



Evidence-based summary for the safety of multiple medication in elderly patients with ischemic stroke

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Background: To retrieve, analyze, and summarize the relevant evidence of home-based medications use for stroke patients, so as to provide evidence for safe home-based medication of elderly patients with ischemic stroke.

Methods: We performed a search in the databases of *British Medical Journal (BMJ)* Best Practice, UpToDate, Joanna Briggs Institute (JBI) Evidence-based Health Care Center Library, Cochrane Library, PubMed, China National Knowledge Infrastructure (CNKI), Wanfang Knowledge Data Service Platform, and others, according to the evidence pyramid model. We retrieved all evidence on the safety of home-based multiple medications use in elderly patients with ischemic stroke, including clinical decision-making, expert consensus, guidelines, systematic reviews, and summary of evidence. The search time limit was from the establishment of the database to March 2021. The literature evaluation standard and evidence grading system of JBI Evidence-based Health Care Center were used to evaluate the quality of the literature, and to classify the extracted evidence.

Results: A total of 17 articles were included in this study, comprising 2 guidelines, 11 systematic reviews, 3 evidence summaries, and 1 expert consensus. This article summarizes the 7 best evidences from 5 aspects: drug dispensing, drug identification, medication time, prescription simplification, and self-management plan.

Conclusions: The evidence of home-based multiple medication use in elderly patients with ischemic stroke provides an evidence-based reference for ensuring the safety of medications for patients, and guides elderly patients with ischemic stroke and their caregivers by applying the best available evidence.

Keywords: Ischemic stroke; home medication; multiple medications; medication safety; evidence-based nursing

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Introduction

Cerebrovascular disease is the third leading cause of death in China, with 1.57 million deaths every year (1,2). Stroke ranks first among the causes of death and disability among the elderly in China (3,4). Among stroke patients over 60 years old, ischemic stroke accounts for 74.7% (2). Elderly patients often present with multiple chronic diseases, and multiple medications are inevitable and very common (5). According to a survey, 95.7% of Chinese elderly patients are currently taking 5 or more drugs (6). Patients with ischemic stroke often experience sequelae such as hemiplegia, poor speech, numbness, facial palsy, and their home-use medication management is variable. There are particularities in medication management at home due to sequelae or excessive medication. Sometimes, harm is caused by medication deviation during in home medication. Reports have shown that 30% of patients will be re-hospitalized within 1 year of illness due to medication deviation. Research on the causes of medication deviation has shown that 50.8% are patient-induced causes and 49.2% are iatrogenic causes (7). At present, there is no systematic home safety guidance strategy (8). Therefore, this study utilized an evidence-based method to retrieve, analyze, and summarize the evidence related to the medication safety of elderly patients with ischemic stroke taking multiple medications at home to provide a basis for their safe medication guidance. Evidence-based summary can effectively help practitioners to grasp the required evidence efficiently, and it has the characteristics of comprehensive retrieval, concise content, easy to understand and spread. Scientific home-based medication is one of the important contents of home-based nurses. The scope of application of this evidence summary is elderly ischemic stroke patients and their caregivers, in conventional medical institutions and at home.

Methods

Search strategy

A search was conducted according to the “6S” systematic retrieval strategy and evidence pyramid model (9). Chinese-language database search terms included “stroke/stroke/cerebral infarction/cerebral infarction/cerebrovascular accident/cerebrovascular disease/cerebral ischemia”, “elderly/elderly patients”, “multiple medication”, and “medication safety/medication compliance/adverse drug reaction/rehospitalization rate/missing service rate/wrong

service rate”. English-language databases were searched using the keywords “stroke/ischemic stroke/cerebrovascular accident/brain infarction/brain ischemia/brain vascular accident” “old person/old patient/elderly/aged/elderly with polypharmacy” “medication safety/medication adherence/patient compliance/medication persistence/drug compliance” and “adverse drug reaction/rehospitalization rate”. Computer searches were conducted in the databases of British Medical Journal (BMJ) Best Practice, UpToDate, Joanna Briggs Institute (JBI) Evidence-based Health Care Center Library, Cochrane Library, PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, China National Knowledge Network (CKNI), Wanfang Knowledge Data Service Platform, and other databases on the safety of medication for elderly patients with ischemic stroke with multiple drugs at home. The search time limit was from the establishment of the database to March 2021.

Literature inclusion and exclusion criteria

The clinical problem of “how to improve the safety of multi-home medication in elderly patients with ischemic stroke” was transformed into an evidence-based problem according to the patient (problem or intervention), intervention, comparison (control or comparator), and outcomes (PICO) strategy (10).

The inclusion criteria were as follows: (I) study participants were stroke patients ≥ 60 years of age who were taking multiple drugs for stroke; (II) research on the safety of multi-homed medicines; (III) outcome indicators included medication safety/medication compliance/adverse drug reactions, and so on; (IV) document type was secondary research, including clinical decision-making, guidelines, evidence summary, systematic review, and expert consensus; (V) revised or updated guidelines were included in the latest edition; and the publication languages were Chinese and English.

The exclusion criteria were as follows: (I) information was incomplete and the full text was unable to be obtained; (II) direct translation and repeated collection of guidelines; (III) documents evaluated as low quality.

Literature quality evaluation standard

The guidelines were evaluated using the Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II) (11), which was updated in 2012 in the United

Kingdom. It includes 6 dimensions and 23 items. Each item is evaluated on a scale of 1 to 7, with 7 points for full compliance and 1 point for complete non-compliance. The scoring formula for each dimension score is (actual score – lowest possible score)/(highest possible score – lowest possible score) × 100%.

The systematic review used the Assessment Tool to Assess Systematic Reviews (AMSTAR) 2017 scale updated in 2017 (12) and the corresponding evaluation standard of the Australian JBI Evidence-based Health Care Center (in 2016) (13) for evaluation. The AMSTAR 2017 scale has 16 items in total, and there are 3 evaluation options: “yes”, “no”, and “partial yes”. The JBI 2016 scale has a total of 11 items, and the evaluation options are “yes”, “no”, “unclear”, and “not applicable”.

Expert consensus was conducted using JBI’s authenticity evaluation tool for expert opinions (13) for evaluation. The scale has 6 items in total, and the evaluation options are “yes”, “no”, “unclear”, and “not applicable”.

The evidence was summarized using the Critical Appraisal for Summaries of Evidence (CASE) list (14). The scale has 10 items, and the evaluation options are “yes”, “no”, and “partially”.

Literature quality evaluation process

The included literature was independently evaluated by 2 (the guideline consisted of 4) researchers, and when they disagreed, they engaged in discussion with a third (5th) researcher to reach a final consensus. All 5 researchers in this study have undertaken systematic training in evidence-based methodology. The selection of contradictory evidence was based on the principle of “evidence-based evidence first, high-quality evidence first, and latest published evidence first” (15).

Results

Basic characteristics of the included literature

A total of 351 articles were obtained, and 17 articles were finally included, including 2 guidelines (16,17), 11 systematic reviews (18–28), 3 evidence summaries (29–31), and 1 expert consensus (32). The basic characteristics of the included literature are shown in *Table 1*.

The quality evaluation results of the included literature

Quality evaluation results of the guidelines

This article finally included 2 guidelines (16,17), and the AGREE II evaluation tool was used to evaluate the quality of the guidelines. The quality evaluation results of the guidelines are shown in *Table 2*.

Quality evaluation results of systematic reviews

This article finally included 11 systematic reviews, 3 from the Cochrane Library (18,20,21), 5 from the JBI Evidence-based Health Care Center Library (22–26), 2 PubMed (27,28), and 1 from China CNKI (19). We used AMSTAR 2017 and JBI 2016 evaluation tools for systematic evaluation quality evaluation. The results of the systematic review are shown in *Table 3*.

The results of the quality evaluation of the evidence summary

This article finally included 3 evidence summaries, 2 from the JBI Evidence-based Health Care Center Library (29,30), and 1 from UpToDate (31). The CASE checklist was used to evaluate the quality of the evidence summary. The evaluation results were as follows: the quality evaluation results of the 3 evidence summaries were consistent, all of which were evaluated as “no” for “is the retrieval method transparent and comprehensive (item 4)”, and the remaining items evaluated as “yes”.

Quality evaluation results of expert consensus

This article finally included 1 expert consensus (32), which came from the China HowNet database. The quality evaluation was conducted using JBI’s authenticity evaluation tool for expert opinions. The evaluation result was as follows: “is there any inconsistency between the proposed viewpoint and the previous literature (item 6)” was evaluated as “unclear”, and the remaining items were evaluated as “yes”.

Evidence summary and description

The 2014 version of the JBI Evidence Pre-grading and Evidence Recommendation Grade System was used to grade the included evidence. According to the different research types, the evidence level is divided into 5 levels,

Table 1 Basic characteristics of the included literature

| Included literature | Issuing time | Source of evidence | Type of evidence | Document content |
|--|--------------|---------------------------|---------------------|---|
| Stroke Foundation, Australia (16) | 2017 | <i>BMJ</i> Best Practices | Management guide | Home visits and medication management |
| Intercollegiate Stroke Working Party of the Royal College of Physicians of London (17) | 2016 | <i>BMJ</i> Best Practices | Practice guide | Reminders, follow-up, and medication management |
| Cross <i>et al.</i> (18) | 2020 | Cochrane Library | Systematic review | Education, behavioral intervention, and medication compliance |
| Chen <i>et al.</i> (19) | 2019 | CNKI | Systematic review | Prescription streamlining and medication safety |
| Rankin <i>et al.</i> (20) | 2018 | Cochrane Library | Systematic review | Drug regulation strategy and drug safety |
| Fryer <i>et al.</i> (21) | 2016 | Cochrane Library | Systematic review | Self-management and medication compliance |
| Braet <i>et al.</i> (22) | 2016 | JBI | Systematic review | Discharge intervention and readmission rate |
| Lo <i>et al.</i> (23) | 2013 | JBI | Systematic review | Self-management and stroke rehabilitation |
| Cameli <i>et al.</i> (24) | 2013 | JBI | Systematic review | Drug management strategy and drug safety |
| Godfrey <i>et al.</i> (25) | 2013 | JBI | Systematic review | Drug regulation strategy and drug safety |
| Lawrence <i>et al.</i> (26) | 2011 | JBI | Systematic review | Social intervention and secondary stroke prevention |
| Zedler <i>et al.</i> (27) | 2011 | PubMed | Systematic review | Packaging with calendar function and medication compliance |
| Kripalani <i>et al.</i> (28) | 2007 | PubMed | Systematic review | Reminders, follow-up, and medication compliance |
| Ishaque (29) | 2020 | JBI | Summary of evidence | Reminders, follow-up, and medication compliance |
| Li <i>et al.</i> (30) | 2018 | JBI | Summary of evidence | Drug management strategy and drug safety |
| Rochon <i>et al.</i> (31) | 2020 | UpToDate | Summary of evidence | Optimize drug treatment and medication safety |
| Hao <i>et al.</i> (32) | 2018 | CNKI | Expert consensus | Family pharmacists and medication safety |

CKNI, China National Knowledge Infrastructure; JBI, Joanna Briggs Institute; *BMJ*, *British Medical Journal*.

Table 2 Standardized scores and evaluation results in all areas of guidelines

| Included literature | Percentage of standardized scores in each dimension (%) | | | | | |
|--|---|--------------|--|---------------------------------------|---------------------------------|---------------------------|
| | Scope and purpose | Participants | The rigor of the guideline development | Clarity of the guideline presentation | Applicability of the guidelines | Independence of the guide |
| Stroke Foundation, Australia (16) | 100 | 100 | 99 | 100 | 85 | 100 |
| Intercollegiate Stroke Working Party of the Royal College of Physicians of London (17) | 100 | 100 | 97.40 | 100 | 70.80 | 100 |

and according to the FAME principle, that is, the feasibility, suitability, clinical significance, and effectiveness of the evidence, the recommendation level is divided into A-level recommendation and B-level recommendation (33). This

study summarized the 7 best pieces of evidence from 5 aspects: drug packaging, drug identification, medication time, prescription simplification, and self-management plan. The evidence is summarized in *Table 4*.

Table 3 Standardized scores and evaluation results of the systematic reviews

| Included article | Evaluation tool [year] | Evaluation results |
|------------------------------|------------------------|--|
| Cross <i>et al.</i> (18) | AMSTAR [2017] | Item 15 is evaluated as “No” and the rest of the items are evaluated as “Yes” |
| Chen <i>et al.</i> (19) | AMSTAR [2017] | Items 2, 7, 10, 12, and 16 are evaluated as “No”; the remaining items are evaluated as “Yes” |
| Rankin <i>et al.</i> (20) | AMSTAR [2017] | Item 10 and item 12 are evaluated as “No”; the remaining items are evaluated as “Yes” |
| Fryer <i>et al.</i> (21) | AMSTAR [2017] | Item 10 and item 12 are evaluated as “No”; the remaining items are evaluated as “Yes” |
| Braet <i>et al.</i> (22) | JBI [2016] | The evaluation of each item is “Yes” |
| Lo <i>et al.</i> (23) | JBI [2016] | The evaluation of each item is “Yes” |
| Cameli <i>et al.</i> (24) | JBI [2016] | The evaluation of each item is “Yes” |
| Godfrey <i>et al.</i> (25) | JBI [2016] | The evaluation of each item is “Yes” |
| Lawrence <i>et al.</i> (26) | JBI [2016] | The evaluation of each item is “Yes” |
| Zedler <i>et al.</i> (27) | JBI [2016] | Item 9 is evaluated as “No”; all other items are evaluated as “Yes” |
| Kripalani <i>et al.</i> (28) | JBI [2016] | Item 5,8,10 is evaluated as “No”; all other items are evaluated as “Yes” |

AMSTAR, A MeaSurement Tool to Assess systematic Reviews; JBI, Joanna Briggs Institute.

Table 4 Summary of the best evidence for the safety of multidrug use at home for elderly ischemic stroke patients

| Category | Evidence content | Level of evidence | Recommended level |
|--------------------------------|--|-------------------|-------------------|
| Pharmaceutical packaging | 1. It is recommended to use blister packaging to pack a variety of drugs according to the time point (18,27-30) | I | A |
| Drug identification | 2. Differentiating drugs by enhancing the specific appearance of drugs can reduce the error rate of complex drug treatment programs (18,25,28,29) | I | A |
| Medication time | 3. Individualized medication schedule (18,28,30) | I | A |
| Simplification of prescription | 4. Continuous drug review and thorough patient education to optimize multi-drug therapy (20,24,32) | I | A |
| | 5. Simplify strategies for individual use of multiple drugs (18,19,29) | I | A |
| Self-management plan | 6. Reduce the readmission rate by setting reminders, self-monitoring, intensive consultation, motivational interviews, family therapy, senior practice nurses (specialist nurses) monthly telephone follow-up, supportive care, and dosing aids (17,18,25,26) | I | B |
| | 7. It is recommended to conduct 3 stages of self-management: 3 different stages. Stage 1: drug container with discharge label, give the drug to the patient at an appropriate time, and fully supervise the selection and administration of the drug. After 7 days, if the patient adapts, enter the second stage. Stage 2: the patient is required to take medication at an appropriate time. After 7 days without error, the patient moves on. Stage 3: the patient is fully responsible for their medication. Medicines are stored in locked cabinets. Check compliance by counting pills (18,21,23,26) | I | A |

Pharmaceutical packaging

The calendar package is used to remind patients to maintain the prescribed dosage plan. The calendar package contains the date, time, and other details. Its types include calendar pill box (CPO) and calendar blister packaging (CBP). The former is based on 1 week and the latter is based on

1 month. The medication is repackaged separately and the time of medication is affixed to visually record the patient's medication status, thereby improving patient compliance with medication (27,28). Cross *et al.* (18) posited in a systematic review on how to improve the ability of patients to take medication, that by changing the packaging, the

use of multi-compartment medicine boxes, calendar packs, automatic drug delivery devices, and other dosage aids are effective measures to increase the rate of patients taking medication. Studies by Ishaque (29) and Li *et al.* (30) have shown that placing reminders on packaging can improve patients' long-term medication compliance.

Drug identification

Kripalani *et al.* (28) summarized the intervention measures to improve patients' compliance with medication as information intervention, behavior intervention, and comprehensive intervention. Studies such as those by Godfrey *et al.* (25) and Ishaque (29) have shown that undergoing personal drug education can improve compliance with drug treatment regimens. Thus, it is advised to carry out drug-related education for patients and their caregivers, enhance the specific recognition of the appearance of drugs, and reduce the error rate of complex drug treatment programs.

Medication time

Li *et al.* (30) highlighted in their evidence summary of residential elderly medication management that it is recommended to use a standardized medication treatment form for all elderly patients, with their name and date of birth clearly printed on the back for identification. Kripalani *et al.* (28) summarized comprehensive interventions to improve patients' medication compliance, and a tailored individualized schedule was presented as 1 of the effective measures to improve patients' medication compliance. Customized medication schedules, including reminder charts and medication lists, remind patients and their caregivers of medication time and medication types like a calendar to improve patient medication safety.

Simplification of prescription

Cameli *et al.* (24) asserted that drug regulation led by pharmacists may play a role in reducing drug errors. Rankin *et al.* (20) showed in their study on how to improve the appropriate use of multiple drugs in the elderly, pharmacists and clinicians cooperate to conduct drug reviews to determine actual and potential drug adverse reactions, optimize drug prescriptions, and improve patients' drug compliance. At the same time, Chen *et al.* (19) showed that a prescription streamlining intervention can reduce the length of hospital stay. Cross *et al.* (18) and Ishaque (29) also showed that by reducing the daily dose to simplify the dosing schedule, fixed-dose combination tablets can improve

compliance with the dosing schedule. In an expert consensus of family pharmacists' service standards and pathways (32), a family pharmacist system was proposed. Family pharmacists manage the whole process of drug treatment for patients at home, conduct drug review, prescription reduction, and drug reorganization, and ensure the safety and improvement of patient medication. These measures could optimize the effect of drug treatment, reduce the patient's burden of disease costs, and improve the national health level. Further, it is recommended to perform continuous drug review and thorough patient education to optimize multi-drug therapy; use drug simplification strategies for patients who use multiple drugs and reduce unnecessary drug types, which could enhance patients' initiative in taking drugs and reduce the rate of missed doses.

Self-management plan

In the 2016 Stroke Practice Guidelines, it is recommended that a stroke discharge team be established, and regular meetings should be held to exchange information about stroke patients under their care; provide information, advice and support for stroke patients, their families, and caregivers (17). Measures such as setting reminders, self-monitoring, intensified consultations, motivational interviews, and monthly telephone follow-ups by specialist nurses have strengthened the administration time and dosage, promoted drug safety, and reduced the readmission rate (18). Lawrence *et al.* (26) pointed out that a stroke nurse specialist provided relevant education and consultation for patients and their families in the outpatient clinic. Patients regularly receive personal advice on lifestyle changes, medication compliance, and lifestyle issues. This is an effective measure to improve secondary prevention after stroke. The 2017 Stroke Management Guidelines (16) recommend that cognitively capable stroke patients and their caregivers should learn about self-management plans before they are discharged from the hospital, and receive support to participate in such plans after they return to the community or family. Intervention before discharge from the hospital was shown to more effectively reduce the readmission rate (22). Fryer *et al.* (21) and Lo *et al.* (23) have shown that the components of self-management intervention can include problem solving, goal setting, decision-making, self-monitoring, and disease response. Nursing staff can increase the patient's self-management ability through face-to-face or online communication on the internet, written materials, mailing manuals, or phone consultation. Self-management plans can improve the

functional capacity and medication compliance of stroke patients. Based on this, 3 stages of self-management are recommended. Stage 1: drug containers with discharge labels, deliver the drugs to the patient at an appropriate time, and fully supervise the selection and administration of the drugs. After 7 days, enter Stage 2 if the patient is compliant. Stage 2: ask the patient to take their medication at an appropriate time. After 7 days without error, the patient moves on. Stage 3: the patient is fully responsible for their medication. Medicines are stored in locked cabinets. Check compliance by counting pills.

Conclusions

This study strictly followed the evaluation criteria to assess the quality of evidence, combined with clinical practice, and comprehensively considered factors such as the feasibility of the evidence. However, most of the evidence included was from countries other than China. It is recommended that the cultural characteristics and medical resources of China are considered when the evidence is interpreted. According to the situation, a comprehensive analysis of elderly patients with ischemic stroke in China was conducted, and a home-based multi-medication safety management plan for elderly patients with ischemic stroke was constructed.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-453/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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