Impact of introducing anticoagulation-related prescribing guidelines in a hospital setting using academic detailing

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Aim: Assess the impact of using academic detailing-assisted guideline roll-out on warfarin initiation, reversal of warfarin overanticoagulation, and uptake of deep vein thrombosis (DVT) prophylaxis across 4 metropolitan teaching hospitals.

Methods: Baseline data were collected for 3 months prior to intervention. Prescribers were then informed about the guidelines, including feedback of current hospital performance and the basis for the guidelines. Post-intervention data were collected for 3 months after guideline implementation.

Results: Uptake of DVT prophylaxis in medical patients increased from 52.8% to 67.0% (p=0.004). No impact on operative surgical patients was seen, possibly due to the high pre-existing rate of uptake (86.1% vs 84.1%, p=0.7). DVT prophylaxis rates in non-operative surgical patients were similar to medical patients, with similar, but non-significant improvements. The time to reach a stable therapeutic international normalized ratio (INR) after warfarin initiation was reduced (p=0.03) as were the number of INR's >4 in the first week of therapy (p=0.03). There were significant improvements in appropriate vitamin K use for warfarin overanticoagulation in patients with an INR above 6 (48% vs 74%, p=0.007), timely follow-up tests (49% vs 62%, p=0.009), and the proportion of next INR's being less than 4 (49% vs 61%, p=0.04).

Conclusions: The use of academic detailing to facilitate guideline roll-out had a positive impact on nearly all areas studied. The academic detailing process within the hospital setting was received enthusiastically by prescribers.

Keywords: warfarin, overanticoagulation, DVT prophylaxis, elderly, academic detailing

Introduction

The anticoagulant group of drugs is consistently one of the top drug groups related to adverse drug events, and the consequences of an adverse event with this group of drugs is likely to be serious (Wilson et al 1995; Roughhead 1999; Runciman et al 2003). The Australian National Mortality Database from 1997–8 indicated that 2.2% of patients experienced an adverse event associated with their death, and 25% of these were drug-related. Anticoagulants accounted for 31% of these adverse drug events.

Several areas within the anticoagulation practice framework were locally identified as areas where strategies to encourage prescribers towards best practice may result in significant improvements in health outcomes. These were:

- Deep vein thrombosis (DVT) prophylaxis in medical patients,
- DVT prophylaxis in surgical patients,
- warfarin initiation,
- treatment of warfarin overanticoagulation.

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The poor uptake of DVT prophylaxis in eligible hospitalized medical patients remains a consistent problem across the health system, despite evidence demonstrating its efficacy. Patient selection, timing and during of prophylaxis, as well as dosing, remain sources of confusion for prescribers. The medical literature reports only 20%–60% of eligible hospitalized medical patients receive DVT prophylaxis (Anderson et al 1994; Ageno et al 2002; Bergmann and Mouly 2002; Goldhaber 2003). Adverse consequences of unprevented venous thromboembolism (VTE) include pulmonary embolism (PE), death, recurrent DVT, venous valvular incompetence and chronic post-thrombotic syndrome. The American Agency for Healthcare Research and Quality reported in its 2002 practice guidelines that the highest ranked safety practice to reduce adverse patient care outcomes was "appropriate use of prophylaxis to prevent VTE in patients at risk".

There are clearly clinical consequences from under-use of DVT prophylaxis. It has been reported that 68% of hospital-acquired DVT's or PE's were potentially preventable, with 48% not receiving any prophylaxis, 23% receiving an inadequate duration of prophylaxis, and 21% receiving the incorrect type of prophylaxis (Arnold et al 2001). The importance of post-operative DVT prophylaxis was highlighted in a group of surgical hip fracture patients (Todd et al 1995). Twelve of 305 patients with no DVT prophylaxis succumbed to fatal PE's compared with none of the 261 patients who did receive prophylaxis.

The initiation of warfarin also presents unique challenges for prescribers. The practice over the last decade towards warfarin use for patients with atrial fibrillation has dictated a shift in prescribing to a much older patient group. This has created a change in how we approach initiation of warfarin, as we are now treating a patient group with much higher warfarin sensitivity. Warfarin initiation approaches that were previously successful are now clearly too aggressive, and likely to overanticoagulate the patient (Roberts et al 1999; Gedge et al 2000). A number of more appropriate methods of warfarin initiation have since been developed (Oates et al 1998; Tait and Sefcick 1998, Crowther et al 1999; Roberts et al 1999).

The management of warfarin overanticoagulation has also become more clearly defined over the last decade. With the advent of treatment of a much older patient group, physicians are more commonly managing patients who

present a challenge with regard to maintaining the international normalized ratio (INR) in the therapeutic range. Episodes of overanticoagulation are now well understood to be associated with serious and sometimes fatal bleeding events. A number of INR reversal strategies have been developed which enable timely reduction of the INR back to the therapeutic range, or if required, total reversal (Wiebert et al 1997; Wentzien et al 1998).

These are all seemingly relatively simple therapeutic areas, and prescribing duties for these areas usually rest at a junior doctor level. Junior medical staff often have no formal training in these areas, and there is often little or no coherence across hospitals, or even within hospitals, towards prescribing. This makes it difficult for junior prescribers to establish a clear practice in their own mind by observing the clinical practice around them.

While it is easy to recognize areas of clinical practice that require improvement, and then draw up practice guidelines, there are barriers at many levels in the implementation and practice of these guidelines. Medical practice is rife with the carcasses of guidelines that have been distributed and never used. Key barriers consistently identified include lack of awareness of the guidelines, inability to access them when needed, and the requirement for a concise quick-reference format rather than detailed text (Mortimer and Ward 2002; Scott et al 2003). Other barriers include lack of agreement with the guidelines, lack of self-efficacy (belief that one can actually perform the behaviour), lack of outcome expectancy (the prescriber doesn't believe the guidelines will have the desired effect) and external barriers (Cabana et al 1999). Clinicians were more motivated to change their practice when provided with hospital-specific feedback demonstrating a need for improvement (Anderson et al 1994).

Academic detailing combines a number of techniques that can be utilized to influence prescribing practices. This involves a number of principles, such as face-to-face sessions, preferably on an individual basis, defining clear educational and behavioral objectives, establishing credibility with respect to objectivity, stimulating physician interaction, use of concise graphic educational materials, highlighting key messages, and when possible, providing positive reinforcement of improved practices in follow-up visits (Avorn and Soumerai 1983). This approach has had a positive impact on prescribing behavior at both the community and hospital setting (May et al 1999; Solomon et al 2001).

Methods
Guideline development
Local best-practice guidelines were developed. These included input from existing published guidelines (SIGN 1999; Geerts et al 2001; Roberts et al 2003), recent primary literature, and expert opinion from within each of the targeted hospitals from both key clinical practitioners and hematologists. Once developed these were then also sent to the respective hospitals' drug committees for further comment and endorsement. This was to help enable credibility both with respect to objectivity, and with respect to ownership from local clinical champions. Each guideline was specifically limited to a single A4 page with an emphasis on clarity and brevity in order to improve prescriber acceptance.

Data collection
Prior to the academic detailing intervention, baseline data for DVT prophylaxis were collected prospectively for a 3 month period, while data on warfarin initiation and treatment of warfarin overanticoagulation were collected both retrospectively and prospectively during this 3-month period. Once the academic detailing was completed, post-intervention data was collected prospectively for a 3–4 month period.

The academic detailing process
Academic detailing was performed by two pharmacists and one doctor, all of whom undertook specific training in this area from experts in the field. The academic detailing process was not carried out until the baseline data collection was complete in order to collect unbiased data on current practice. Prescribers were targeted for one-on-one interviews, in keeping with the true form of academic detailing, but larger groups were occasionally catered for to incorporate the uniqueness of hospital dynamics. Interviews were conducted at a place of the prescribers' choice, and took between 20–60 minutes depending on the level of prescriber interest and prescriber time constraints. Selected medical and surgical teams at each hospital were detailed, and only patients treated by these teams were studied.

The interview was structured to inform the prescriber why there was a problem in this area and the medical literature supporting this. An important part of the process was collation and feedback of local data, indicating the extent of the problem within that particular hospital. The

guidelines were then introduced, with reference to their origins, particularly input from any local hospital champions. They were explained in a clear simple manner, emphasizing their standardization across the hospitals with a view to making life easier for the prescriber. Detailing materials were designed to be clear, brief, easily interpreted, and where possible presented as graphs.

Key messages
DVT prophylaxis
a)   Eligible medical patients defined as those who are immobilized (temporary or otherwise) in conjunction with an acute disease process. Patients were considered to be mobile if they ambulated independently three times daily for at least 5 minutes each time.

b)   Eligible surgical patients determined by adding the risk associated with both the patient and the type of surgery

c)   Low molecular weight heparin (LMWH) dose reduction or non-LMWH prophylaxis for those patients with impaired renal function (estimated creatinine clearance <30 ml/min).

Warfarin initiation
a)   Use of the guidelines avoids overanticoagulation during the loading phase

b)   Achieves a stable therapeutic INR in a shorter time

c)   Use of a recognized initiation approach allows for early discharge to community physicians.

Warfarin overanticoagulation
a)   An INR >6 puts the patient at unacceptable risk and requires immediate treatment with an appropriate dose of vitamin K (Hylek et al 2000; Oden and Fahlen 2002).

b)   The course of an INR is unpredictable, and timely follow-up of INR testing after any intervention is essential.

c)   Look for signs of bleeding

d)   Try and identify the cause of overanticoagulation.

Endpoints
DVT prophylaxis
a)   Proportion of eligible patients receiving prophylaxis

b)   Uptake of appropriate therapy for patients with reduced renal function (defined as estimated creatinine clearance <30 ml/min using optimized Cockroft-Gault equation) (Kirkpatrick et al 1999). Appropriate alternative therapy was defined as either a reduced DVT prophylaxis dose of LMWH, use of unfractionated heparin, or mechanical prophylaxis.

Warfarin initiation

a) Time to reach a stable therapeutic INR, defined as either the first of two consecutive INR's in the range of 2–3, or the first measurement in the therapeutic range when the previous or subsequent INR was within 0.5.

b) The number of patients experiencing an INR ≥ 4 during the first week of warfarin initiation.

Warfarin overanticoagulation

a) Use of vitamin K for INR >6

b) Follow-up INR within 24 hours

c) Next INR >4

d) Time between INR being performed and vitamin K administration for INR's >6.

An episode of warfarin overanticoagulation was defined as an INR >4.5

Guideline availability

Guidelines were posted as A4 sheets in critical points on the wards and in doctors' offices, prescribers were given their own pocket-sized charts, electronic copies were available, and the guidelines were placed in patient drug charts to enable immediate access at the time of decision making. Doctors were also given a drug information contact number specifically for questions regarding the guidelines.

Statistics

Comparison of continuous variables pre and post intervention utilized a Student's t-test. Dichotomous variables were compared with simple non-parametric tests such as Fisher's Exact Test. Time to a stable therapeutic INR was determined using survival analysis, comparisons being made with the log-rank test.

Sample size

DVT prophylaxis – non-parametric power calculations indicated at least 120 patients in each group (pre and post intervention) were required to detect a decrease from 30% inappropriate prescribing to 15%. No background data was available for warfarin initiation and treatment of overanticoagulation. A minimum of 30 patients from each hospital in each of these categories was collected for the baseline data.

Results

Patient characteristics are indicated in Table 1.

Medical DVT prophylaxis

During the pre-intervention period 198 patients were identified as being eligible for DVT prophylaxis, including 26 patients admitted under surgical teams for medical reasons. Of these, 180 patients had no obvious contra-indication for DVT prophylaxis and were not on oral anticoagulants, with 52.8% receiving DVT prophylaxis. There were 266 patients assessed post-intervention, 49 of who were admitted under surgical teams. Of these, 230 patients had no obvious contra-indication for DVT prophylaxis and were not on oral anticoagulants, with 67.0% receiving DVT prophylaxis, an absolute increase of 14.2% (p=0.004) (Figure 1).

Table 1 Patient characteristics

	Pre-intervention	Post-intervention
Medical DVT prophylaxis		
n	198	266
Hospital (%)	23/25/28/24	24/29/25/22
Age (years, mean ± 1 SD)	79+10	77+14
Gender (% male)	59	50
Weight (kg, mean ± 1 SD)	67+20	70+18
Type of admission (%)		
heart failure	24	32
airways disease	32	27
days immobile (median, range)	5.5 (1–225)	5.0 (1–96)
Surgical DVT prophylaxis		
n	166	221
Hospital (%)	16/32/22/31	24/32/22/23
Age (years, mean ± 1 SD)	70+16	67+18
Gender (% male)	45	45
Weight (kg, mean ± 1 SD)	75+18	73+15
Type of DVT surgery (%)		
Orthopaedic	44	49
General	44	35
Vascular	9	8
Warfarin initiation		
n	173	91
Age (years, mean ± 1 SD)	71.4+14.8	72.9+13.5
Gender (% male)	54	47
Weight (kg, mean ± 1 SD)	75+19	74+16
Serum albumin	33.5+6.5	33.9+5.1
Hospital (%)	27/21/24/28	30/32/26/12
Warfarin overanticoagulation		
Episodes of overanticoagulation	192	106
N	161	89
Age (years, mean ± 1 SD)	76+13	78+10
Gender (% male)	47	57
active bleeding (%)	21	14

Abbreviations: DVT, deep vein thrombosis; SD, standard deviation.
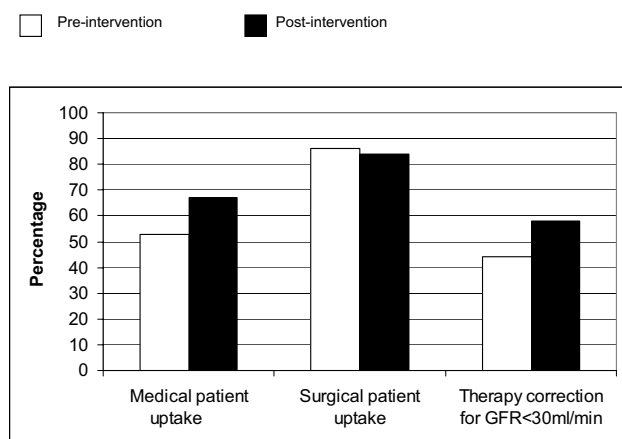
Figure 1 DVT prophylaxis outcomes (p<0.01).
Abbreviations: DVT, deep vein thrombosis; GFR, glomerular filtration rate.

When medical and non-operative surgical patients were considered separately, the trends were similar. For medical patients in the pre and post-intervention stages, the rate of DVT prophylaxis uptake was 51.6% and 65.2% respectively (p=0.016). This was compared with 61.9% and 73.5% respectively in the small sample of non-operative surgical patients (p=0.3).

Patients with poor renal function (glomerular filtration rate [GFR] <30 ml/min) were considered ineligible for full LMWH DVT prophylaxis. Appropriate therapy was considered to be either a reduced dose of LMWH, use of unfractionated heparin or use of mechanical prophylaxis. During the pre-intervention phase 7 of 21 patients (33%) received appropriate therapy alteration compared with 19 of 32 (59%) in the post-intervention phase (p=0.3), (Figure 1).

Surgical DVT prophylaxis

During the pre-intervention phase 136 of 158 (86.1%) clearly eligible patients received prophylaxis, compared with 174 of 207 (84.1%) in the post-intervention phase (p=0.7) (Figure 1). Appropriate therapy for patients with impaired renal function was given for 12 of 22 patients (55%) in the pre-intervention phase compared with 7 of 13 patients (54%) after the intervention (p=0.98). Operative surgical patients also received a significantly higher use of mechanical DVT prophylaxis compared with medical patients. This was nearly always in combination with pharmacologic prophylaxis and was evident during both the pre and post-intervention stages (p<0.001 for both, see Table 2).

Warfarin overanticoagulation

Use of vitamin K to reverse INR's >6 in patients with no clinically obvious bleeding increased from 48.1% in the pre-intervention phase to 74.4% post-intervention (p=0.007). The median time taken to administer vitamin K was 13.3 hours before the intervention, decreasing to 7.2 hours after the intervention (p=0.099) in this group. The next INR taken was below 4 in 48.7% of patients pre-intervention compared with 61.1% after the intervention (p=0.04). A follow-up INR was performed within 24 hours in 48.7% of cases pre-intervention compared with 62.4% after (p=0.009). For patients experiencing some form of bleeding, use of vitamin K increased from 40% to 67% (p=0.17), with no change in the median time to administer vitamin K (3.7 vs 3.9 hours).

Warfarin initiation

Post-intervention patients initiated on warfarin were quicker to get to a stable therapeutic INR (p=0.03, see Figure 2). They were also less likely to experience an episode of overanticoagulation in the first week of initiation (31.8% vs 18.7%, p=0.03).

Discussion

With the exception of DVT prophylaxis for the operative surgical patients, there were clear improvements in the outcome indicators in all areas. While the endpoints were not direct measures of patient safety outcomes, it is reasonably expected they would have a positive flow-on effect for patient safety. It is likely the improved DVT prophylaxis uptake would translate to a decreased number of hospital-acquired DVT, a situation illustrated by Arnold and colleagues (2001).

The improvements from more aggressively reversing INR's >6 and paying closer attention to timely follow-up

Table 2 Modality of DVT prophylaxis

	LMWH only (%)	Heparin only (%)	Mechanical only (%)	Combination mechanical plus drug(%)
Pre-intervention				
Medical	55	22	5	18[1]
Surgical	31	9	2	58
Post-intervention				
Medical	57	21	5	16[1]
Surgical	45	12	3	40

Note: [1]p<0.001 compared with surgical use of mechanical plus drug DVT prophylaxis.
Abbreviations: DVT, deep vein thrombosis; LMWH, low molecular weight heparin.

Pre-intervention • • • Post-intervention ─────
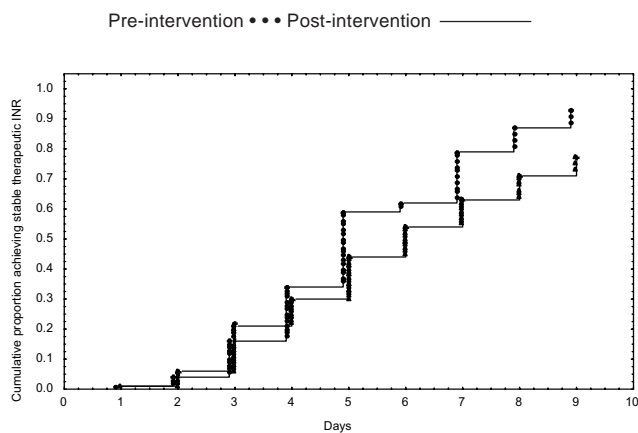
Figure 2 Time to a stable therapeutic INR during warfarin initiation (p=0.03).
Abbreviations: INR, international normalized ratio.

may be expected to translate to a decreased likelihood of bleeding as a serious adverse event (Hylek et al 2000; Oden and Fahlen 2002). The same might be expected of the decreased number of high INR's during warfarin initiation bought about by use of the guidelines.

The baseline rate of medical DVT prophylaxis uptake was similar or better than that found by other groups. Anderson et al (1999) noted a 21%–40% baseline uptake in a study performed in the late 1980's when there was possibly less awareness of this issue. Ageno et al (2002) noted a 46% uptake in Italian hospitals on a background of passive guideline dissemination, while a 32% uptake in medical patients was noted in France (Bergmann and Mouly 2002). The uptake rates in this study at baseline were marginally better, but consistent with these figures at 52.8%, a number based on patients who had a clear indication for DVT prophylaxis with no contra-indications to prophylaxis and no other ongoing therapeutic anticoagulation. The increase to 67.0% after guideline implementation was pleasing, but indicates there is still room for further improvement.

This study noted a far superior uptake of DVT prophylaxis in operative surgical patients compared with that in medical patients. This was 86.1% versus 52.8% at baseline, and 84.1% versus 67.0% after guideline implementation, for surgical and medical patients respectively (p<0.001 for both). This difference has been noted previously and may be due to the more structured, protocol-driven nature of procedural surgery that allows prescribers to pre-empt the need for DVT prophylaxis (Goldhaber 2003; Goldhaber and Tapson 2004). This decreased markedly in non-operative patients admitted under surgical teams, who experienced a similar rate of DVT prophylaxis uptake as medical patients (62% and 74% DVT

prophylaxis uptake before and after guideline implementation).

The number of patients experiencing overanticoagulation during the first week of warfarin initiation decreased with the implementation of the warfarin initiation guidelines, in conjunction with a small improvement in the time to reach a stable therapeutic INR. However both these endpoints fell far below what has been shown to be achievable with these guidelines previously (Roberts et al 2003).

Possibly the most impressive impact was seen with the warfarin overanticoagulation guidelines. This was possibly a reflection that these were the simplest, and clearest of the four guidelines. There were only 2 factors to focus on: the patients INR, and whether the patient was experiencing clinically significant bleeding. It is well recognized that prescribers are more likely to follow guidelines if they are specific (Michie and Johnston 2004). This excellent uptake may also have been driven by the clear message from the academic detailing process that highlighted the increasing risk of death/hemorrhage with increasing INR's (Oden and Fahlen 2002). The prescriber is also "rewarded" within a relatively short timeframe after an intervention with this guideline, via noting the satisfactory reduction in INR. With the other guidelines, there was no obvious or immediate feedback to the prescriber indicating the new course of action was having an impact, eg, increased prescribing for DVT prophylaxis.

Despite the satisfactory improvement in practice as a result of this form of guideline implementation, several issues need to be addressed. At all hospitals the rotation of junior medical and surgical staff, who are likely to do the bulk of the prescribing for issues related to these guidelines, is at least three-monthly. This can be even more frequent when some staff are on holidays, sick leave, etc. The academic detailing relies of course on timely interaction with those who are likely to prescribe, which dictates an ongoing commitment and the resources to do this. The second issue is that there was still a lot of room for improvement, especially for the medical patient DVT prophylaxis and the warfarin initiation. The only approach that has come close to 100% compliance involves computerization, often with forcing functions. This has worked particularly well in the setting of surgical DVT prophylaxis, where admissions are generally planned, and the need for prophylaxis is pre-empted (Mosen et al 2004). This is more difficult for the acute and somewhat more random nature of medical patient admission.

The approach of using academic detailing within the hospital setting was greeted with almost unanimous enthusiasm. A sample of 36 doctors was taken to judge the interest in the concept of academic detailing within hospitals, the interest in anticoagulation as a topic, and their general participation in the visit. On a scale of 0 (hostile) to 4 (very interested) the mean ranking was 3.5, 3.6, and 3.7 respectively for each of these areas. Prescribers were very interested in the feedback from within their own hospitals, and this undoubtedly helped in their acceptance of the guidelines. The more junior prescribers were very keen to absorb this information and found it most useful, as the need for education in the areas covered by the guidelines was not being formally met elsewhere. There were occasional barriers to guideline acceptance, and this appeared more likely in the senior ranking prescribers, who are possibly less likely to make a change in their set prescribing habits if this was required. Resistance to guideline acceptance was also encountered when the occasional individual consultant had a very set approach to a particular therapy, eg, using 10 mg, 10 mg, and 5 mg on the first 3 days of warfarin initiation.

Ideally, academic detailing would be performed each time a new prescriber (or more commonly, group of prescribers) commenced at the hospital, so sustainability issues would need to be considered. It may be more likely to have a long term effect on younger prescribers, who are often still seeking input and clarification on clinical issues, in order that they may develop an appropriate clinical approach. They are also the group most likely to be doing the prescribing. Academic detailing appears to be an effective approach welcomed by prescribers for encouraging uptake of clinical guidelines within the hospital setting. It should be strongly considered either by itself or in conjunction with other strategies as a means of improving guideline compliance and patient care within the hospital setting.

Disclosure

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