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Use of therapeutic outcomes monitoring method for performing of pharmaceutical care in oncology patients

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Abstract

This study aimed to implement pharmaceutical care using the therapeutic outcome monitoring (TOM) method for pharmacotherapeutic follow-up of oncological patients. This was a prospective longitudinal study involving patients undergoing oral chemotherapy. The study environment was an outpatient pharmacy at a tertiary-level oncology hospital. Ninety patients who received oral chemotherapy were evaluated, and 27 patients were followed up in accordance with the exclusion criteria and acceptability of participation in the study. The patients were predominantly diagnosed with gynecological tumors, with a mean age of 57.56 ± 13.06. The average consumption of drugs per patient was 4.63 ± 4.85, and more than 55% of patients had undergone oral antineoplastic therapy for more than a year. The main therapeutic groups used were drugs that acted on the gastrointestinal tract and metabolism (34%). All patients had at least one drug-related problem (DRP). In total, 133 DRP were identified. Approximately 33% of patients had DRPs related to antineoplastic therapy; non-adherence, incorrect administration, and the probability of adverse events were among the frequently reported DRPs. We identified 43 negative outcomes associated with medication (NOM), with untreated health problems (47%) and non-quantitative insecurity (30%) being the most frequently reported. 81 pharmaceutical interventions were performed, and 96% were accepted. The main errors avoided with the interventions were untreated health problems, misuse, and interruptions associated with medication administration. The TOM method effectively achieved the desired results of therapy, improving the use of medicines, and thus increasing patient safety.

Keywords

Pharmaceutical care, medications errors, oral antineoplastic

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Introduction

Cancer is a disease with many stigmas, and antineoplastic therapy is one of the main concerns of patients. In such a scenario, preconceived ideas may diminish the possibility of finding a suitable cure. The pharmaceutical industry has seen a significant advancement in the production of oral anticancer agents. It is a high-cost technology for two reasons: oral formulation of anticancer agents administered intravenously and the innovation cost associated with new chemotherapeutic agents.[1]

Oral chemotherapy drugs have a high incidence of adverse events and are associated with various types of medication errors.[2] Gilbar and Carrington (2005) found 106 errors related to the use of oral methotrexate; 25 deaths were reported, and 48 serious outcomes were identified. Over 50% of the errors were due to

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overdose. The lack of treatment adherence is also a problem associated with the use of oral chemotherapy since these treatments, for the most part, involved prolonged exposure to the drug, and the effectiveness of the treatment depends on the appropriate use of the therapy.[3,4]

Problems involving failure of the use of drugs are a global concern. Pharmaceutical care has emerged as a tool to solve problems related to the misuse of drugs.[4,5] Pharmaceutical care is based on the agreement between the pharmacist and the patient[6,] and professional practice enables the patient to benefit from this process.

Pharmaceutical care can improve health and reduce costs through direct patient care, including patient assessment, identifying problems related to therapy, and the cause of these problems. This process develops health goals, including those associated with the treatment, monitoring, and evaluation of results.[6,7] It follows the active character of pharmaceutical care detection of drug-related problems (DRPs) for the prevention and resolution of the negative outcomes associated with medication (NOM).[8] Several pharmacotherapeutic follow-up initiatives have been implemented for cancer patients to monitor antineoplastic pharmacotherapy, including assessing adherence, therapy counseling, and interventions related to medication errors.[9–14]

Pharmacists have proposed several methods to achieve the objectives of pharmaceutical care.[7,15,16] Among the clinical techniques, the therapeutic outcomes monitoring (TOM) method has been highlighted to perform pharmacotherapeutic follow-up. According to Dader and Martínez (1999), the model proposed by the TOM method is indicated for the achievement of pharmaceutical care for patient groups that are considered at risk, such as patients with chronic diseases, the elderly, and those who are polymedicated, including cancer patients.

This study aimed to implement pharmaceutical care using the TOM method for pharmacotherapeutic follow-up of cancer patients receiving oral chemotherapy to identify DRP and prevent NOM.

Patients and methods

This longitudinal prospective study was conducted between 6 months. The study was conducted at the outpatient pharmacy of a cancer hospital at the tertiary level. The target population for this study was patients who received oral chemotherapy. The inclusion criteria were patients >18 years who were treated with Tamoxifen 20 mg, Anastrozole 1 mg, Etoposide 50 mg, and Megestrol 160 mg. Patients unable to respond to the interviewer's questions were excluded.

The Pharmaceutical Care methodology used was the TOM method, developed by Hepler.[17] This method guides the development of a specific form, according to the needs of the study group.[15] In addition to that, we elaborated the Pharmacotherapeutic Follow-up form for Ambulatory Patients for data collection.

In the hospital where the study was carried out, the drugs were dispensed monthly to the patients. Thus, pharmaceutical consultations were conducted at the pharmacy on the day that the patient received their medicines. All patients underwent at least three pharmaceutical queries. The first interview was applied to the first part of the form designed for this study, and in subsequent interviews, the second part of this form.

The DRP was classified according to the proposal of the Third Consensus of Granada (2007)[8]: wrong drug administration, personal characteristics, improper storage, contraindications, dosage or inadequate duration, duplicity, dispensing error, prescription error, noncompliance, interactions, other health problems that affect treatment, likelihood of adverse events, and untreated health problems. The DRP with unwanted outcomes that could cause any harm to the patient was also classified as NOM.

Pharmacological classes were analyzed according to the therapeutic groups of Anatomic Therapeutic Chemistry (ATC).

Pharmaceutical interventions were performed whenever DRP was detected. The interventions were classified into two groups: clinical interventions, in which the DRP was solved, orally or in a written form, with physicians or other health care providers who could help in resolving the DRP, and interventions with the patient, in which the DRP was solved by direct instructions or by guiding the patient.

Descriptive statistics were used to organize the data collection, classification, and data description. Thus, the qualitative variables were expressed as absolute or percentage rates, whereas quantitative variables were expressed as mean and standard deviation.

Institutional Ethics Committee approved this study (CAAE 03808912.0.0000.5274).

Results

Of the total eligible patients, 90 were evaluated; according to the exclusion criteria, 30 patients were excluded; contact could not be established with 15 patients, and 18 patients did not participate in the study. The main reasons reported for not participating were lack of time and poor health due to the disease. This study included 27 patients. We performed 78 pharmaceutical consultations, with an average of 2.88 consultations/patients.

For data collection, an outpatient pharmacotherapeutic follow-up form was created (Table 1). The TOM

Table 1. Pharmacotherapeutic follow-up form for outpatients using oral chemotherapeutics.

Part I (first consultation)	Part II (others consultations)
Personal and socioeconomic data	**Identification**
Clinical and physical evaluation	**Clinical and physical evaluation**
Oncological diagnosis	Evolution of the patient Laboratory and imaging exams
Comorbidities	
Allergies	
Social, physical and food habits	
Pharmacotherapeutic evaluation	**Pharmacotherapeutic evaluation**
Antinoplastic treatment (previous and current) Medicines prescribed in use	Medicines prescribed in use
Non-prescription drugs in use	Non-prescription drugs in use Use of herbal medicine and other alternative therapies
Use of herbal medicine and other alternative therapies	
Pharmaceutical pipelines	**Pharmaceutical pipelines**
Identification of drug-related problems Pharmaceutical interventions carried out	Identification of drug-related problems
	Pharmaceutical interventions carried out
Pharmaceutical guidelines performed	**Pharmaceutical guidelines performed**

method advises that the document be prepared according to the needs of the study group to analyze personal and clinical characteristics (Castro et al., 2008). Thus, the form was divided into two parts: the first part was to be applied in the first consultation, and the second part to be used in other meetings. Figure 1 shows the elements that constitute the form. In the first part, personal and socioeconomic data, lifestyle habits, treatments performed, health problems, information detailing identified medications, and pharmaceutical behaviors are described. The second part describes the treatments performed, clinical examinations, the patient's evolution concerning the proposed plan, and the pharmaceutical procedures.

The demographic profile of the patients showed a predominance of females (93%), with gynecological tumors (63%), low educational qualifications (56%), and a mean age of 57.56 years (± 13.06) (Table 2).

Only 11% of the patients did not present with any type of comorbidity (Figure 1). Diseases related to the cardiovascular system (51%) were the most common comorbidities, with hypertension (28%) being the most prevalent, followed by heart disease (13%), diabetes (6%), and dyslipidemia (6%). Another comorbidity commonly reported by the studied population was depression, which was reported in 13% of patients.

The average consumption of medications was 4.63 (± 4.85) medications per patient, ranging from 2 to 15 medicines in each pharmaceutical appointment. Approximately 33% of patients had used oral chemotherapy for more than a year, and 22% had used it for more than two years. The main therapeutic groups used by patients were drugs that act on the gastrointestinal tract and metabolism (34%), nervous system (28%), and cardiovascular system (21%). Patients were asked about the use of drugs without a prescription. Among the 27 patients, 11 (38%) reported that they were self-medicating. Most of these patients reported using analgesics, and four patients (37%) used herbal medicines.

All patients reported at least one drug-related problem (DRP) during the consultations. Hundred and thirty-three DRP were identified, with an average of 4.71 (± 2.47) per patient. The frequency and classification of the DRP are shown in Table 3. Approximately 33% of patients had DRPs related to oral chemotherapy. Most of the reported DRPs were related to other therapies used by patients.

The main DRP was related to untreated health problems (18%). This DRP included cases in which there was a lack of medication in the unit. Most health problems were not related to gastrointestinal issues. Non-adherence DRP (16%) was identified as one of the most frequently reported DRPs. To classify it, any report that showed a lack of adherence to some medication in all consultations was considered non-adherent. Wrong administration (14%) was the third most commonly found DRP. The pharmacist evaluated all situations that diverged from medical recommendations such as dosage, administration of medication with or between meals, taking a whole tablet, or break/grinding the tablet. For DRP contraindications (8%), we considered all self-medications.

Of the reported DRPs, 43 were NOMs (Table 4). Among the NOMs reported, untreated health problems (47%) and non-quantitative insecurity (30%) were the most frequently reported. In cases where there was non-quantitative insecurity, negative results related to the interaction and the appearance of adverse effects were considered. Seven patients had side effects that could be associated with the use of oral chemotherapy.

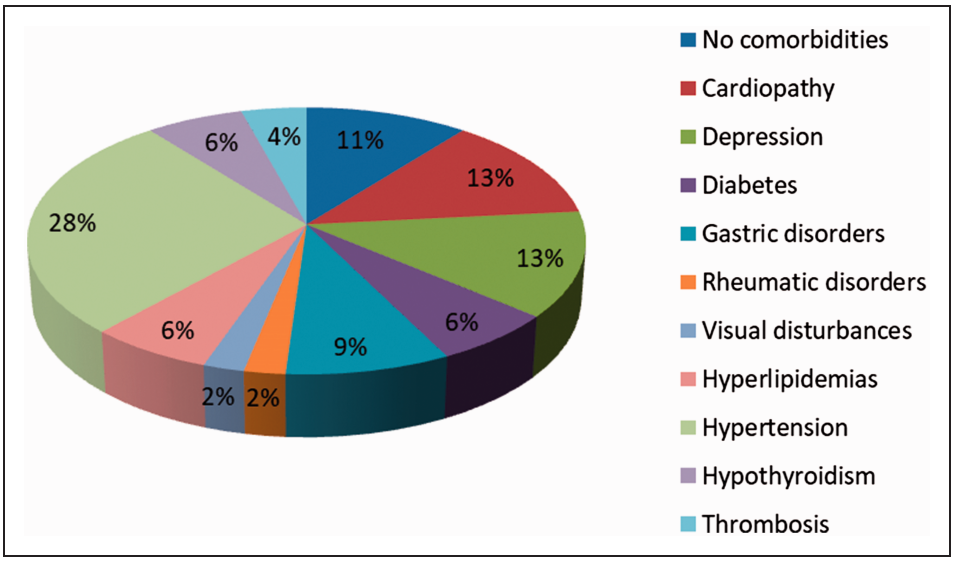

Figure 1. Comorbidities found in 27 patients followed in the study. It was found 42 comorbidities. Some patients had more than one comorbidity.

Table 2. Demographic profile of the study population.

Variables	Mean ± SD
Age (years)	57.56 ± 13.06
Variables	**n (%)**
Gender	
Female	25 (93)
Male	2 (7)
Marital status	
Single	8 (30)
Married	9 (33)
Divorced	5 (19)
Widow(er)	5 (19)
Location of residence	
Reside in the city of Rio de Janeiro	13 (48)
Reside outside the city of Rio de Janeiro	14 (52)
Level of education	
Literate	3 (11)
Middle school–uncompleted	7 (26)
Middle school–completed	5 (19)
High school–uncompleted	0
High school–completed	4 (15)
University–uncompleted	1 (4)
University–completed	7 (26)
Oral chemotherapy used	
Tamoxifen	8 (30)
Anastrozole	8 (30)
Etoposide	4 (15)
Megestrol	7 (26)
Diagnosis	
Ovarian tumor	6 (22)
Endometrial tumor	11 (41)
Breast tumor	5 (19)
Desmoid tumor	5 (19)
Legend:	
SD: standard deviation	

Table 3. List of drug-related problems (DRP), classified according to the III Granada Consensus (CONSENSUS COMMITTEE, 2007).

DRP	n (%)
Health problems untreated	24 (18)
Noncompliance	21 (16)
Wrong administration	19 (14)
Probability of adverse events	18 (13)
Other health problems that affect treatment	11 (8)
Contraindication	11 (8)
Prescription errors	8 (6)
Interactions	9(7)
Personal caracaterísticas	7 (5)
Dose and/or wrong duration	4 (3)
Duplicity	3 (2)
Improper storage	1 (1)
Dispensingerrors	0 (0)
Total	133 (100)

Table 4. Negatives outcomes associated with medications rating (NOM), classified according to the III Granada Consensus (CONSENSUS COMMITTEE, 2007).

NOM	n (%)
Necessity	
Health problem untreated	20 (47)
Effect of unnecessary medication	5 (12)
Effectiveness	
Not quantitative ineffectiveness	3 (7)
Ineffectiveness quantitative	1 (2)
Security	
Not quantitative in security	13 (30)
Insecurityquantitative	1 (2)
Total	43 (100)

Table 5. Pharmaceutical interventions performed in monitoring patients on oral chemotherapy.

Clinical interventions	n (%)
Referral to other health professionals	17 (53)
Inclusion of drugs	3 (9)
Adverse drug reaction notification	4 (13)
Substitution drug	6 (19)
Drug interaction alert	2 (6)
Total:	32 (100)
Interventions with the patient	n (%)
Administration Schedule Change	4 (9)
Correct administration of drugs	4 (9)
Patient barriers removal (myths)	3 (7)
Table orientation with schedules	4 (9)
Drug Interaction alert	7 (15)
Patient education	8 (17)
Correct storage	2 (4)
Rational use	11 (24)
Explanation of correct indication	1 (2)
Advice on health care	2 (4)
Total:	46 (100)

We performed 81 pharmaceutical interventions, of which 78 (96%) were accepted. Of the total interventions, 59% were performed with patients (Table 5). Many DRPs did not require interventions to be resolved in the range of pharmaceutical consultations.

Through interventions, it was possible to prevent therapy errors from occurring or perpetuating themselves. Among the main errors avoided are untreated health problems, in which referral to health professionals (physician and non-physician) and inclusion of medications represented about 62% of medical interventions performed. Other avoided errors were misuse and insecurity in medication administration, through interventions conducted directly involved the patients. Among them, 56% were related to drug interaction alerts, patient education for rational use, and risks of self-medication.

Discussion

This study demonstrates that the TOM method is useful for the pharmacotherapeutic follow-up of patients. Usually, cancer patients using antineoplastic drugs are exposed to a greater number of adverse events, especially the main polymedicates, so it is necessary to follow up with them.[15] In addition to the particular control of pharmacotherapy, DRP could be identified, and NOM could be prevented, increasing the patient's safety. Using another monitoring methodology, a study conducted by Battis et al. (2017) identified that 45% of patients using oral chemotherapy had problems related to therapy. They concluded that strict monitoring and follow-up of patients undergoing oral chemotherapy are crucial to achieving therapeutic goals, improving patient safety and adherence, and reducing adverse drug events and healthcare costs.[11] In the present study, one-third of patients using oral chemotherapy had problems related to antineoplastic drugs. The probability of adverse events is more frequent due to the appearance of the effects, followed by the infectivity of the drug.

Although few studies have reported using the TOM method for analysis of cancer patients, several studies show positive results with its use for other patients' profiles.[18–20] A survey by Alvarez de Toledo and colleagues (2001) compared two groups of patients with coronary heart disease: a group had received pharmaceutical care through the TOM method, called "Study TOM COR," and another group received no monitoring. They found that the group receiving follow-up had lower demand for emergency care, hospitalizations, and days in intensive care centers. The author concluded that patients receiving pharmaceutical care knew the reasons for their pharmacotherapy and therefore used an efficient health system, helping them achieve the highest level of health.[18] Two other studies with asthmatic patients, using the TOM as a Pharmaceutical care method, demonstrated that therapy counseling and correct guidance concerning the use of drugs, mainly inhalers, showed better clinical outcomes and improved patients' quality of life.[19,20]

One of the limitations of this method is the development of an appropriate form for the type of service provided, which may fail to consider the patient holistically as methods with structured forms such as the Dader Method and the Pharmacist's Workup of Drug Therapy (PWDT).[7] The pharmacotherapeutic monitoring methods originate from the classic health care and registration system called subjective, objective, assessment, and plan (SOAP). The PDWT way is one of these methods and was a pioneer in Pharmaceutical Care. This method has the data analysis, effectiveness, and safety of pharmacotherapy, an action plan through the resolution of DRP, monitoring, and evaluation.[7] The Dáder and TOM methods are derived from the PDWT method, essentially presenting the same components. However, the Dáder process uses a standardized form, independent of the group of patients. It allows more time for data analysis, while TOM emphasizes the importance of a specific format for different patients according to their needs.

In the present work, the methodology and form used were efficient in the pharmacotherapeutic follow-up of cancer patients. Follow-up was conducted using other methodologies, making it possible to identify DRP, perform pharmaceutical interventions that would

enable the prevention of errors and patient education, thus improving their safety and handling.[11,13,21,22]

When analyzing therapy problems, 133 DRPs (4.71 DRP/patient) were identified in the present study, with the most prevalent DRPs including untreated health problems, non-adherence, incorrect administration, and probability of adverse events. Similar results were found in studies conducted on cancer patients using other pharmacotherapeutic follow-up methodologies. A study performed by Souza and Cordeiro (2012), using the Dáder method to monitor 18 patients using capecitabine, identified 66 DRPs (3.66 DRP/patient), with the most prevalent DRPs including health problems not being treated due to the lack of medication supply, occurrence of adverse events, and incorrect administration.[22] Another study used the Dáder and PWDT method adapted for the follow-up of 31 breast cancer patients using capecitabine, and 289 DRPs (9.32 DRP/patient) were identified, 82.7% of which were related to the occurrence of adverse events related to oral chemotherapy.[21] In the study carried out by Battis et al. (2017), 68 oncological patients were followed, 31 DRPs (0.45 DRP/patient) were identified, with non-adherence and adverse events among the most frequently reported DRPs. This study did not specify the monitoring methodology used.[11]

The pharmacist's role in identifying and resolving DRP is paramount for patient safety, as it is associated with medication errors. An oral chemotherapy management program carried out by Muluneh et al. (2018) detected 196 adverse events, 92% of which required pharmaceutical interventions.[13] This data corroborates the results of the present study, in which the 96% of pharmaceutical was accept. The survey conducted by Olinto et al. (2013) carried out around 197 treatments for the 289 identified DRPs, with an acceptance rate of around 80%.[21]

In the present study, 43 NOMs were identified, corresponding to 32% of the identified DRPs. Untreated health problems and non-quantitative insecurities were the most prevalent NOMs. Non-quantitative insecurity corresponded to the adverse reactions identified. Similar results were found in a study conducted on cancer patients treated with capecitabine. 59 NOMs were identified, with untreated health problems and quantitative and non-quantitative insecurities among the most prevalent.[22] In the study conducted by Souza and Cordeiro (2012), there is no report concerning the severity of the adverse reactions found.[22] However, other studies with oncological patients have shown lower ADR rates than those reported in the present study. In the survey conducted by Battis et al. (2017), with cancer patients, around 2.9% of patients had severe adverse reactions (Grade 3 and 4)[11], in another study of breast cancer patients using capecitabine, 0.8% of patients had severe adverse reactions.[21] In the present study, 18.5% of the patients had Grade 3 reactions.

Demographic data revealed that most patients were women, with a prevalence of gynecological tumors. The age range is also consistent with the findings in the literature for this type of neoplasia. The cervix tumor is more common in women aged 46 - 50 years, while the ovarian tumor is more common between 51 - 55 years old.[23] Similar results were found in the study conducted by Birand and collaborators (2019), in which 65.4% of the population using oral chemotherapy was female, with a mean age of 59.1 years ($\pm$ 11.34).[14]

The most commonly used therapeutic groups corroborate the profile of cancer patients. Gastrointestinal disorders, such as nausea and vomiting, are common and are usually caused by use of several medications or chemotherapy. Chronic pain is another symptom that is closely associated with cancer. It is estimated that this symptom occurs in 30% of patients with early-stage disease and in 70% of advanced cases.[24] Usually, the protocols to treat pain proposed by the World Health Organization (WHO), according to the pain scale, call for the use of a combination of non-opioid analgesics, opioid analgesics, and adjuvant drugs such as antidepressants, anticonvulsants, antihistamines, corticosteroids, and anxiolytics, among others.[25,26] In this study, hypertension was the main comorbidity reported by patients, justifying the high frequency of drugs for the cardiovascular system. These data reflect a public health problem that is the high prevalence of hypertension in Brazil, estimated to be prevalent in 35% of the population over 40 years[27] and corroborate with other studies conducted with patients using oral chemotherapy.[14,22]

In this study, we found that more than one-third of patients were self-medicated. In 2002, a survey in the US found that 35% of adults surveyed had used complementary medicines independently.[28] In Brazil, it is estimated that at least 35% of the purchased drugs are used for self-medication, making it a public health problem.[29] This scenario depicts the weakness of public health services.

Another important finding of this study was the occurrence of polypharmacy. According to Secoli (2010), polypharmacy can be defined as the use of five or more medications, configured as a security problem related to drug use.[30] The elderly population is the group of patients who have an increased occurrence of polypharmacy because of the clinical conditions of this group, mainly characterized by chronic disease, which requires prolonged treatment and varied.[30–32] In a study conducted in Canada, the average prescribed drugs were five prescription drugs

before starting any cancer treatment.[33] These results corroborate with the results of the present study. The classes of medications most commonly used by elderly cancer patients are also similar to those found in this study's results, with a predominance of drugs for cardiovascular problems.[33] All studies concluded that the main negative effects of polypharmacy are drug interactions, adverse reactions, and increased health care costs.[30–33]

The lack of adherence to oral antineoplastic therapy was also one of the main DRPs found in the present study. The adherence rates can vary between 16% and 100%, with breast cancer patients undergoing hormone therapy with tamoxifen presenting better rates between 50% and 98%.[4] Lack of adherence is one of the main problems associated with oral antineoplastic therapy, and several factors may be related to its occurrence. Studies have demonstrated that pharmaceutical care programs, including therapy monitoring, guidance, and counseling, are of paramount importance to ensure better adherence rates for oral antineoplastic therapy.[4,9–14]

Interventions in this study reflect the problems related to the use of drugs and the needs of patients. In clinical interventions, the majority referred to other health professionals, indicating that there are factors besides the use of drugs that interfere with the quality of life. Alano et al. (2012) identified the doubts of patients related to their health problems and therapy. It also identified the need for referral to other health professionals.[34] Most interventions with patients were related to their security to ensure rational use and prevent adverse events. These results corroborate with Sabater et al. (2005), who showed that the most prevalent interventions were related to the use of additional medication, reduction of non-voluntary compliance, withdrawal of self-medication-related medicines, and the number of drugs used by the patient.[35]

Conclusion

The TOM method proved to be an efficient method of pharmaceutical care for patients with cancer. It managed to achieve the desired results in therapy, improving the use of medicines by patients, making it possible to identify DRP and prevent NOM, thereby increasing their safety. The study also demonstrated the importance of multidisciplinary teams in treating patients with cancer. Through interdisciplinary communication, it is possible to solve problems related to the patient's health and therapy, ensuring a better quality of life.

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