European Geriatric Medicine 8 (2017) 250–255

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www.em-consulte.com/en

Research paper

The relationship between polypharmacy and recovery of activities of daily living among convalescent stroke patients: A propensity score-matched analysis

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ARTICLE INFO

Article history:
Received 25 February 2017
Accepted 20 April 2017
Available online 8 May 2017

Keywords:
Polypharmacy
Rehabilitation
Functional independence measure effectiveness
Propensity score

ABSTRACT

Introduction: Polypharmacy induces side effects or drug interaction for elderly patients. Whether polypharmacy negatively affects stroke rehabilitation of patients is unclear in Japan. The aim of this study was to assess the relationship between polypharmacy and recovery of daily activity among convalescent stroke patients.
Methods: In this retrospective cohort study, we screened 719 stroke patients who were admitted to and discharged from the Sagami Rehabilitation Hospital or the Tsurumaki Onsen Hospital between April 2012 and July 2014 in Kanagawa, Japan. Among 719 patients screened, 509 were excluded because of propensity score matching. The primary outcome was Functional Independence Measure-Motor (FIM-M) effectiveness, and participants were divided according to FIM-M effective scores into the following two groups: non-improvement (105 patients) or improvement of FIM-M effectiveness (105 patients).
Results: Risk factors associated with non-improvement of FIM-M effectiveness included epilepsy and number of drugs used upon admission. FIM-M effectiveness in the patients in whom five or more drugs were used upon admission was significantly lower than in those in whom one drug was used. Through this finding, we defined the use of five or more drugs as polypharmacy. Drugs with significant differences regarding polypharmacy included antihypertensive and antidiabetic drugs.
Conclusions: These findings suggested that polypharmacy negatively affects stroke rehabilitation outcomes. Thus, pharmacists should make attempts to respond to individual patient outcomes to optimize prescriptions, which may minimize the brunt of polypharmacy on patient outcomes.

1. Introduction

According to a recent survey by the Ministry of Health, Labor, and Welfare of Japan, stroke is the fourth ranked killer; in addition, stroke is the primary cause of disease that requires nursing care. Although the number of deaths due to stroke has decreased annually, prevalence of stroke will continue to increase until 2025, and the number of stroke patients in need of nursing care is also expected to increase. Per the 2015 Japanese guidelines for stroke management [1], hypertension, dyslipidemia, and diabetes mellitus are risk factors. Therefore, stroke patients are more likely to be exposed to polypharmacy because it is extremely important to control blood pressure (BP) and levels of lipids and plasma glucose (PG). In addition, upon strictly controlling BP, lipids, and PG, polypharmacy also manifests, and undesirable drug interactions or side effects are likely to occur. In addition, Kojima et al. reported that when stroke patients are taking 5–6 or more drugs, side effects or fall are likely [2,3]. Therefore, polypharmacy may negatively affect rehabilitation outcome of patients. We hypothesized that the increased use of drugs and cognitive dysfunction and decreased activities of daily living (ADL) may be integral in setting

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http://dx.doi.org/10.1016/j.eurger.2017.04.009
1878-7649/

the tone of stroke rehabilitation. Therefore, the aim of the present study was to investigate the impact of polypharmacy on rehabilitation of stroke patients.

2. Methods

2.1. Participants

We screened 719 stroke individuals who were admitted to and discharged from Sagami Rehabilitation Hospital or Tsurumaki Onsen Hospital between April 2012 and July 2014 in Kanagawa, Japan. In Japan, patients with stroke who require intensive rehabilitation to improve ADLs and return to their own home are usually then admitted to convalescent rehabilitation wards and covered by public health insurance [4]. In our patient cohort, they received comprehensive rehabilitation support from a multidisciplinary team, including a rehabilitation physician, experienced nurses, a physical therapist, occupational therapist, speech-language-hearing therapist, care worker, social worker, and pharmacist.

2.2. Survey items

Information regarding study participant's characteristics, including age, gender, body weight, length of stay (LOS), days from stroke onset to admission to the convalescent rehabilitation ward, primary diagnosis (e.g., cerebral infarction, cerebral hemorrhage, and subarachnoid hemorrhage), complications (e.g., Parkinson's disease, hypertension, type 2 diabetes mellitus, epilepsy, and dyslipidemia), number of comorbid conditions, number of drugs upon admission and discharge, and presence of high risk drug use were collected via medical records. Information regarding study participant's laboratory data, including serum creatinine (Scr), estimated glomerular filtration rate (eGFR), white blood cell counts (WBC), albumin (Alb), and total cholesterol (T-Cho) were collected via medical records as well. We collected data on the number of drugs and Functional Independence Measure (FIM) at admission and discharge and paired this with other aspects of participant's characteristics and laboratory data upon admission. In addition, we used high-risk drugs, which were indicated by guidelines from the Ministry of Health, Labor, and Welfare. Number of drugs upon admission was classified into eight categories.

2.3. Outcome measure

We assessed ADLs using the FIM. FIM is one of the most common measurements to assess ADLs and includes 13 lower-order items regarding motor function (FIM-M) and 5 lower-order items regarding cognitive function (FIM-C) [5–7]. Each item is scored on a scale of 1–7 points (total assistance to complete independence). The FIM-total (FIM-T) score ranges from 18 to 126 points. The FIM scores upon admission and at discharge were assessed by the multidisciplinary rehabilitation team. FIM effectiveness is calculated as FIM-M gain/(91 points – FIM-M upon admission) [8]. FIM gain is the FIM change from admission to discharge. This is used to check what percentage of potential improvement has been achieved by setting the points that actually improved as numerator. The primary outcome was FIM-M effectiveness. The participants were divided according to FIM-M effective scores in the following two groups: non-improvement of FIM-M effectiveness (negative score to 0 points) and improvement of FIM-M effectiveness (above 0 points; positive score). The same units of rehabilitation were carried out for all participants regardless of their FIM score, stroke severity, or LOS.

2.4. Sample size calculation

A study size analysis was performed using Power and Sample Size Calculation software (version 3.0, 2009, William D. Dupont, PhD, and Walton D. Plummer, Department of Biostatistics, Vanderbilt University). Per a previous study, the mean FIM gain of stroke patients in convalescent rehabilitation wards in Japan was 19.6 ± 9.6 [4]. Although available data for detecting clinically relevant FIM gains in convalescent stroke patients were limited, a previous study of Japanese convalescent rehabilitation wards demonstrated that the mean difference of the FIM gains between the oral intake and tube-feeding group was 11 [9]. Therefore, we inferred that the mean difference was 11 between the groups in our study. When the ratio is 1:1, 51 patients are needed in each of the two groups for a power $(1 - \beta)$ of 0.8 and α of 0.05.

2.5. Statistical analysis

We used the propensity score method to mitigate the influence of nonrandom selection of improvement and non-improvement patients. The propensity score for an individual is defined as the conditional probability of the presence of non-improvement given the individual's covariates. To estimate these scores, we created a logistic regression model using the following covariates: demographic variables, such as age [10], gender, LOS [11], days from the stroke onset to admission [12], and FIM at admission [13]; clinical variables, such as stroke subtype (cerebral infarction, cerebral hemorrhage, or subarachnoid hemorrhage). We performed a one-to-one nearest neighbor match on the logit of the propensity score with a caliper value of 0.2.

A normality test was performed to compare the continuous data between the two patient groups. Student's *t*-test for normally distributed data or Mann-Whitney *U* test for data that were not normally distributed was used. A χ^2 test or Fisher's exact test to compare categorical data was used before matching. Paired *t*-test for normally distributed data, Wilcoxon signed-rank test for data that were not normally distributed, or a McNemar's test for categorical data was used where appropriate for propensity score-matched data. A multiple logistic regression analysis with a stepwise backward selection method was performed to identify the factors affecting non-improvement of FIM-M effectiveness. All variables that were significantly different between the groups upon performing univariate analysis before and after matching were included in the regression analysis. Age, LOS, days from stroke onset to admission in rehabilitation wards, FIM-M score at admission, epilepsy, number of drugs at admission, and Alb were included in the regression analysis. Multicollinearity among factors was confirmed using the variance inflation factor. In addition, a multiple logistic regression analysis with a stepwise backward selection method was performed to identify the factors affecting polypharmacy. All variables between the groups assessed during univariate analysis were included in the regression analysis. The Kruskal-Wallis test was used to analyze the differences among eight groups stratified based on each drug used and performed multiple comparisons using the Steel-Dwass test. Results are presented as the mean ± standard deviation (SD). $P < 0.05$ was considered statistically significant. All statistical analyses were performed using JMP® Pro (Version 12, SAS Institute Inc., Cary, NC, USA).

3. Result

3.1. Participants

Among 719 individuals screened, 509 were excluded because of propensity score matching. A total of 210 stroke participants