Drug-related problems among community-dwelling elderly with ischemic stroke in China

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Abstract

Background. Ischemic stroke incidence is increasing amongst elderly patients in China; this is closely associated with drug-related problems (DRPs).

Objectives. To evaluate the influencing factors of DRPs among elderly patients with a history of ischemic stroke in the Chinese community and the role clinical pharmacists play in providing solutions.

Materials and methods. This study was conducted in 2 community health service centers in Putuo District, Shanghai, China, between December 2018 and June 2019. Demographics and clinical characteristics of the 130 selected patients were collected. Drug-related problems were classified using the Pharmaceutical Care Network Europe (PCNE)-DRP V8.03 classification system. The number, types, causes, interventions, and status of DRPs were then analyzed.

Results. The average number of DRPs per patient was 1.3, corresponding to 256 causes. "Treatment effectiveness P1" was identified as the most common problem (75.0%). The main causes were "drug selection C1" (33.2%) and "patient-related C7" (30.9%). Antihypertensive drugs, statins, aspirin, and Chinese patent medicines were the top 4 drugs for DRPs. Age, unintentional medication discrepancy and medication compliance were independent predictors of DRPs. Pharmacists provided 339 interventions, mainly "at drug level I3" (38.9%) and "at patient level I2" (30.7%). Most of the interventions (85.5%) were accepted by the patients and 65.9% of the problems were solved.

Conclusions. The number, types and etiology of DRPs in elderly patients with ischemic stroke in our community are diverse and treatment effectiveness is the main cause of their occurrence. Clinical pharmacists play an important role in providing interventions for major causes of DRPs.

Key words: community, ischemic stroke, drug-related problem, treatment effectiveness, clinical pharmacists

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Background

Chronic diseases have become the main cause of death for the Chinese elderly, with stroke identified as the leading cause.[1,2] Stroke can be divided into ischemic stroke and hemorrhagic stroke, with the former accounting for about 70% of strokes.[3] Ischemic stroke patients have a high rate of recurrence, mortality and disability. Secondary prevention can effectively reduce the recurrence and mortality. Effective secondary prevention strategies include dietary modification, exercise, as well as the use of aspirin, statins and antihypertensive agents.[4,5] However, it has been reported that few follow-up patients with ischemic stroke present good compliance with secondary prevention for 1 year after discharge from hospital, and only 1/2 of the patients adhere to secondary prevention medication.[6,7]

Quality of life has also been researched in relation to ischemic attacks. Hohmann et al. evaluated the impact of pharmaceutical care on health-related quality of life in patients after a transient ischemic attack or ischemic stroke.[8] In addition, ischemic stroke and problems related to drug use, selection and dose, duration of treatment, and results of follow-up of drug use were also examined.[9] In the study by Hohmann et al., a 61-year-old patient was diagnosed with acute ischemic stroke due to sudden numbness and thrombolysis in the right upper extremity, and was hospitalized in the stroke unit. This case was evaluated according to the Simple Object Access Protocol (SOAP) .[10] In a review by Poels et al., the relationship between the use of immune checkpoint inhibitors and atherosclerotic cardiovascular disease was analyzed. It has been stated that the incidence of atherosclerotic cardiovascular disease increases in pathologies such as cardiac problems, ischemic stroke and coronary artery disease due to the use of immune checkpoint inhibitors.[11] In a randomized controlled study, parameters of patients with ischemic attack and stroke who received pharmacist intervention were compared. The intervention consisted of a focused drug review, motivational interview, and 3 follow-up phone calls. Clinical outcomes were reported as cardiac death, ischemic stroke or acute myocardial infarction.[12]

In recent years, DRPs in the elderly have been the focus of research in China. In one study, possible DRPs were followed up for 1 year in 184 elderly patients hospitalized in the geriatric clinic. The percentage of elderly patients who had problems related to at least 1 drug was determined as 34.5%. It was observed that the most important reason for potential DRPs was drug selection.[13] In another study, 291,944 drug prescriptions given to 10,643 patients were examined and the rate per patient according to the drugs used was reported as 3548 DRPs. The authors reported that noteworthy problems were related to treatment efficacy (39.9%) and drug doses (47.0%).[14] In yet another study, data of elderly patients over 60 years of age who were using at least 5 medications were compared, and it was stated that DRP was caused by economic reasons and deficiencies related to the correct drug protocols.[15] In a study comparing systemic blood pressure values, a total of 525 DRPs were detected. It was reported that the efficacy of treatment in the detected problems was resolved with drug changes (48.76%). More than 90% of the patients accepted these interventions.[16] Additionally, the elderly patients often take multiple medications and have more comorbidities, which can lead to DRPs.[17] Pharmacological databases from different provinces in China were compared. Patients over 64 years of age have the highest mortality rates, according to the databases. When the death rates were evaluated in terms of gender, the rate was higher in men than in women.[18] More specifically, in studies related to DRPs, problems in ambulatory patients,[19] neurological problems,[20] respiratory problems, and cardiac problems have been reported.[21,22]

A drug-related problem (DRP) is defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.[23] Many studies showed that DRPs can increase morbidity, length of hospitalization, mortality and medical expenditures, and cause a heavy burden on patients and society.[24–26]

The majority of previous studies on DRPs for patients with ischemic stroke concerned patients in the acute phase of ischemic stroke treated in a hospital. As a member of the multidisciplinary care team (MDT), the pharmacist participated in the treatment process from admission to discharge, and there were 0.32–1.8 DRPs on average. The acceptance rate of pharmacist's recommendations for doctors and patients reaches 89–94%.[27–29] However, research on DRPs in patients with a history of ischemic stroke in the community was seldom reported. The authors stated that the elderly with chronic diseases in the community generally were taking many types of medications (more than 5 types). The medication compliance was poor, and multiple referrals between clinics led to problems, such as repeated medications.[17,30] After receiving acute treatment in hospitals, patients who have had an ischemic stroke usually receive drug therapy in the community. Currently, they are out of the supervision of the MDT. Therefore, it is very important to investigate the DRPs for patients in the community with a history of ischemic stroke, as well as the intervention effect of clinical pharmacists on DRPs.

Objectives

The primary objective of the study was to evaluate DRPs and analyze the factors influencing them among Chinese community-dwelling elderly who have had an ischemic stroke. The secondary objective was to assess the interventions provided by clinical pharmacists.

Materials and methods

Study design

Data on drug-related problems among community-dwelling elderly who have had an ischemic stroke were prospectively collected from December 2018 to June 2019. The research subjects were elderly who have had an ischemic stroke and were treated at either Cao Yang Community Health Service Center or Gan Quan Community Health Service Center. Both institutions are class 1 hospitals located in Putuo District, Shanghai, China. The Health Service Centers have 6 community health service stations and nursing homes, covering more than 220,000 citizens. The study was conducted by a pharmacist team from Shanghai Tongji Hospital, China, with support from the 2 Health Service Centers. The study was approved by the Medical Ethics Committee of Shanghai Tongji Hospital, Tongji University School of Medicine (Shanghai Tongji Hospital Ethics Committee, approval No. 2018-055). The study was carried out in accordance with the Declaration of Helsinki. All enrolled patients signed an informed consent form.

The inclusion criteria were: 1) age ≥65 years; 2) history of ischemic stroke; and 3) regular (>28 days) taking of more than 5 drugs. Exclusion criteria were: 1) severe or end-stage disease; 2) mental disorder or severe cognitive dysfunction; or 3) inability to complete the questionnaire.

Data collection

A total of 8 general practitioners from the 2 Health Service Centers received the training to assist in the collection of data. There were 6 clinical pharmacists who received different training, including the Pharmaceutical Care Network Europe-drug-related problem (PCNE-DRP) classification system, medication therapy management for ischemic stroke and inappropriate medications evaluation for older adults in China. Among them, 3 were senior clinical pharmacists (with more than 5 years of experience and a clinical pharmacist qualification certificate) and 3 were junior clinical pharmacists (with less than 2 years of experience). Patient demographics and clinical information were collected using one-to-one interviews, patient medical records and hospital information systems. Patient medication compliance was evaluated according to the 8-item Morisky Medication Adherence Scale (MMAS-8 ≥ 6 means high medication compliance, MMAS-8 < 6 means low medication compliance).

PCNE-DRP classification

Drug instructions, clinical guidelines and drug databases, such as UpToDate (https://www.wolterskluwer.com/en/solutions/uptodate) and Micromedex (https://www.micromedexsolutions.com), were used to identify DRPs and propose interventions. Drug-related problems were classified according to the PCNE-DRP V8.03 classification system. This system has 5 primary domains, namely Problems (P), Causes (C), Planned Interventions (I), Intervention Acceptance (A), and Status of the DRP (O). The implementation plan is shown in Fig. 1. Drug-related problems were investigated and classified by a clinical pharmacist, reviewed by a senior clinical pharmacist, and then re-investigated and reclassified by another senior clinical pharmacist to reach a consensus. If there was a variation in classification, the final decision would be determined through group discussion.

Statistical analyses

A patient may have multiple medication problems, and each problem can have more than 1 cause and can lead to more interventions. As a result, statistical analyses were carried out separately at patient and drug level. Data were analyzed with IBM SPSS software v. 20.0 (IBM Corp., Armonk, USA). Categorical variables were described as frequencies or percentages, and continuous variables were described as mean ± standard deviation (M ±SD) if the data passed the normal distribution test. Medians and quartiles (quartile 1 (Q1), quartile 3 (Q3)) were used for skewed data.

The incidence of DRPs with various influencing factors were analyzed using binary logistic regression. All the reported variables were independent. For all continuous variables greater than 0, the Box–Tidwell test was conducted to check the linear relationship between explanatory variables and the logit of the response variables. For all interaction variables, p-value > 0.05/22 = 0.0023 is considered a linear relationship. The absence of multicollinearity among independent variables was checked using linear regression. For all variables, the tolerance was >0.1 and the variance inflation factor (VIF) was <10. No multicollinearity was found. Studentized residuals after regression were used to check the assumption of the lack of strong influential outliers. Four cases had higher studentized residuals and these cases were checked and determined to be reasonable. Therefore, those cases were included in the regression. Basic assumptions for conducting the logistic regression were met.

The binary logistic regression used the "Forward LP" method. The likelihood ratio test (LR test) was used to evaluate whether the calculated model with added variables was statistically significant. The Hosmer–Lemeshow test and Nagelkerke's R^2 were used to check the goodness-of-fit. The Wald coefficient test was conducted for each regression coefficient.

Results

Baseline characteristics

As shown in Fig. 1, a total of 134 (considering that contact with 2 was lost and 2 died) elderly patients who had

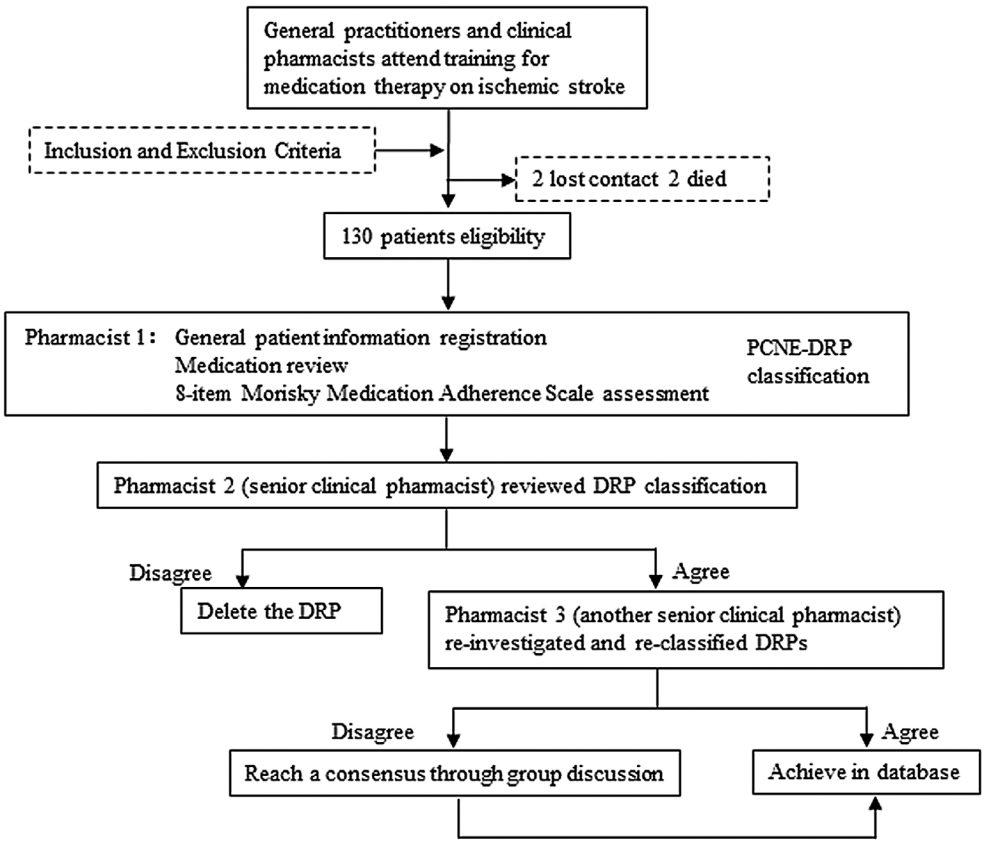

Fig. 1. Flowchart of patient enrollment and drug-related problems classification

PCNE-DRP – Pharmaceutical Care Network Europe-drug-related problem.

ischemic stroke were initially recruited. Of these, contact with 2 patients was lost and 2 patients died, and therefore 130 patients were enrolled. The clinical characteristics of the enrolled patients were shown in Table 1. The median age of the subjects (Q1, Q3) was 76.5 years (Q1, Q3: 70, 83) and 54.6% (71/130) were male. Of the subjects, 25.4% (33/130) had a history of drug allergy and the average body mass index (BMI) was 23.7 ±3.6 kg/m^2. There were 9.2% (12/130) current smokers, 15.4% (20/130) current drinkers, 69.2% (90/130) were married and lived with family, and 16.9% (22/130) were educated at primary school or below. The most common comorbidities were hypertension (86.9%, 113/130), atrial fibrillation or coronary heart disease (69.2%, 90/130), hyperlipidemia (57.7%, 75/130), skeletal diseases (49.2%, 64/130), and sleep disorders (46.9%, 61/130). The median (Q1, Q3) number of daily prescription drug kinds was 7 (Q1, Q3: 6, 9), mean daily intake of oral drugs was 15 tablets (Q1, Q3: 8, 23), and mean daily intake of oral dietary supplements was 0 tables (Q1, Q3: 0, 1). Of the patients, 26.9% (35/130) had unintentional medication discrepancies due to referrals between clinics. The median points of MMAS-8 were 5.5 (Q1, Q3: 3.5, 7).

Indentification of drug-related problems

As shown in Table 2, all 130 patients had DRP reported in their files. A total of 164 DRPs were found, averaging 1.3 per patient. Of these, 75.0% (123/164) were related to "treatment effectiveness P1", 12.8% (21/164) to "treatment safety P2" and 12.2% (20/164) were related to "other problems P3". There were 256 causes, and the top 3 were "drug selection C1" (33.2%, 85/256), "patient related C7" (30.9%, 79/256) and "other C8" (21.9%, 56/256). The pharmacists provided 339 planned interventions, with an average of 2.1 for each DRP. Interventions were mainly made "at drug level I3" (38.9%, 132/339), followed by "patient level I2" (30.7%, 104/339) and "prescriber level I1" (18.6%, 63/339). The top 3 drugs associated with DRPs were antihypertensive drugs (22.0%, 36/164), statins (18.9%, 31/164) and aspirins (15.9%, 26/164), which accounted for more than 1/2 of all DRPs. The 4th-ranked drugs associated with DRPs were Chinese patent medicines (7.3%, 12/164). The distribution of the causes for these 4 types of DRPs is shown in Table 3. The most common cause of antihypertensive DRPs was "no or inappropriate outcome monitoring C8.1", while the most common cause of aspirin DRPs was "patient uses/takes less drug than prescribed or does not take the drug at all C7.1". Both C8.1 and C7.1 were the main causes of statin DRPs. The main cause of Chinese patent medicine DRPs was "dosage regimen not frequent enough C3.3".

Analysis of factors associated with the incidence of drug-related problems

The regression coefficient, Wald test, p-value, and odds ratio (OR) values are listed in Table 4. The χ^2 for LR test was 11.688, degrees of freedom (df) was 3, and the p-value

Table 1. Demographics and clinical characteristics of participants (n = 130)

Characteristics		Value
Age, median (Q1, Q3) [years]		76.5 (70, 83)
Gender, male, n (%)		71 (54.6)
Drug allergy history, n (%)		33 (25.4)
BMI[a], M ±SD [kg/m^2]		23.7 ±3.6
Smoking status, n (%)	current smoker	12 (9.2)
	ex-smoker	13 (1.0)
	non smoker	105 (80.8)
Drinking status, n (%)	current drinker	20 (15.4)
	ex-drinker	16 (12.3)
	non drinker	94 (72.3)
Living status, n (%)	married and living with family	90 (69.2)
	unmarried/divorced/widowed and living alone	11 (8.5)
	unmarried/divorced/widowed and living with family	29 (22.3)
Education level, n (%)	primary school or below	22 (16.9)
	junior high school and above	108 (83.1)
Comorbidities, median (Q1, Q3), n		6 (5, 8)
Comorbidity, n (%)	hypertension	113 (86.9)
	atrial fibrillation or coronary heart disease	90 (69.2)
	hyperlipidemia	75 (57.7)
	skeletal disease	64 (49.2)
	sleep disorder	61 (46.9)
	diabetes	58 (44.6)
	digestive disease	56 (43.1)
	urinary disease	47 (36.2)
	renal disease	31 (23.8)
	depressive and anxiety neurosis	20 (15.4)
	tumor	17 (13.1)
	infectious disease	16 (12.3)
	COPD	13 (10.0)
	blood disease	9 (6.9)
	Parkinson's disease	2 (1.5)
	others	39 (30.0)
Daily prescription drug kinds, median (Q1, Q3), n		7 (6, 9)
Daily oral drugs, median (Q1, Q3), number of tablets		15 (8, 23)
Daily oral dietary supplements, median (Q1, Q3), number of tablets		0 (0, 1)
Unintentional medication discrepancies due to referral[b], n (%)		35 (26.9)
MMAS-8 score, median (Q1, Q3)		5.5 (3.5, 7)

M ±SD – mean ± standard deviation; BMI – body mass index; COPD – chronic obstructive pulmonary disease; MMAS-8 – 8-item Morisky Medication Adherence Scale; Q1 – 1st quartile; Q3 – 3rd quartile. Gender, drug allergy history, smoking status, drinking status, living status, education level, comorbidity, and unintentional medication discrepancies due to referral were categorical variables described as percentages. Age, BMI, comorbidities, daily prescription drug kinds, daily oral drugs, daily oral dietary supplements, and MMAS-8 score were continuous variables described as M ±SD, or medians and quartiles (Q1, Q3, as appropriate). [a] Obesity: BMI ≥ 28 kg/m^2; [b] unintentional medication discrepancies due to referral: number of patients have unintentional medication discrepancies between self-reported use of prescribed drugs and the medication record due to referrals between clinics; MMAS-8 ≥ 6 means high medication compliance, MMAS-8 < 6 means low medication compliance.

was 0 (<0.05). The Nagelkerke's R^2 of the model was 0.324, which shows a good fit. The Hosmer–Lemeshow test was conducted and the χ^2 was 11.688, and p-value of the Hosmer–Lemeshow test was 0.166 (greater than 0.05), meant that Hosmer–Lemeshow goodness of fit test result was statistically significant. The model can predict DRP incidence with 79.2% accuracy, as shown in Table 5.

Multivariate binary logistic analysis showed that patients' age, unintentional medication discrepancy and medication compliance were significantly correlated to DRPs. As shown

Table 2. Distribution of the types, causes and interventions for drug-related problems according to the PCNE-DRP classification V8.03

Domain	Code	Details	n	%
Types of problems	P1	treatment effectiveness	123	75.0
	P1.1	no effect of drug treatment	6	3.7
	P1.2	effect of drug treatment not optimal	95	57.9
	P1.3	untreated symptoms or indication	22	13.4
	P2	treatment safety	21	12.8
	P2.1	adverse drug event (possibly) occurring	21	12.8
	P3	other	20	12.2
	P3.1	problem with cost-effectiveness of the treatment	5	3.0
	P3.2	unnecessary drug treatment	8	4.9
	P3.3	unclear problem/complaint	7	4.3
Prescribing and drug selection-related causes	C1	drug selection	85	33.2
	C1.1	inappropriate drug according to guidelines/formulary	6	2.3
	C1.2	inappropriate drug (within guidelines but otherwise contraindicated)	11	4.3
	C1.3	no indication for drug	18	7.0
	C1.5	inappropriate duplication of therapeutic group or active ingredient	3	1.2
	C1.6	no or incomplete drug treatment in spite of existing indication	29	11.3
	C1.7	too many drugs prescribed for indication	18	7.0
	C2	drug form	1	0.4
	C2.1	inappropriate drug form (for this patient)	1	0.4
	C3	dose selection	28	10.9
	C3.1	drug dose too low	10	3.9
	C3.2	drug dose too high	5	2.0
	C3.3	dosage regimen not frequent enough	12	4.7
	C3.4	dosage regimen too frequent	1	0.4
	C4	treatment duration	4	1.6
	C4.1	duration of treatment too short	1	0.4
	C4.2	duration of treatment too long	3	1.2
Drug use-related causes	C6	drug use process	3	1.2
	C6.1	inappropriate timing of administration or dosing intervals	2	0.8
	C6.3	drug over-administered	1	0.4
	C7	patient-related	79	30.9
	C7.1	patient uses/takes less drug than prescribed or does not take the drug at all	31	12.1
	C7.2	patient uses/takes more drug than prescribed	3	1.2
	C7.3	patient abuses drug (unregulated overuse)	4	1.6
	C7.4	patient uses unnecessary drug	5	2.0
	C7.5	patient takes food that interacts	3	1.2
	C7.6	patient stores drug inappropriately	1	0.4
	C7.7	inappropriate timing or dosing intervals	17	6.6
	C7.9	patient unable to use drug/form as directed	15	5.9
	C8	other	56	21.9
	C8.1	no or inappropriate outcome monitoring (including TDM)	49	19.1
	C8.2	other cause	5	2.0
	C8.3	no obvious cause	2	0.8
Planned interventions	I0	no intervention	4	1.2
	I0.1	no intervention	4	1.2
	I1	at prescriber level	63	18.6
	I1.1	prescriber informed only	1	0.3
	I1.2	prescriber asked for information	5	1.5
	I1.3	intervention proposed to prescriber	56	16.5
	I1.4	intervention discussed with prescriber	1	0.3
	I2	at patient level	104	30.7
	I2.1	patient (drug) counselling	64	18.9
	I2.3	patient referred to prescriber	40	11.8
	I3	at drug level	132	38.9
	I3.1	drug changed to…	19	5.6
	I3.2	dosage changed to…	27	8.0
	I3.3	formulation changed to…	1	0.3
	I3.4	instructions for use changed to…	24	7.1
	I3.5	drug paused or stopped	31	9.1
	I3.6	drug started	30	8.8
	I4	other intervention or activity	36	10.6
	I4.1	other intervention	29	8.6
	I4.2	side effect reported to authorities	7	2.1

P – problems; C – causes; I – planned interventions; PCNE-DRP – Pharmaceutical Care Network Europe-drug-related problem; TDM – therapeutic drug monitoring. All items in the table were categorical variables described as percentages.

Table 3. Top 4 drug classes causing drug-related problems

Domain	Antihypertensive drugs		Statins		Aspirins		Chinese patent medicine	
	details	n	details	n	details	n	details	n
Types of problems	total	36	total	31	total	26	total	12
	P1.2 Effect of drug treatment not optimal	27	P1.1 No effect of drug treatment	2	P1.1 No effect of drug treatment	1	P1.2 Effect of drug treatment not optimal	7
	P2.1 Adverse drug event (possibly) occurring	6	P1.2 Effect of drug treatment not optimal	20	P1.2 Effect of drug treatment not optimal	14	P1.3 Untreated symptoms or indication	2
	P3.3 Unclear problem/ complaint	3	P1.3 Untreated symptoms or indication	1	P1.3 Untreated symptoms or indication	2	P2.1 Adverse drug event (possibly) occurring	1
			P2.1 Adverse drug event (possibly) occurring	2	P2.1 Adverse drug event (possibly) occurring	7	P3.2 Unnecessary drug treatment	2
			P3.1 Problem with cost-effectiveness of the treatment	2	P3.3 Unclear problem/ complaint	2		
			P3.2 Unnecessary drug treatment	1				
			P3.3 Unclear problem/ complaint	3				
Major causes	C8.1 No or inappropriate outcome monitoring (incl. TDM)	17	C7.1 Patient uses/takes less drug than prescribed or does not take the drug at all	9	C7.1 Patient uses/takes less drug than prescribed or does not take the drug at all	9	C3.3 Dosage regimen not frequent enough	3
	C1.6 No or incomplete drug treatment in spite of existing indication	6	C8.1 No or inappropriate outcome monitoring (incl. TDM)	8	C7.7 Inappropriate timing or dosing intervals	6	C1.7 Too many drugs prescribed for indication	2
	C7.1 Patient uses/takes less drug than prescribed or does not take the drug at all	5	C1.6 No or incomplete drug treatment in spite of existing indication	6	C1.6 No or incomplete drug treatment in spite of existing indication	4	C7.1 Patient uses/takes less drug than prescribed or does not take the drug at all	2
	C1.2 Inappropriate drug (within guidelines but otherwise contraindicated)	4	C7.9 Patient unable to use drug/form as directed	5	C1.2 Inappropriate drug (within guidelines but otherwise contraindicated)	3		

P – problems; C – causes; TDM – therapeutic drug monitoring. All items in the table were categorical variables counted in numbers.

Table 4. Forward stepwise regression for the influencing factors of DRPs

Variables	Regression coefficient	Wald χ^2	p-value	OR (95% CI)
Age	–0.061	4.528	0.033	0.941 (0.889–0.995)
Unintentional medication discrepancy	1.746	6.797	0.009	5.734 (1.543–21.311)
Medication compliance	–0.428	14.520	0.000	0.652 (0.523–0.812)
Constant	7.449	9.232	0.002	1718.704 (–)

OR – odds ratio; DRPs – drug-related problems; 95% CI – 95% confidence interval. A value of $p < 0.05$ is considered statistically significant. The Nagelkerke's R^2 of the model was 0.324. Age, unintentional medication discrepancy and medication compliance were influencing factors ($p < 0.05$) of DRPs obtained using binary logistic regression analysis.

in Table 4, OR of age was 0.941, which means that age had only little effect on the incidence of DRPs. Medication compliance was a protective factor (less DRP risk). Unintentional medication discrepancy was more likely to cause DRPs, since the OR of unintentional medication discrepancy was 5.734.

Acceptance of interventions and the status of DRPs

As shown in Table 6, a total of 85.5% (290/339) of the interventions were accepted, 66.1% (224/339) received interventions were implemented completely, and 65.9% ((81+27)/164) drug-related problems were partially or completely resolved.

Discussion

To the best of our knowledge, this is the first prospective study on DRPs in Chinese community-dwelling elderly who have had an ischemic stroke. We found that DRPs were common among elderly ischemic stroke patients

Table 5. Predicted correct percentage of the DRP incidence model

Observed		Predicted DRPs		Percentage correct (%)
		no	yes	
Observed DRP	no	29	16	64.4
	yes	11	74	87.1
Overall percentage		–	–	79.2

DRPs – drug-related problems.

Table 6. Acceptance of interventions and the outcomes of drug-related problem

Domain	Code	Detailed	n	%
Intervention accepted	A1	Total	290	85.5
	A1.1	intervention accepted and fully implemented	224	66.1
	A1.2	intervention accepted, partially implemented	24	7.1
	A1.3	intervention accepted but not implemented	14	4.1
	A1.4	intervention accepted, implementation unknown	28	8.3
Intervention not accepted	A2	total	5	1.5
	A2.1	intervention not accepted: not feasible	2	0.6
	A2.2	intervention not accepted: no patient consent	3	0.9
Other	A3	total	44	13.0
	A3.1	intervention proposed, acceptance unknown	40	11.8
	A3.2	intervention not proposed	4	1.2
Not known	O0	total	47	28.7
	O0.1	problem status unknown	47	28.7
Solved	O1	total	81	49.4
	O1.1	problem completely solved	81	49.4
Partially solved	O2	total	27	16.5
	O2.1	problem partially solved	27	16.5
Not solved	O3	total	9	5.5
	O3.1	problem not solved, lack of patient cooperation	3	1.8
	O3.3	problem not solved, intervention not effective	3	1.8
	O3.4	no need or possibility to solve problem	3	1.8

A – intervention acceptance; O – status of the drug-related problem (DRP). All items in the table were categorical variables described as percentages.

in the community, since 65.4% of patients had at least 1 DRP. The average incidence of DRPs per patient was relatively high (1.3) compared with previous studies. One study in Germany found the DRP incidence of 1.8 per person among ischemic stroke inpatients categorized by the hospital setting.[27] Another study identified the DRP incidence of 1.04 per person among hospitalized stroke patients using the Hepler–Strand classification,[28] and another identified the DRP rate of 0.32 among hospitalized ischemic stroke patients using the PCNE-DRP V8.0 classification system.[29] The differences in DRP may be due to the classification system utilized.

Chen et al. reported that the mean DRP rate of ischemic stroke patients hospitalized in China was 0.32. They stated that DRP rates were high, especially in patients with kidney failure (0.91) and liver failure (0.65). The authors found that drug selection and treatment safety were the 2 main problems encountered the most frequently. They reported that proton pump inhibitors, followed by cerebrovascular/nootropics and sedative-hypnotics were associated with DRPs, respectively (in this sequence of decreasing frequency). They also observed that the most common type of DRPs was "treatment safety P2" (60.2%),[29] likely because inpatients were monitored by MDT. In inpatients, it was easier to monitor the efficacy of the drug, and the potential safety hazards of the drug were less understood. Additionally, hospitalized patients were generally in the acute phase of ischemic stroke. There were numerous types of treatment drugs in the acute phase for hospitalized patients, such as the use of antibiotics and proton pump inhibitors, larger drug doses and multiple drug delivery modes. Furthermore, the use of injections also increased the risk of adverse drug events. Similarly, Hohmann et al. found problems related to DRPs in 105 patients (67.7%). They found the ratio of DRPs per patient to be 1.8 ±2.0. They stated that the main criteria related to DRPs were

drug type, indication and dosage.[27] Harris et al. conducted an evaluation of the Pharmacists Act on Care Transitions in Stroke service. As in other studies, correct drug use, dosage, treatment duration, and dispensing, as well as drug use parameters were evaluated. In a study in which 27 patients were evaluated, they detected 30 DRPs.[9] Apart from the DRPs in people who have had ischemic strokes, researchers have also examined the clinical causes of ischemic strokes. In a study that prospectively examined the effects of blood pressure on stroke in China, they observed that pulse pressure and mean arterial pressure were indicative criteria for stroke. It was also stated that mean arterial pressure is a more important criterion than pulse pressure in terms of stroke. They also found that blood pressure was slightly lower in patients with hypertension.[31] Tang et al. suggested that lobar microhemorrhages in the brain may affect the outcome of poststroke depression. It has been stated that lobar microhemorrhages in the brain are an important factor in the clinical course of depression in Chinese stroke patients.[32]

In this study, among all the DRPs in elderly patients in the community who have had an ischemic stroke, "drug selection C1" (33.2%) and "patient related C7" (30.9%) were the 2 main causes. For example, aspirin or statins in the secondary prevention strategies for ischemic stroke were not taken consistently by patients or the way of taking them was wrong. Patients increased or decreased antihypertensive drugs doses without pharmacist instruction. Some drugs used for alleviating symptoms were taken for a long time. Patients should stop taking those drugs according to pharmacist's instruction. However, in fact some patients did not stop taking since they liked those drugs. Correspondingly, pharmacists put forward suggestions for interventions mainly at the drug level (38.9%) and the patient level (30.7%). Based on these findings, the drugs most commonly associated with DRPs were antihypertensive drugs, followed by statins, aspirin and Chinese patent drugs. The main problem with antihypertensive drugs was that patients had poor blood pressure control. Some patients followed the regimen continuously when they were discharged from hospital. The regimen was not adjusted in time when the efficacy was poor or adverse reactions occurred. At the same time, some patients increased or decreased the dosage by themselves. Aspirin DRPs were mostly due to incorrect usage and dosage. For example, aspirin enteric-coated tablets were not taken on an empty stomach. Sometimes, the frequency of every day administration was automatically changed to every other day by patients since some patients were afraid of side effects. There were numerous statin-related DRPs, and a number of patients did were not taking statins every day. Some thought that the treatment was finished after discharge, some thought that their blood lipids were not high and there was no indication for statin use, and some stopped taking the medication or reduced its dose due to the fear of possible adverse effects.

In contrast with previous studies,[27–29] we found that the proportion of Chinese patent medicine DRPs (7.3%) was not low, which may be related to the preference of the Chinese elderly for selecting Chinese patent medicines. A considerable number of patients believed that Chinese patent medicines had less side effects. They tended to use *Ginkgo biloba* preparations instead of aspirin and take Danshen tablets in the long term. This study also showed that the specific causes for Chinese patent medicine DRPs were related to the inconsistent dosage or frequency of administration. Sometimes, drug safety of the Chinese patent medicines was not fully clarified by drug instructions, so patients, especially the older ones, used these drugs at will. In this case, DRPs such as potential drug–drug interactions and adverse reactions occurred frequently.

Patient's age, unintentional medication discrepancy and medication compliance were independent predictors of DRPs. Unintentional medication discrepancy was a risk factor that caused DRPs. Such discrepancies were usually caused by referral between different hospitals. Pharmacists can remind patients of drug change caused by referral to reduce DRPs.

The high rates of intervention acceptance (85.5%) and resolved problems (65.9%) were consistent with other study of in-hospital stroke patients.[13–15] This indicated that the community and home pharmaceutical care led by clinical pharmacists could be fully trusted by patients. The full-course pharmaceutical care model (hospital–community–home) is worth promoting.

This study may have 2 potential effects. Elderly ischemic stroke patients in the community could fully understand and improve compliance with the secondary prevention strategies for ischemic stroke thanks to patient explanations and targeted medication education by clinical pharmacists. Extending pharmaceutical services provided by clinical pharmacists from hospital to community and even the patient's home is worthy of reference by peers.

Limitations

The sample size was small and there might be deviations in the results. Moreover, no control group was set, so we were unable to compare the influence with or without clinical pharmacists on DRPs among elderly ischemic stroke patients in Chinese communities. The economic aspects of drugs were not investigated.

Conclusions

This study indicates that DRPs are very common in elderly ischemic stroke patients in Chinese communities, since 2/3 (65.4%) of the study subjects had at least 1 DRP. The average incidence of 1.3 DRPs per patient is relatively high in comparison to previous research. The major

type of problem was "treatment effectiveness P1" (75%). The rates of intervention acceptance (85.5%) and solved problems (65.9%) are quite high. The number of DRPs was increased due to unintentional medication discrepancy due to referral. Meanwhile, patients' medication compliance can help decrease the DRPs.

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