Dabigatran Adherence Among Nonvalvular Atrial Fibrillation Patients Is Associated with Pharmacist-Based Activities


Study Overview

Objective. To assess site level adherence to dabigatran among patients with atrial fibrillation and to determine if specific practices at the site level are associated with adherence.

Design. Mixed-methods study involving retrospective quantitative and cross-sectional qualitative data.

Setting and participants. 67 Veterans Health Administration sites with 20 or more patients with dabigatran prescription for nonvalvular atrial fibrillation between 2010 and 2012 were included. Among these sites, 41 sites participated in an inquiry about practices related to dabigatran use. A total of 47 pharmacists among the 41 sites were interviewed. The investigators identified from the interviews 3 specific practices related to dabigatran use: appropriate patient selection (review of indications, contraindications, and prior adherence to other medications), pharmacist-driven patient education, and pharmacist-led adverse event and adherence monitoring. Sites were characterized as having adopted these specific practices or not, based on the interviews.

Main outcome measure. Dabigatran adherence defined by proportion of days covered (ratio of days supplied by prescription to follow-up duration) of 80% or more. Site level variance in dabigatran adherence among the 67 sites were described. Site level adherence was adjusted by patient level factors and site level factors. The association between site level practice and adherence was examined with Poisson models using generalized estimate equation to account for clustering of patients within sites.

Main results. A total of 67 sites with 4863 patients with prescriptions of dabigatran for atrial fibrillation were included in the analysis. There was wide variation among sites on adherence rate, with a range of 42% to 93% (median, 74%). The sites were categorized as high performing if their site level adherence rate was at least 74%. Among the 41 sites that participated in the qualitative study that defined exposure variables, appropriate patient selection was performed at 31 sites, pharmacist-led education was provided at 30 sites, and pharmacist-led monitoring at 28 sites. There was variation in the duration of monitoring among sites, with 18 of 28 monitoring for 3 to 6 months while the rest of the sites monitor indefinitely. Site level practices differed between low and high performing sites, with high performing sites more likely to have adopted appropriate patient selection with review...
of adherence (83% vs. 65% in low-performing sites), have pharmacist-driven education (83% vs. 59%), and have pharmacist-led adverse event monitoring (92% vs. 35%). After adjustment for patient level and site level characteristics, the association between adherence and appropriate patient selection (adjusted risk ratio [RR], 1.14; 95% confidence interval [CI], 1.05–1.25) and pharmacist-led adverse event monitoring (RR, 1.25; 95% CI, 1.11–1.41) remained.

Conclusion. There is wide variability in dabigatran adherence among patients with atrial fibrillation at different VA sites. Site level pharmacist-based practices are associated with the level of adherence at the sites.

Commentary

Studies have demonstrated that in a clinical trial setting, dabigatran is as effective as warfarin in stroke prevention among patients with atrial fibrillation and is associated with a lower risk of major hemorrhage [1]. However, outside of clinical trials, effectiveness of a treatment regimen is highly related to whether treatment is adhered to. In contrast with warfarin treatment, where treatment adherence is regularly tracked through monitoring of blood levels and clinic visits, dabigatran does not require monitoring and thus, adherence to dabigatran may not be monitored. A recent study finds that poorer adherence likely contributes to increased risk of stroke and death among patients on dabigatran [2]. The current study examines the variation in adherence rates on a site level and identifies factors that are associated with better adherence. The findings suggest that better patient selection through examination of prior adherence to warfarin and other medications and pharmacist-led adverse event and adherence monitoring are practices that are associated with better adherence. These are potentially important findings that may impact care for patients with atrial fibrillation.

These results need to be interpreted cautiously because of the limitations of the observational study design. Several factors need to be considered when interpreting the study findings. First, despite the VA being a comprehensive system of care, veterans often use care outside of the VA, including obtaining medications outside of VA [3]. Because of the prevalent concurrent use of care outside of VA, examining adherence to medication with only VA records may be incomplete and may erroneously categorize patients as low adherence. Second, the number of patients on dabigatran per facility is rather small and quite variable as well, with some sites that have very few number of patients. Although the investigators have excluded sites with fewer than 20 patients on dabigatran, the variability in the use of dabigatran may reflect site-specific factors, some of which may affect patient selection on the site level, that ultimately may affect outcome. Finally, the interview of pharmacist at each site may reflect the view of one to two pharmacists at each site, and thus may not truly reflect practices at the site throughout the period where patients were selected and outcomes defined.

Applications for Clinical Practice

Although it is tempting to conclude that instituting the pharmacist-based activities in patient selection and adverse event monitoring will lead to better adherence to dabigatran and thus improved patient outcomes, considering the limitations in the study a follow-up intervention study where sites are randomized to institute-specific practices for dabigatran use will be very important to demonstrate definitively the impact of these interventions. Also, as the use of dabigatran and other novel anticoagulants become more prevalent [4], a follow-up study to include a larger sample of patients may also be valuable to demonstrate if the conclusions are upheld.

—William Hung, MD, MPH

References

For Worksite Weight Loss: Something Is Better than Nothing, but Is Something More Even Better than That?


Study Overview

Objective. To compare the effectiveness of 2 employee weight management programs—a less-intense program versus a more intense, individually-targeted program with financial incentives—at producing weight loss.

Design. Cluster randomized controlled trial.

Setting and participants. The setting for the “Tailored Worksite Weight Control Programs Project” was 28 small and medium-sized employers in and around Roanoke and Richmond, Virginia. Investigators enrolled the firms after a series of conversations with worksite leaders and conducted stratified cluster randomization based on worksite size (categorizing small firms as those with 100–300 employees and medium firms as those with 301–600 employees). For worksites to be considered for inclusion, the researchers required that the employer have between 100–600 employees total, provide internet access to employees, provide access to a weigh-in kiosk for the weight management program, and be willing to conduct a brief health survey of all employees at baseline to facilitate identification of eligible employees. Once eligible and interested worksites were identified, there were further inclusion criteria for employees themselves. To enroll in the study, an individual employee had to be over 18 years of age, have a BMI ≥ 25 kg/m², not be pregnant or with a medical condition that would contraindicate participation, and not already participating in a structured weight loss program. Of 73 worksites deemed eligible upon review of local companies, 39 (53.4%) initially agreed to enroll in the study. Of those, 11 dropped out before the intervention due to lack of managerial support and/or employee interest. Within the 28 enrolled worksites that were randomized, 6258 employees were felt to be eligible based on baseline screening. Of those, 1790 (29%) enrolled in the study.

Intervention. At worksites randomized to the INCENT program, study participants received an internet-based, tailored weight loss advice intervention coupled with a financial incentive. The behavioral intervention was based in social cognitive theory. It focused on advising healthier diet and increasing physical activity levels to 150 min/wk. Participants in this group received daily emails from the program that were “tailored” according to their gender and according to their preferred features of physical activity. The modest financial incentive they received was tied to weight loss. They were paid $1 for each percent of body weight lost per month. All INCENT participants also had access to a comprehensive website where they could access information about exercise, including videos, and logs for monitoring activity and dietary intake.

At worksites randomized to the less intense LMW (“Livin’ My Weigh”) program, employees who enrolled received an intervention that also included information about diet and physical activity but did not include daily tailored emails or financial incentives. These participants did receive quarterly newsletters. Both programs were designed to last for 12 months, with a 6-month weight-loss phase followed by a 6-month weight maintenance phase. The results reported in this study focus on weight loss achieved at 6 months.

Main outcome measures. The primary outcome in this study was weight change, measured in 2 ways: mean weight loss at 6 months, and percentage of participants in each arm who had achieved clinically meaningful weight loss (defined as ≥ 5% of body weight) at 6 months. Weight change was measured using calibrated scales at kiosks that were provided within each workplace. Secondary outcomes of interest focused on behavioral measures based on self-report using repeated surveys of participants. These included change in physical activity levels (measured using 6 Behavioral Risk Factor Surveillance System (BRFSS) items, and 8 Rapid Assessment Physical Activity (RAPA) scale items), and change in dietary behaviors (using the Block Fruit-Vegetable
Fiber Screener, and the Beverage Intake Questionnaire). Analysis was intention-to-treat (last observation carried forward for those who disenrolled before 6 months) and was conducted at the level of the individual participant, with generalized linear modeling including a time indicator and interaction terms for study group by time, to account for clustering effects.

Results. Of the 1790 participants who enrolled in the study, 1581 (88%) had complete follow-up data for analysis. Study participants were predominantly female (74%), Caucasian (77%), and well educated (only 17% had a high school diploma or less). Participants in the study differed from the overall eligible population for the study in a couple of important ways: they were more likely to be Caucasian and more likely to be women. The groups were well balanced with respect to most baseline characteristics, however, INCENT participants were significantly younger (45.7 vs. 48.2 years) and reported having worked at their current jobs for less time (8.1 vs. 11.6 years on average) than LMW participants. A significantly higher percentage of INCENT participants also reported meeting physical activity recommendations at baseline (10.2% vs. 6.8%, \( P < 0.05 \)).

At the 6-month mark, participants in both groups lost weight on average (–2.3 lbs in INCENT, and –1.3 lbs in LMW), but there were no significant between-group differences. Likewise, although slightly more participants in INCENT (14.6%) achieved a 5% weight loss compared to those in LMW (9.7%), this difference also was not statistically significant.

For self-reported outcomes, some differences did emerge between the groups. INCENT participants reported a statistically significantly larger increase in daily fruit and vegetable intake (0.2 servings, \( P < 0.001 \)) and fiber intake (0.58 g, \( P < 0.001 \)). Within group change measured for self-reported water intake was significant for INCENT participants (increased by 0.47 fl oz per day), whereas it was not for LMW participants. Between group differences were presumably not significant for this measure, as they were not reported.

Conclusion. The authors conclude that both an individually targeted internet-based intervention and a minimal intervention can lead to improvements in activity and diet behaviors, and that both produce a modest amount of weight loss for employees.

Commentary

Given the high prevalence of overweight and obesity in the United States, employers are increasingly interested in programs that can promote more healthful behaviors and achieve weight loss for workers. Because many employers are faced with bearing the health care costs of obese employees [1], and because chronic health conditions linked to obesity may impact worker productivity through increased absenteeism [2], the financial benefits of successful employer-based weight management programs may be significant. Unfortunately, to date, many such programs have gone unevaluated. Those that have been evaluated tend to be lacking in empirical basis (eg, too brief and not based on principles of behavior change). Perhaps because of these programmatic weaknesses, evaluations have not generally shown that employer-based weight management programs are able to move the needle very much on weight [3]. It seems that having \textit{any} program in place is better than having nothing at all, but it is unclear whether programs of greater intensity are able to produce better results.

In this study by Almeida and colleagues, the researchers tested whether a more intense, tailored internet-based behavioral intervention with financial incentives produced greater weight loss than a less-intense program, hypothesizing that it would. Surprisingly, they actually found very little difference between the 2 groups with respect to weight outcomes, and only minimal differences with respect to behavior change. The strengths of this study include a randomized trial design with a strong comparison group, and the use of intention-to-treat analysis. Additionally, both interventions that were tested were “real-world friendly” programs, meaning that they could, in theory, be implemented relatively easily in a wide variety of settings. This is in stark contrast to traditional behavioral weight loss programs that tend to be incredibly intense and costly in nature—probably unappealing to most employers. Despite being of lower intensity, both of the interventions in this study had a clear basis in behavior change theory, which was a strength. Additionally, the retention rates at the end of the 6-month study period were excellent, with almost 90% of participants having complete follow-up data. Although this trend was probably facilitated by having a “captive” employee population, it speaks to the ease of participating in and hosting the programs.

Although the randomized design was a definite strength of this study, the demographic imbalances between the
groups at baseline (resulting from individual-level factors that could not be randomized) may have been important. INCENT participants were younger and earlier in their careers, and although the researchers conducted multivariable analyses to try to eliminate confounding, this baseline imbalance raises concerns for whether or not other unmeasured confounding variables might have been unequally distributed between the groups.

It is not surprising that neither intervention produced large amounts of weight loss. Although the interventions were evidence-based in that they were grounded in behavior change theory, the specific behaviors focused on were not those that would be expected to yield significant weight loss. Both interventions, at least as described in this paper, seemed to put a greater emphasis on physical activity than diet (in terms of resources available for participants). While activity is critical for health promotion and weight maintenance [4], it is probably less important than diet for achieving meaningful weight loss. This is particularly the case when one considers the level of activity that was targeted in this study (150 min/wk). Although this is the recommended level for adults in order to maintain health, it is not believed to be sufficient to result in weight loss [5]. In terms of the dietary recommendations described in these programs, a focus on low-fat, high-fiber diets would be only expected to promote weight loss assuming that significant overall caloric reductions were met. Without stating specific caloric limits (which perhaps they did, even if not mentioned in the methods section), it’s hard to know how effective these diets would be at reducing weight, despite their likely positive impacts on overall health. In keeping with these points of emphasis for dietary change, the places where statistically significant differences emerged between the groups were not those that would be expected to produce differential weight loss. Fruit and vegetable intake, while important for health, will not produce weight loss independent of an overall decrease in caloric intake. The other dietary outcome that was significantly different between the groups was fiber intake, likely a correlate of the increased fruit and vegetable intake.

One of the key assumptions driving this study was that INCENT was a more intense program than LMY, and thus would produce greater weight loss. In reality, though, neither of the programs was particularly intensive—there were no face-to-face contacts in either, for example. This issue captures a fundamental trade-off between the need to achieve results and the need for pragmatism in designing interventions. Although less intense interventions are likely to produce less weight loss (as was the case in this study), they are probably also infinitely more likely to be adopted in the real world, making it very important to do studies such as this one.

One area where the INCENT arm could have enhanced its effectiveness without sacrificing pragmatism was in the size of the financial incentive used. The researchers mentioned not wanting to use large incentives in order to avoid “undermining intrinsic motivation,” a concern often raised in these kinds of interventions. Unfortunately, the “$1 per percent weight lost” reward probably went too far in the other direction, being too small to provide any kind of additional motivation. Studies of financial incentives for weight loss reveal that weight loss increases in proportion to the size of the incentive [5], and perhaps this incentive was too tiny to register with most participants, particularly in this population of well-educated, high-earning adults.

Applications for Real-World Implementation

For employers and others considering how to design pragmatic weight management interventions, this study shows that even relatively simple, low-key, internet-based interventions are able to produce some measureable behavior changes and a little bit of weight loss, which is likely meaningful when considered in a large population. On the other hand, reconfiguring the resources in such an intervention to provide greater focus on caloric consumption, higher physical activity levels, and the use of larger financial incentives might well be worth the bang for the buck in trying to improve upon these results.

—Kristine Lewis, MD, MPH

References