Adverse Drug Reactions among Critically Ill Patients at Cairo University Hospital: Frequency and Outcomes

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Abstract

Background: Adverse drug reactions (ADRs) are common problem in intensive care units where the polypharmacy is involved in treating patients. Control of such events is possible if it is identified and reported. However, reporting of adverse drug reactions still in its infancy. Aim: the aim is to assess the frequency and outcomes of adverse drug reactions among critically ill patients at Cairo university hospital. Research questions: 1- What is the frequency of adverse drug reactions among a selected sample of critically ill patients at Cairo university hospital? 2- What is the outcome of adverse drug reactions among a selected sample of critically ill patients at Cairo university hospital? 3- What is the degree of severity of adverse drug reactions among a selected sample of critically ill patients at Cairo university hospital? Design: Descriptive exploratory design was utilized. Setting: The study was carried out at the Critical Care Department affiliated to Cairo University Hospitals. Subjects: A convenience sample of 150 male & female critically ill adult patients receiving different types of medications constituted the study sample. Tools: Two tools were utilized in the study, 1. Sociodemographic and medical data sheet and, 2. Adverse drug reactions assessment sheet. Results: The study results revealed that one of fifth (21%) of study sample were suffered from adverse drug reactions. ADRs were represented on the patients in the form of dry mouth, abdominal distension, headache, insomnia, constipation, tachycardia, peripheral edema, hypertension, hypotension, cough, drowsiness. Severity of adverse drug reactions was ranged from mild severity (41.9%) to moderate and severe reaction (9.7%). Conclusion: The prevalence of adverse drug reactions among critically ill patients is prevalent in a ratio of nearly (21%); and, more than half of these reactions were life-threatening. Recommendation: A written hospital policy describing basic standards in management of ADRs is recommended to be established and before initiation of new medication, assess for potential drug–disease and drug–drug interactions, check dosages, and check the most common causes of ADRs, then starting new drugs.

Key words: Adverse drug reactions, poly pharmacy, critically ill patients, Frequency, Outcomes

1. Introduction:

Although health care personnel are looking for patient’s safety, mistakes and errors inevitably occur, particularly in a complex environment such as intensive care unit (ICU). Such errors have serious implications for patient’s wellbeing and safety and are a major public motivation to strive for a safer health care system. One factor that influences morbidity and mortality is a harmful unpredicted reaction to a drug that is an almost daily occurrence in hospitals. The ICU has been known to be the land of poly pharmacy for many years. Poly pharmacy is known to increase the risk of adverse drug reactions (ADRs), drug-drug and drug-disease interaction. It has been claimed that patients taking two drugs face a 13% risk of adverse drug interactions, rising to 38% when taking four drugs and to 82% if seven or more drugs are given simultaneously (Kathiria, Sattigeri, Desai, & Patel, 2013).

In general, ADRs means any undesired responses to drug administration, as opposed to therapeutic effect, which is the desired response, (Abrams & Goldsmith, 2004). ADR is defined by the World Health Organization (WHO) as "one which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function" (WHO, 2008). Reis & Cassiani (2011) added that ADRs are any non-intentional harmful response to medication that occurs with doses normally used in previous mentioned purposes. Also, the concept of ADRs includes all responses that place patients at risk or expose them to harm. Serious adverse drug events are defined by the United State Food and Drug Administration (FDA) as events caused by a drug which results in a patient's death, hospitalization, or disability, or cause a congenital abnormality, or a life-threatening event, or require an intervention to prevent permanent damage.

ADRs are common; it contributes to significant morbidity and healthcare costs, and carry the single greatest risk for harm to patients in hospitals. It has been estimated that, each year, over 770,000 people in the United States who are hospitalized suffer ADRs, which costs major hospitals up to $5.6 million per year.
Researchers assert that ADRs are the sixth most common cause of death after heart disease, cancer, stroke, lung disease, and accidents. In our drug-consuming society, we often expect side effects, such as an upset stomach from aspirin, sleepiness from an antihistamine or nausea caused by a pain pill. However, in the event of a hospitalization or an unexpected death possibly related to an adverse drug reaction blame may be directed at the drug manufacturer, the health care facility or the physician who prescribed the medication (Mutnick, 2004, and Loes, 2006).

Although published reports indicate that thousands of deaths occur each year as a result of medical errors, the true numbers of deaths attributed to ADRs is unknown (Osterberg & Blaschke, 2007). In the US, 3 to 7% of all hospitalizations are due to ADRs. ADRs occur during 10 to 20% of hospitalizations, about 10 to 20% of which are severe. Incidence of death due to ADRs is unknown; suggested rates of 0.5 to 0.9% may be falsely high because many of the patients included had serious and complex disorders. Incidence and severity of ADRs vary by patient characteristics (eg, age, sex, ethnicity, coexisting disorders, genetic or geographic factors) and by drug factors (eg, type of drug, administration route, treatment duration, dosage, and bioavailability). Incidence is probably higher and ADRs are more severe among the elderly, although age of the person may not be the primary cause. The contribution of prescribing and adherence errors to the incidence of ADRs is unclear (Tarloff, 2007).

Chamberlain (2011) classified ADRs into four types; type A, extension of pharmacologic effect, often predictable and dose dependent, responsible for at least two-thirds of ADRs e.g., propranolol and heart block, anticholinergic and dry mouth, type B, idiosyncratic or immunologic reactions, rare and unpredictable e.g., chloramphenicol and a plastic anemia, type C, associated with long-term use, involves dose accumulation, e.g., phenacetin and interstitial nephritis or anti-malarial and ocular toxicity, and type D, delayed effects (dose independent), carcinogenicity e.g., immunosuppressant, teratogenicity e.g., fetal hydantoin syndrome. Symptoms and signs may manifest soon after the first dose or only after chronic use. They may obviously result from drug use or be too subtle to identify as drug-related. In the elderly, subtle ADRs can cause functional deterioration, changes in mental status, failure to thrive, loss of appetite, confusion, and depression. Symptoms include itching, rash, fixed-drug eruption, upper or lower airway edema with difficulty breathing, and hypotension. Idiosyncratic ADRs can produce almost any symptom or sign and usually cannot be predicted (Tarloff, 2007).

Nurses who work in critical care must assess and monitor the patient closely in order to identify subtle changes in a patient’s condition that warrant immediate intervention. Patients who are admitted to critical care tend to be medically unstable, requiring constant cardiac and respiratory monitoring and continual adjustment of treatments, such as the titration and dosing of multiple intravenous medications and changes in ventilatory support. Because of the critical nature of patients’ conditions, nurses working in critical care are often confronted with dealing with end-of-life issues and sometimes other ethical dilemmas related to withholding, withdrawing or medical futile care . Critical care nurses must be able to interpret, integrate and respond to a wide array of clinical information (futures in nursing, 2003).

2. **Significance of the study:**

ADRs can be life-threatening, particularly in the critically ill population. Life-threatening events associated with ADR occur in 26% of ICU patients as compared to 11% in non-ICU patients (Kane-Gill, Kirisic, Verrico, & Rothschild, 2012). WHO reported in 2012, that the ADRs are estimated to be between fourth and sixth leading cause of death in USA and more than 10% of ADRs lead to hospitalization according to some studies. Worldwide, more than 50% of all medicines are prescribed, dispensed or sold inappropriately, and 50% of patients fail to take them correctly. 30% of the total health budget accounts for use of medicines in many countries. Therefore, assessing prevalence and outcomes of ADRs among critically ill patients will be beneficial in many ways; it will alert health care professionals to this problem, help in its reduction/prevention, save patients’ life, lead to a cost effective care at the Critical Care Departments and might generate an attention and motivation for further researches into this area. So, the aim of this study is to assess the frequency and outcome of adverse drug reactions among critically ill patients at Cairo university hospital.

3. **Aim of the study:**

The aim of this study is to assess the frequency and outcomes of adverse drug reactions among critically ill patients at Cairo university hospital.

4. **Research questions:**

To fulfill the aim of this study, the following research questions were formulated:
1. What is the frequency of adverse drug reactions among a selected sample of critically ill patients at Cairo university hospital?

2. What is the outcome of adverse drug reactions among a selected sample of critically ill patients at Cairo university hospital?

3. What is the degree of severity of adverse drug reactions among a selected sample of critically ill patients at Cairo university hospital?

5. Subjects and Methods:

5.1 Research Design

Descriptive exploratory research was utilized in this study.

5.2 Setting

The study was carried out at Critical Care Department affiliated to Cairo University Hospital, in Cairo Governorate. It is one of the largest educational university hospitals in Egypt in this field, and it receives patients from all Egyptian governorates and other countries. It consists of 3 units over 3 floors; first, second and the third unit, the first floor containing 18 beds, the second floor containing 31 beds; and the numbers of occupied beds not exceed 35 bed /day.

5.2 Subjects

A convenience sample of 150 male & female critically ill adult patients receiving different types of medications & stayed for at least two days after admission constituted the study sample.

5.3 Tools

Two tools were utilized to collect data pertinent to the study.

These tools are:

1- Sociodemographic and medical data sheet which covers patient’s gender, age, diagnosis, co-morbidity diseases and etc.

2- Adverse Drug Reaction assessment sheet which covers the following areas: drug groups, adverse drug reactions that appear on the patient through general observation (signs & symptoms) & laboratory results, then report about onset, duration, severity, outcomes, intervention & duration of the treatment for ADRs.

5.4 Ethical consideration

An official permission to conduct the study was obtained from directors of the Critical Care department at Cairo University Hospital. Patients' agreements to be included in the study were obtained after explanation of the nature and purpose of the study. Each patient was free to either participate or not in this study and had the right to withdraw from the study at any time without any rationale; also, patients were informed that data will not be included in any further researches without another new consent if they do not mind. Confidentiality and anonymity of each subject were assured through coding of all data.

5.6 Techniques for data collections

Structured interview, reviewing medical /nursing records and direct patients observation were utilized to fill out the study tools.

5.7 Procedure

The current study was carried out on two phases, designation and implementation phases which are:

5.7.1 Designation phase:

It was concerned with the construction and preparation of the different data collection tools, in addition to obtaining managerial arrangement to carry out the study.

5.7.2 Implementation phase:

Implementation phase: The researchers visited the critical care departments on daily bases, reviewing the medical/nursing records to identify patients who fulfill the criteria of inclusion. Then those patients were interviewed to obtain informed consent after explaining the nature and purpose of the study. Then sociodemographic and medical data sheet (tool1) was filled at the first contact with the patient. Then adverse drug reaction assessment sheet (tool 2) was filled on daily bases after two days from admission to ICU until patient discharge to follow any physical changes from disease or drug administration.
5.8 Statistical analysis data

Upon completion of the data collection, data were tabulated and analyzed using statistical package for social sciences (SPSS); relevant statistical analysis was used to test the obtained data. Descriptive statistics were applied (e.g. mean, standard deviation, frequency, percentage). Also relevant inferential statistics was applied.

6. Results

Findings of the current study are presented in two main sections; section (1) related to socio-demographic data, medical data, hospitalization period, and drug groups (table 1 and figures 1-2-3), section (2) is concerned with the answer of research questions 1.2 & 3 (table 2 and figure 4,5).

Section 1:

Figure (1) shows that, 28% of study sample's age ranged between 40-60 years, and 24.7% of them were aged between 20 to 40 years. Figure (2) shows that, more than half of study sample (57.3%) were males. Figure (3) shows that, 40.7% of studied sample stayed in hospital for less than or equal to five days and 38% of them stayed from 5 to 10 days and only 1.3% stayed more than 20 days.

Table (1) revealed that, the most common medical diagnosis of the study sample were IHD, CHF, HTN, MI, COPD with a percentage of 16.5%, 13.3%, 13.3%, 10.7% & 8% respectively; and 12% of patients having more than one disease.

Section (2):

Figure (4) showed that more than one fifth (21%) suffered from adverse drug reactions. Figure (5) revealed that more than half of the study sample (51.6%) had life threatening reactions.

Table (2) revealed that, less than half of the study sample (41.9 %) who were having adverse drug reactions developed gradual onset of reaction and 41.9% with mild severity and 32.3% lasted for minutes in addition to, 45.2% of patients were developed adverse drug reactions received medical management.

7. Discussion:

The present study findings documented that about one quarter of study sample's age were between twenty to forty years and another quarter of them were aged between forty to sixty years and more than half of them were male. Regarding this issue, Public Citizen's Health Research Group, (2007) reported that more adverse drug reactions occur in patients aged 60 or older; the odds of suffering an adverse drug reaction really begin to increase even before age of 50. Almost half (49.5%) of Food and Drug Administration (FDA) reports of deaths from adverse drug reactions and 61% of hospitalizations from adverse drug reactions were in people younger than 60. The risk of an adverse drug reaction is about 33% higher in people aged 50 to 59 than it is in people aged 40 to 49. In accordance with this Kane-Gill, Kirisic, Verrico, & Rothschild, (2012) in a research article entitled as “analysis of risk factors for adverse drug events in critically ill patients” found that, out of a sample of 1101 patients 54% were male, with a mean age of 59.4 ± 17.5 years. Accordance with this, Gill, Rea, Verrico & Weber (2006) who investigated adverse-drug-event rates in an intensive care unit revealed that a total of 280 ADEs were identified in 181 ICU patients, age of these patients was 59 ± 17 years, with 52% of ADEs occurring in men.

In relation to length of hospital stay the study findings revealed that more than two fifth of study sample stayed in hospital for less than or equal to five days and more than one third of them stayed from 5 to 10 days. The rational for this may be due to multiple medical diagnosis that these patients have and polypharmacy which leads to adverse drug reactions. In the same line, Conforti, Costantini, Zanti, Moretti, Grezzana &Leone, (2012) found that one hundred fourteen hospital admissions (11.1%) were caused by ADRs, and out of 1023 patients, 256 patients (25.0%) had an ADR during their hospital stay. The duration of hospital stay was significantly longer in patients who developed an ADR during their time in hospital, 18.7 (95% CI: 17.2–20.1) days versus 12.6 (95% CI: 11.9–13.3) days. In contrary, Tumwikirize, et al (2011) in a longitudinal observational study, conducted in Kabale Regional Referral and Itojo District Hospitals. The study was conducted from July to December 2005. The study population consisted of patients aged 13 years and above, admitted on the medical wards of the two hospitals during the study period. They stated that, Length of hospital stay for most of the patients (50.3%) was 1 - 3 days. ADRs did not significantly affect duration of hospital stay in both hospitals.

Regarding to medical diagnosis the study findings documented that the most common medical diagnosis of the study sample was IHD, CHF, HTN, patients having more than one disease, MI, COPD. This may be due to
patients’ age were one quarter aged from 40 to 60 in whom these diseases are more common. In these regard, Shankar, et al., (2005) found that the most common illness, which warranted admission to the ICU, were chronic obstructive pulmonary disease (COPD), cerebrovascular accident, myocardial infarction, alcoholic liver disease, congestive heart failure, pneumonia and septicemia. One hundred and forty eight patients admitted to the ICU were suffering from more than one illness.

Findings of this study revealed that, more than one fifth (21%) suffered from adverse drug reactions. Also, regarding to onset, severity, duration, intervention & outcomes of ADRs, the study findings documented that less than half of study sample who were having adverse drug reactions developed gradual onset of reaction with mild severity and lasted for minutes in addition to, receiving medical management. And more than half of adverse drug reactions was life threatening. The underlying rational of less prevalence of the adverse drug reactions among ICU patients may be the documentation system which is not available in the critical care department.

In relation to this, Jha, Bajracharya & Namgyal, (2007) in their study about prevalence of adverse drug reactions with commonly prescribed drugs in different hospitals of Kathmandu valley showed that during the study period from May 2007 to September 2007, 37 ADR reports were received out of 4287 patients in four different hospitals with a prevalence of 0.86% and male to female ratio of 0.85, among the cases of ADR, 54.1% were female and 45.9% were male (P=0.65). In accordance with this, Hitchings (2012) in a study entitled as “The Incidence of Serious Adverse Drug Reactions in Critical Care and their Reporting Rate: a Prospective Study” which undergone between 1 January and 31 March 2012, 358 patients were admitted to the adult critical care units of this hospital, of whom 143 (40%) were included in the study. 1026 patient-days of ICU care were reviewed. Serious ADRs were detected in 9 cases (6.3%), equating to a rate of 8.8 events per1000 patient-days. In 6 cases, the ADR was the main reason for ICU admission. Eight of the ADRs (89%) were classified as life-threatening (death occurred in 1 case), and 4 (44%) to have been potentially avoidable.

In the same context, Lazarou & Pomeranz, (2004) in a research article entitled as “Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies” found that, the overall incidence of serious ADRs was 6.7% and of fatal ADRs was 0.32% of hospitalized patients. It is estimated that in 1994 the overall 2, 216, 000 (1721000-271 000) hospitalized patients had serious ADRs and 106000 (76000-137000) had fatal ADRs, making these reactions between the fourth and sixth leading cause of death. In this regard, Gill, Rea, Verrico, & Weber, (2006) who studied adverse-drug event rates in an intensive care unit, revealed that, a total of 280 ADEs caused by 97 unique medications were identified in 181 ICU patients, no ADEs caused a disability. Life-threatening reactions and prolonged hospital stays occurred with less than 3% of ADEs. Also, In survey done by, Pirmohamed, et al., (2004), when the adverse drug reactions as cause of admission to hospital, a prospective analysis of 18, 820 patients, showed that 1225 admissions related to an ADR, giving a prevalence of 6.5%, with the ADR directly leading to the admission in 80% of cases. The median bed stay was eight days, accounting for 4% of the hospital bed capacity. The overall fatality was 0.15%. Most reactions were either definitely or possibly avoidable.

Regarding to, American college of medical toxicology (2007) medication errors and adverse drug reactions are common and costly. Estimates of hospitalized patients experiencing them has ranged from 1.5% to 35%, depending on the population studied, the adequacy of reporting, and the case definitions used. Fatal drug reactions are estimated to occur in 0.32% of hospitalized patients. Between 1.1 % and 8.5 % of all hospital admissions are reportedly caused by adverse drug reactions. Also, Wester, Jönsson, Spigset, Druid, & Hägg, (2008) reported that adverse drug reactions are known to be responsible for between 3% and 12% of admissions to hospitals, and fatal adverse drug reactions (FADRs) account for about 5% of deaths of those patients in US hospitals.

8. Conclusion:

Based on the results of the current study, it can be concluded that, the frequency of adverse drug reactions among critically ill patients was (21%). The most common clinical manifestation of ADRs were, blurred vision , dry mouth, headache, insomnia, depression, drowsiness , tachycardia, bradycardia, peripheral edema, hypertension, hypotension, cough, abdominal distension, constipation, anorexia heartburn, nausea, polyuria, & petechia. Also, more than half of these reaction were life-threatening outcomes.

9. Recommendations:

1. Replication of the study on larger probability sample selected from different geographical areas in Egypt is recommended to determine national magnitude of this problem.
2. Before initiation of new medication, assess for potential drug–disease and drug–drug interactions and apply the rules of medication administration, the most common causes of ADRs, then starting new drugs.

Acknowledgment

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References:


American College of Medical Toxicology. (2007). Medication Errors and Adverse Drug Reactions or Events. Available at www.acmt.net/mht.


Figure (1): Distribution of the studied patients regarding their age (n=150).

Figure (2): Distribution of the studied patients in relation to gender (n=150).

Figure (3): Distribution of hospital stay for the studied patients (n=150).
Table (1): Distribution of Medical Diagnosis of the Studied Subjects (n=150).

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<th>Medical diagnosis</th>
<th>Frequency</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease (IHD)</td>
<td></td>
<td>25</td>
<td>16.5</td>
</tr>
<tr>
<td>Non independent diabetes mellitus (NIDDM)</td>
<td></td>
<td>13</td>
<td>8.7</td>
</tr>
<tr>
<td>Congestive heart failure (CHF)</td>
<td></td>
<td>20</td>
<td>13.3</td>
</tr>
<tr>
<td>Independent diabetes mellitus (IDDM)</td>
<td></td>
<td>7</td>
<td>4.7</td>
</tr>
<tr>
<td>Hypertension (HTN)</td>
<td></td>
<td>20</td>
<td>13.3</td>
</tr>
<tr>
<td>Liver Cirrhosis</td>
<td></td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td></td>
<td>12</td>
<td>8.0</td>
</tr>
<tr>
<td>Systemic Lupus</td>
<td></td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
<td>5</td>
<td>3.3</td>
</tr>
<tr>
<td>Renal Impairment</td>
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<td>1.3</td>
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<tr>
<td>Septic Shock</td>
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<tr>
<td>Gilliane Barrie</td>
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<tr>
<td>Cancer</td>
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<td>Renal Impairment</td>
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<tr>
<td>Septic Shock</td>
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<td>0.7</td>
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<tr>
<td>Disturbed conscious level (DCL)</td>
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<td>Disseminated intravascular coagulopathy (DIC)</td>
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<tr>
<td>More than one disease</td>
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<td>18</td>
<td>12</td>
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Figure (4): Prevalence of ADRs among studied subjects (n=150).

Figure (5): Distribution of the outcomes of reactions among studied subjects (n=150).
Table (2): Distribution of the onset of reactions, severity, duration, outcome and intervention for reactions of study sample (n=150).

<table>
<thead>
<tr>
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<tr>
<td><strong>Onset of reactions</strong></td>
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<tr>
<td>Slow</td>
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</tr>
<tr>
<td>Gradual</td>
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<tr>
<td>Immediate</td>
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<tr>
<td><strong>Severity of reactions</strong></td>
<td></td>
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<tr>
<td>Mild</td>
<td>13</td>
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<tr>
<td>Moderate</td>
<td>3</td>
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</tr>
<tr>
<td>Severe</td>
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<td>9.7</td>
</tr>
<tr>
<td><strong>Duration of reactions</strong></td>
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<td></td>
</tr>
<tr>
<td>Minutes</td>
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<tr>
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</tr>
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