THE APPLICATION OF TWO ANALYTIC METHODS TO INVESTIGATE THE INFLUENCE OF POOR INR CONTROL ON RISKS OF HOSPITALISATION FOR PATIENTS RECEIVING WARFARIN

Oflori B1, Davey P1, Goudie B2, Timoney A2, Donnan P1
1University of Dundee, Dundee, Scotland, UK; 2NHS Tayside, Dundee, Scotland, UK

OBJECTIVES: Adverse drug reactions to oral anticoagulants are a cause of significant morbidity. Treatment decisions will depend on effective means of risk stratification and a better understanding of changes that occur in the immediate period just before an event. METHODS: Cox proportional hazards modelling and the case crossover methodology were applied to determine the hazards associated with the outcome of hospitalisation due to bleeding or over-anticoagulation. The study population comprised an inception cohort of 735, accumulating 583 patients years follow up. Under Cox proportional hazards modelling pre-specified clinical and laboratory variables were tested, including measures of quality of anticoagulation. Under the case-crossover methodology changes in biochemical, haematological, anticoagulation parameters, drug exposures, and their relation to outcome were analysed by conditional logistic regression analysis. Measurements from a 3-month case window immediately before the outcome event were compared to a control window four to six months before the outcome event. In both analyses factors univariately associated at p < 0.3 were considered in a multivariate backward-stepwise analysis. RESULTS: Under multivariate Cox proportional hazards modelling four variables were found to be significantly and independently correlated with the outcome; % days over INR 4.4 (p < 0.001), history of malignancy (p = 0.048), history of any bleed (p < 0.001), number of current comorbidities (p = 0.046). The case crossover analysis suggested that patients experiencing an outcome event were more likely to have spent time above INR 4.4 in the case period just before the event compared to the control period. For every increase of 1% in the time spent above INR 4.4 the odds of an event increased by 27% (95% CI 4%–54%). CONCLUSION: This study provides further evidence of the importance of monitoring and reporting time spent over INR 4.4 to minimise the risk of adverse outcomes to warfarin therapy.

PCV76

USING A PATTERN MIXTURE MODEL TO UNDERSTAND THE IMPACT OF NON-RANDOM MISSING DATA IN HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS UNDERGOING NON-CARDIAC VASCULAR SURGERY

Lee WC1, Cappelleri JC1, Sheikh S1, Haider S1, Gold KP1, Stephens JM1
1Abt Associates Inc, Bethesda, MD, USA; 2Pfizer Inc, Groton, CT, USA; 3Quanta Scientific, Silver Spring, MD, USA

OBJECTIVE: Non-randomness of missing data in longitudinal health-related quality of life (HRQoL) studies causes potential bias of estimates using conventional generalized linear model (GLM). The study objective was to compare a pattern mixture model (PMM) with GLM. METHODS: HRQoL data were collected using the SF-12 acute at baseline and postoperative Day 30 as part of a clinical trial assessing perioperative myocardial ischemic injury (PMII) in high-risk noncardiac vascular surgery patients. A PMM, where the indicator variable of drop-out and the interaction term of drop-out and the presence of PMII event were included as covariates, was fitted using physical component scores (PCS) of SF-12 as the outcome variable. The main predictor was the presence of PMII event adjusted for a host of control variables. This PMM was compared with a GLM where a change in PCS on SF-12 was used as a dependent variable. RESULTS: Of the 370 subjects in the U.S. clinical population, 229 subjects provided information on the SF-12 at baseline and 195 subjects at Day 30. Mean PCS were 30.6 (SD = 10.7) at baseline and 32.8 (10.6) at Day 30. Drop-out was not independent of the presence of PMII event (p = 0.0085). With the GLM using only completed cases (N = 190), an unexpected result emerged; the presence of PMII event was positively associated with improvement in the PCS of SF-12. In contrast, PMM (N = 229) indicated a more realistic result of a change in direction that, although statistically insignificant (p = 0.11), reflected a detrimental effect on PCS in the presence of a PMII event. CONCLUSION: GLM on complete data can give a spurious result when sicker patients are more likely to be excluded from analysis. While the PMM provided a logical direction of effect, a longer follow-up may have been necessary to detect a statistically significant and noticeable improvement in the PCS.

PCV77

ASSESSING THE LIKELIHOOD OF FRACTURE WITH ORAL ANTI-SPASTICITY MEDICATIONS: A CASE-CONTROL STUDY

Nichol MB1, Shi SG1, Knight TK1, Barron RL2
1University of Southern California, Los Angeles, CA, USA; 2Allergan Corp, Irvine, CA, USA

OBJECTIVES: To estimate the odds ratio of hip or vertebral fracture associated with oral anti-spasticity medications in a California Medicaid stroke/spasticity population. METHODS: A case-control design matched each hip or vertebral fracture patient to five patients without fracture on date of first prescription of oral spasticity medication. Oral spasticity medications were grouped according to their sedative qualities (light headedness, somnolence or drowsiness). Logistic regression was used to estimate adjusted odds ratios of fractures for medication groups while controlling for patient demographics, comorbidity, and other concurrent medications, through a propensity score approach. RESULTS: The adjusted odds ratio of having a hip or vertebral fracture for patients using medication classified in the somnolence group (Dronabinol, Lamotrigine, Riluzole or Tizanidine) was 1.88 (p = 0.003). The odds ratio was reduced to 1.65 after propensity score adjustment, but remained statistically significant (p = 0.024). Light headedness and drowsiness medication groups did not show a significant effect on fracture. Concurrent use of Diazepam, a member of the drowsiness medication group, was individually associated with the likelihood of fracture (raw odds ratio = 1.48, p = 0.002; odds ratio after propensity score adjustment = 1.39, p = 0.014). CONCLUSIONS: Care should be taken when prescribing sedating oral spasticity agents in elderly stroke patients.

HEALTH POLICY

RETAIL PRICES DECREASED 30% IN FINLAND IN 1994–2003 EVEN BEFORE INTRODUCTION OF GENERIC SUBSTITUTION: A COHORT ANALYSIS

Jorma启动nen V, Hahl J, Eranko P
GlaxoSmithKline Oy, Espoo, Finland

OBJECTIVES: We followed the retail prices of the year 1994 cohort of new chemical entities (‘the 1994 NCE cohort’) in Finland until March 15, 2003, before the introduction of generic and parallel import substitution on April 1, 2003. METHODS: The 1994 NCE cohort did not have any sales in 1993 by defin-