values of estimated GFR [emphasis added].”

Finally, the authors of the letter are Pierre Delanaye, MD; Etienne Cavalier, MD; and Jean-Marie Krzesinski, MD, PhD. They are from the University of Liège, Centre Hospitalier Universitaire de Liège, 4000 Liège Sart Tilman, Belgium.

**Reference**