





Original article

Pattern of drug prescribed and drug related problems among hospitalized elderly patients

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Abstract: Prescribing drugs for elderly patients is not an easy task since elderly patients are frequently with comorbid conditions. In Libya, there are no guidelines for the management of medications used in elderly patients and no specialized geriatric health institutions. The aim of this study is to assess the pattern of medication use among hospitalized elderly patients in Sebha Medical Centre and the drug-related problems associated with these patterns. This report is descriptive and retrospective cross-sectional study that is conducted at Sebha Medical Center during 2021. Potential drug-related problems were assessed based on the classification of Hepler and Strand. In this study, out of 195 participants, most of the patients have been given antibiotics (92.0%). The majority of patients have been prescribed anti-gastric agents, vitamins and anti-thrombotic agents which accounted for 75.0%, 62.0% and 55.0%, respectively. To less extent, anti-hypertensive agents, analgesics and anti-hyperlipidemics were reported by 45.0%, 43.0% and 38.0%, correspondently. Almost all the patients have at least one event of drug-related problem and more than three-quarters of the patients had more than one event of drug-related problems. The highest rate was untreated indications which were reported for 77.0% then followed by drug use without indication nearly a half of the events 48.0%. To fewer extent rates were reported: “in improper drug selection”, “drug interaction” and “adverse effects” which were reported for 25.0%, 23.0% and 18.0% of the total events, respectively. Almost all elderly patients have been prescribed antibiotics, analgesics and vitamins. Drug-related problems are predominant prevalent in the clinical practice at the center. This study highlights the importance of activation of clinical pharmacist interventions at hospitals which can contribute to reducing the chance of risk of drug-related problems events among hospitalized elderly patients and ensuring rational drug prescribing in the geriatric clinical settings.

Introduction

Pharmacotherapy is one of the essential components of geriatric care and management of elderly comorbidity diseases. Several characteristics of aging can influence the medication prescribing for them and making the appropriate selection process of their medications is an uneasy task. Study report that elderly people use a substantial number of drugs between 4 - 6 drugs a day per a person. Particularly for the treatment of chronic diseases, elderly patients were found to use about three times more drugs than younger patients [1]. In Libya, the first part of the present study that has been published showed that nearly two-thirds of the patients had three to five comorbidity diseases at the same time and almost all elderly patients have polypharmacy [2]. The treatment of multiple comorbidities and symptoms of elderly patients require understand how drugs affect the aging pharmacodynamic and pharmacokinetic aspects [3].

Optimizing the treatment based on medical guidelines in presence of many comorbid conditions is not easy task since elderly patients with comorbid conditions are frequently excluded from clinical trials [4] and as a consequence the evidence coming from these studies may not be generalizable to this population [5]. Many unplanned admissions are medication related [6] and a considerable number could be prevented [7]. The geriatric population is at high risk of drug related problems (DRPs) due to the age-related pharmacokinetic and pharmacodynamic changes, chronic disease conditions and polypharmacy may make elderly people to respond differently than expected [8]. Inappropriate prescribing can cause substantial morbidity and represents a clinical and economic burden to patients and society [9]. Medication related problems have been identified as the third or fourth cause of death among the elderly and can cause disability, gait disturbance and falls [10]. Therefore, drug related problems (DRPs) are significant for the pharmaceutical care practitioner and they can occur in any phase of the medication use process. The

essential element of DRPs is the impact of the problem on the health-outcome of the pharmacotherapy. Thus, a DRP can be defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [11]. DRP originated from the Hepler and Strand [12] who defined eight problems that could result in poorer health outcomes in an attempt to categorize DRP (**Table 1**). Inappropriate prescribing is one of the major challenges face the physicians and it is a major their concern particularly in developing countries where the effective infrastructure health is often not well established. Rational drug prescribing is necessary for elder's health care since they are a vulnerable group of people because of the increased prevalence of comorbidities and poly-pharmacy [2].

Examining patterns of drug prescribing and identification of prescribing problems can contribute to drawing successful policies to improve the quality of prescribing and ensure medication safety. A previous Libyan study evaluated 106 elderly prescriptions from different community pharmacies according to Beers criteria revealed that about 15% of the total drugs prescribed are inappropriate [13]. However, there is limited data on pattern of drug prescribed to elderly hospitalized patients in Libya, therefore, the aim was to assess pattern of medication use among the hospitalized elderly patients and drug related problems associated with such pattern.

Materials and methods

This study is descriptive and retrospective cross-sectional study which was conducted at Sebha Medical Centre (SMC) located in South region of Libya in 2021. Convenient sampling technique was used to select the sample size from patient's records who fulfill the inclusion criteria were enrolled. Patient records were eligible for inclusion if the patient's age is 65 years and above. Patients with more than 24 hours of length of stay in the hospital were included. Letter of ethical clearance was obtained from the ethical review committee of Sebha University (1/2021). Permission also obtained from

SMC office for cooperation from Department of Medical Record at SMC. Two independent data collectors “senior pharmacy students” were well-trained retrieved the documentation of the medication review from the medical records. We used the standardized data extraction sheet to collect relevant information from patient medical records and data collected by trained pharmacy students using pre-tested data collection checklist. They review the medications, medical record and laboratory data to identify and address DRPs. The sheet had three main sections patient demographics, medical history and laboratory data. The following data were recorded for each patient: age, gender, body weight, family and social histories, history of

drug allergies, relevant medical and medication history, vital signs, drugs used at admission, drugs started during the hospital stay and at discharge reports, results of routine laboratory tests and the diagnosed diseases which are important for identification of drug therapy problems. Potential DRPs were assessed based on classification of Hepler and Strand [12] as shown in this study. However, failure to receive drugs category could not assessed since this study was retrospectives study. Two senior trained students of pharmacy for all medications used on the data of inclusion and documented on a standardized report form. The researchers were trained by professional a clinical pharmacist (principal investigator).

Table 1: Classification of drug related problems [12]

	Drug related problems	Description
1	Untreated indication	Does the patient have an untreated medical condition or indication which may benefit from drug therapy?
2	Drug use without indication	Is the patient taking a drug for which there is no valid indication?
3	<i>Failure to receive drugs*</i>	<i>Does the patient have a medical condition that is the result of him/her not receiving a drug</i>
4	Improper drug selection	Does the patient have a medical condition for which the incorrect drug is being taken?
5	Adverse drug reactions	Does the patient have a medical condition which is the result of an adverse drug reaction?
6	Drug interactions	Does the patient have a medical condition that is the result of a drug-drug or drug-food interaction?
7	Sub-therapeutic dosage	Does the patient have medical condition for which too small of the correct drug is being taken?
8	Over dosage	Does the patient have medical problem for which too much amount of the correct drug is being taken?

* Failure to receive drugs category could not assessed since this study was retrospectives study.

All data with prescribed medications and identification of potential DRPs by the individual researchers were reviewed, documented, categorized and entered into a data collection sheet and when necessary adjusted by the principal investigator. Each documented drug therapy was evaluated for the presence of DRPs using standard textbooks as a pathophysiologic approach applied therapeutics: The clinical use of drugs. Medscape website is also used which providing access to medical information for clinicians. The reliability and accuracy of each drug

therapy problem was assessed by supervisor clinical pharmacist.

Statistical analysis: All data from the recorded collection sheet were classified and coded, then were feed into the computer and tabulated by using Microsoft Excel and IBM. Statistical Package for the Social Sciences (SPSS-20 software) was used and analyzed. DRP were then classified according to Hepler and Stand classification (1990) as mentioned above in the introduction.

Results

Pattern of drug prescribed: As it is shown in **Table 2**, a total of 2223 prescribed drugs were dispensed for 195 elderly patients recruited in the study, corresponding to 12 drug categories. In **Table 2**, the three major groups of medications use by elderly inpatients are antibiotics (n = 179, 92.0%), anti-gastric agents (n = 146, 75.0%) and vitamins and minerals (n = 120, 62.0%). Regarding to anti-gastric agents, the highest rate was proton-pump inhibitors (PPIs) which accounted for 65.5% (n = 127) followed by metoclopramide by 29.3% (n = 57) while ranitidine accounted for 06.6% (n = 13). More than half of the patients (n = 65, 55.0%) uses antithrombotic agents and just less than half of the patients (45.0%) use anti-hypertension drugs and 43% use analgesics. Over one third of the patients use anti-hyperlipidemic drugs (38.0%), 37.0% use fluid supplements and 34.0% for diuretics. However,

less than one third (31.0%) use hematinic agents. The lowest types of drugs that use among the elderly patients are calcium supplements (19.0%) and anti-diabetics (08.0%).

Drug related problem: Regard to frequency of DRP among the elderly inpatient, as is shown in **Table 3**, more than one-third of the participants (38.0%) had 3 - 4 DRPs events. Female elderly patients have more prevalence (44.0%) compared to male patients (33.0%), followed by 29.0% of the patients had 1 - 2 DRPs. Just over one fifth of the patients held 5 - 6 DRPs. The lowest rate (n = 12, 06.0%) was reported for having more than six DRPs. Only 06.0% (n = 12) of the participants did not expose to any event of DRPs. Moreover, nearly two thirds of the participants (n = 127, 65.0%) had at least three DRPs. In general, the mean number of DRPs was 2.9 which nearly close to three events per patient.

Table 2: Pattern of drug use among Libyan participants

Drugs	Male patient	Female patient	Total
Antibiotics	97 (95%)	82 (88%)	179 (92%)
Anti-gastric agents	77 (75%)	69 (74%)	146 (75%)
Vitamins	70 (69%)	50 (54%)	120 (62%)
Anti-thrombotic agents	35 (34%)	30 (32%)	65 (55%)
Anti-hypertension agents	42 (41%)	46 (49%)	88 (45%)
Analgesics	44 (43%)	40 (43%)	84 (43%)
Anti-hyperlipidemic	36 (35%)	39 (41%)	75 (38%)
Fluid supplements	45 (44%)	27 (29%)	72 (37%)
Diuretics	35 (34%)	32 (34%)	67 (34%)
Hematinic agents	36 (35%)	25 (27%)	61 (31%)
Ca supplements	14 (04%)	18 (19%)	32 (16%)
Anti-diabetics	11 (11%)	07 (08%)	18 (09%)
Total	102 (52%)	93 (47.6%)	195

Patient may have more than one drug

Table 3: Frequency of patients who have drug-related problems

DRP	Male patient	Female patient	Total
3 - 4	34 (33%)	41 (44.0%)	75 (38%)
1 - 2	32 (31%)	24 (26.0%)	56 (29%)
5 - 6	22 (22%)	18 (19.0%)	40 (21%)
> 6	07 (07%)	05 (05.0%)	12 (06%)
00	07 (07%)	05 (05.0%)	12 (06%)
Total	102 (52%)	93 (47.6%)	195

Drug related problems: **Table 4** shows the most commonly identified DRPs. From 195 participants, there were 407 events of DRPs and nearly equal ratio between genders. The highest rate was untreated indications which was found in 155 patients (77.0%) from the total events of untreated indications (306). In this category, over one third of the events 113 (37.0%) were untreated electrolyte imbalance followed with untreated anemia in (18.3%) of untreated indication conditions. Over one tenth of untreated

conditions (n = 33, 10.7%) were diabetic patients. Minority untreated conditions reported with hypertension (n = 18, 05.8%), thrombocytopenia (05.5%), fever (03.5%) and hypotension (n = 10, 03.2%). The second highest DRP category was drug use without indication which reported in about half of the patients 48%. Prescribing of antibiotics without clearly indication was the majority which was represented by 157 patients (84.4%) of the total events (n = 186) of this category (**Table 5**).

Table 4: Drug-related problems identified from the patients

Drug-related problems	Male patients	Female patients	Total
Untreated indication	83 (81%)	68 (73%)	151 (77%)
Drug use without indication	57 (56%)	36 (39%)	93 (48%)
Improper drug selection	25 (25%)	24 (26%)	49 (25%)
Drug interaction	13 (13%)	31 (33%)	44 (23%)
Adverse reaction	11 (11%)	25 (27%)	36 (18%)
Over dosage	10 (10%)	09 (10%)	19 (10%)
Sub therapeutic dosage	07 (07%)	08 (09%)	15 (08%)
Failure to receive drugs	00 (00%)	00 (00%)	00 (00%)
Total	206 (50.6%)	20 (49.4%)	407 events

In **Table 5**, to less extent rates of cases under category of in improper drug selection (n = 54, 17.6%) was reported from the total drug related problems. Out of these 54 cases, 15 cases represent prescribing ranitidine and five cases use oral hematinic agents. Potential drug interaction cases were accounted with 54 patients (17.6%) of total DRP events included 45 cases were potential risk of bleeding due to use combination of anti-platelets agent. For category adverse effect cases, they were found to be of 12.7% (n = 39). Hyponatremia or a dry

cough (n = 15) and hypotension (n = 09) cases could be associated with angiotensin converting enzyme inhibitors and furosemide, respectively. Minority events were represented among over dosage (23, 07.5%) as using prescribing aspirin 300 mg as tablet represented seven cases or metoclopramide eight cases. Similarly, the rate of sub-therapeutic dosage was reported by 03.2% (n = 10) for instance normal doses for end stage renal failure and three cases of low doses of atorvastatin based on lipid profile data.

Table 5: Types of drug related problems associated with their causes

Drug related problem	Example	n	Details
Drug without indication	Antibiotics	157	Mostly ciprofloxacin & metronidazole
	Others	11	Tranexamic acid, diazepam & nystatin
	Total	186	
Inappropriate drug selection	Ranitidine	15	Outdate regime
	Oral hematinic agents	05	Must be replaced by blood transfusion
	Others	24	Metformin & ACE
	Total	54	
	Anemia	56	
	Hyponatremia	45	
	Hypocalcemia	34	
	Diabetes mellitus	33	
	Hypokalemia	21	

Un-treated diseases	Hypertension	18	
	Hypotension	10	
	Fever	11	
	Thrombocytopenia	17	
	CVA	09	
	Infection	06	
	Hyperkalemia	05	
	Hypernatremia	05	
	IHD	05	
	Diarrhea	05	
	Prostatic hyperplasia	04	
	Others	16	Constipation & hypercalcemia
Total	306		
Adverse effect	ACEIs	15	Causes hyponatremia or dry cough
	Furosemide	09	Causes hypotension
	Others	15	Thrombocytopenia
	Total	39	
Drugs interaction	Risk of bleeding	45	Due to more than an anti-platelet
	Others	09	Risk of bradycardia when given carvedilol with bisoprolol & digoxin
	Total	54	
Over-dose	Aspirin	07	Aspirin dose needs to be adjusted
	Metoclopramide	08	Metoclopramide needs to be decreased in dose according to GFR
	Others	08	Insulin, azithromycin & ciprofloxacin
	Total	23	
Sub-therapeutic doses	Furosemide	07	
	Atorvastatin	03	Needs to be adjusted
	Total	10	

Discussion

Evidence suggests the use of drugs in elderly people is often inappropriate partly because of the complexities of prescribing, patient, provider, and health-system factors. Antibiotic is frequently prescribed among all the hospitalized elderly patients [14]. Consumption of antibiotic by elderly population is up to 45.0% with significant rise over the past decades [15]. Accordingly, this study revealed the highest category compared with other drugs with the majority of elderly patients prescribed antibiotics. High rate of antibiotic use observed may be due to absence of standard protocols or guidelines for antibiotic use. PPIs class exerts greater acid-suppressing effect than other traditional therapies [16]. There is significant increase in use of PPIs over the last 15 years, particularly, in older population [17]. This suggests high number of drugs per a prescription led to an increased prescription of these

gastrointestinal drugs to avoid gastric irritation. In this study, nearly two-third of the patients had received PPIs during their staying. However, inappropriate PPI use is of a great concern, especially in the elderly, who are often affected by multiple comorbidity and polypharmacy. Thus, this long-term PPI among elderly can increase risk of adverse outcomes and DDIs [18]. Previously, the main inappropriate indication of PPIs is prophylaxis of gastrointestinal bleeding in low-risk patients [19]. As the use of drugs with potential gastrointestinal toxicity is associated with prescribing of various drugs, it is perhaps not surprising that PPI is associated with the polypharmacy, appropriate or inappropriate. The elderly is at a high risk of developing nutritional deficiencies due to low dietary intake or impairment in the mechanism of absorption or failure to conversion to active forms [20]. This trend of deficiency of vitamins could be

consistent with high prescribing rate of vitamins for two-third of population.

Positive correlation between dyslipidemia and heightened CVD risk [21, 22] which increases significantly with increase of age [23]. Currently, 15.0% of the population have hyperlipidemia, 35.0% with heart disease and similar rate for patients receiving antihyperlipidemics. Certain studies demonstrated that treatment with statins reduces CVD events and mortality rate with well-tolerated in elderly [24, 25]. 40.0% of elderly patients have diabetes mellitus [2]. In contrast, the patients who documented taking anti-diabetic whether oral hypoglycemic agent or insulin were low. This can be justified by the fact that diabetic inpatients are always under direct surveillance and treating. Health practitioners usually suppose patients were already taking diabetes drugs even though the medical records miss this information in the file. This inconsistency may reflect non-observance of complete recording all medical information among clinicians. Missing information of pharmacotherapy will negatively influence on patients' therapy and exposed them to DRPs and medication errors.

The elderly population is at greatest risk for DRPs due to the age-related pharmacological changes, multi-comorbidity and poly-pharmacy [8, 26]. Any symptom in patient should be considered as drug side effect until proved otherwise [27]. In this study, most patients have one DRP and every patient had average of two which is in line with other studies [28 - 30]. DRPs are associated with increased healthcare cost and hospital admission, prolonged hospital stay and reduced quality of life with increased mortality [31, 32]. The most common DRP is untreated condition account for 50.0% out of the total DRPs with prevalence rate of 75.0%. Similar trend of incidence of inappropriate treatment that required additional therapy has been reported [33] with less extent in Indian's study [34]. This high prevalence rate can be explained by high burden of comorbidity and could be illustrated that physicians are more likely focusing on major conditions and giving less attention to

minor conditions. As it was mentioned, 35.0% of the patients having infection. About half of the antimicrobial agents prescribed to hospital inpatients are considered inappropriate [35]. The inappropriate use of antibiotic contributes to emergence and spread of antimicrobial resistance [36]. For patients with hyperlipidemia and on statins are in line others [37]. It is important that elderly patients need to establish successful plan for prevention and reducing risk factors or need intensively treated of this dyslipidemia to prevent recurring of complications [38].

Drug use without indication phenomenon was stated in developing countries [39]. The unnecessary drug therapy problems frequently tend to be overlooked in polypharmacy prescribing. In Jimma University specialized hospital, polypharmacy was the only independent predictor for unnecessary drug therapy [40]. Prevalence rate of drug use without indication is more frequent than problems due to prescribing of drugs for elderly patients [41]. Drug use without indication was the second DRP occurrence among our population. Nevertheless, health practitioners are often not fully updated with their patient's actual medication use [42, 43]. Physician prescribing errors can arise from the choice of the wrong or improper drug selection when prescribing ineffective drug where more effective drug available. In this study, prescribed drugs were under improper drug selection and its prevalence rate is 25.0%. Evidence found that omeprazole is significantly more effective than ranitidine in gastritis and heartburn [44] and normalized physiological well-being [45]. Thus, older drugs tend to be less expensive and this may be factor in drug selection. Inappropriate polypharmacy occurs when patients use or prescribed more medicines than are clinically indicated [46]. Beers criteria provide evidence-based recommendations on medications that health care providers should pay attention to, as these medications are probably not the most appropriate, safest or the best choice for patients of 65 years and above [47].

In this study, 25.0% of the patients have potential DDI between their prescribed drugs during hospitalization. This is in line with studies who reported 25 - 50% clinically relevance potential DDIs in elderly patients [42, 48]. DDIs present unfavorable outcomes which causing 03% of all hospitalizations of older patients and cost health care system more than US\$ one billion [49, 50]. Concomitant administration of anticoagulant and antiplatelet therapies increases risk of bleeding [51]. COMPASS study indicated that dual antiplatelet combination therapy significantly reduces incidence of adverse CVD events. The bleeding events occurred is significantly more among the patients who treated with combination therapy [52]. It is especially difficult to obtain therapeutic benefit that outweighs the risk of bleeding from the concurrent use of antithrombotic drugs, since tendency of bleeding increases with advanced age. DDIs are more likely to happen in the elderly because they tend to use multiple medications and have altered pharmacokinetic aspects [53]. Evidence shows increasing risk of potential DDIs with increasing use of prescribed medication [53]. Advanced age is associated with increased risk of acquiring ADR [54], more than half of all the hospitalizations due to ADR had occurred in elderly patients [55]. Polypharmacy increases risk of DDIs and ADRs [56], thus, increased with number of drugs use [57]. Currently, 20.0% of the patients have potential adverse effects from their drug received in hospital and from all drug prescribed. However, even adherence to these guidelines of treatments, still may cause reaction particularly in patients with hypotension [58]. Accomplish fully understanding the adverse effects by using why, how and where could provide clinician to choose appropriate intervention to reduce occurring and preventable side effects. One of possible cause of complication of preventable side effects is that once the medication is initiated, it is not always regularly reviewed and titrated to adjust prescribed drugs for physiological changes in elderly and DDI of concurrent drugs [59].

Based on fact that renal function falls with increasing age [60], elderly should be considered as renal insufficient patient. Unsuitable dosing or frequency of administration is considered be responsible for medication errors with overdosing being significant problem [61]. In this study, 10.0% of the patients have over-therapeutic dose. The over-therapeutic doses in metoclopramide in patients needed to be decreased to 50.0 - 75.0% according to patient's GFR. Drug dosing in renal insufficiency needs to be individualized whenever possible to optimize therapeutic outcomes and minimize toxicity. Use of aspirin to prevent development of CVD is associated with development of gastrointestinal ulcer [62]. Indeed, a systemic review study reported that low-dose of aspirin increases risk of major bleeding [63]. In Iran, most prescribing errors were happened during selecting drug dose and frequency [64]. The disquiet from prescribing overdose to the patient leads to give under-dosing of the drug which undermine exploit the full potential of the particular drugs. Unnecessary decreases in dosage may result in under-treatment or changing to an alternate drug with a narrower therapeutic index and lower efficacy. In this study, 10.0% of the patients have sub-therapeutic dose. Out of half of these cases, seven patients advanced CKD, were taken furosemide dose that normally given for patient with normal GFR. The threshold dose of intravenous furosemide is 10 mg in population with normal renal function. This increases to 80 - 160 mg in patients with declining renal function [65]. Hence, furosemide doses lower than 80 mg are not effective in advanced CKD patients.

In Libya, there are no active local guidelines for management of medications for elderly patients, no specialized geriatric health institutions and no specialized physicians in geriatric medicine. The traditional relationship between physicians and pharmacists is no longer to ensure rational prescribing and adherence to clinical guidelines of therapy particularly in clinical settings. Pharmacist interventions are nowadays considered as valuable input in elderly care process by rationalizing the

pharmacotherapy and reducing medication errors [66]. Pharmacists can improve the quality of drug prescribing [29, 67]. However, Libyan pharmacists as health providers represent potential, currently underused for optimizing drug use. Professional healthcare in certain developing countries lacks local working guidelines assessing the potential of inappropriate drugs. A Palestine's study demonstrates that physicians and pharmacists have relatively low awareness about appropriate medications for elderly patients [68]. This study highlighted the importance that clinical pharmacist should enabled to engage in hospital medical teams for treatment of geriatric inpatients to optimize pharmacotherapy. The optimizing of clinician prescribing can be achieved as a result of the physician accept recommendations introduced by clinical pharmacists and scientifically dealing toward these suggestions in his/her medical practice. Professional cooperation between all healthcare

providers are essential to delivery of personalized and effective patient services [69].

Conclusion: Antibiotics, analgesic and vitamins are the common prescribed medications for Libyan elderly patients. DRPs predominant prevalence in clinical practice in Libya. Pharmacists should actively participate and intervene in clinical activities to reduce incidence of DRPs in clinical settings. Clinical pharmacists can reduce chances of experiencing DRPs and ensuring patients receive effective, safe and efficient drug therapy. The hospital committee should encourage pharmacists to give their effort regarding the medication use. This study can serve as data-base for researchers and academic institutions for geriatric medication appropriateness. It may also help different health care providers to minimize the burden of DRPs and their consequences.

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Ethical issues: Including plagiarism, informed consent, data fabrication or falsification and double publication or submission have completely been observed by authors.

Author declaration: The authors confirm that all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.

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