ORIGINAL RESEARCH

Analysis and causality assessment of Adverse Drug Reactions of Antipsychotics in a tertiary care hospital: A Prospective study.

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Abstract

Aim: To determine the causality assessment of Adverse Drug Reactions of Antipsychotics in a tertiary care hospital

Methods

Total 150 eligible patients were enrolled from outpatient and inpatient Department of Psychiatry, GGSMCH Faridkot by using non probability convenient sampling technique. Each enrolled patient was followed up every 15 days for a period of 6 months for monitoring of adverse drug reactions. Causality assessment of adverse drug reactions if any, was done by using suitable scales like Naranjo Algorithm and WHO UMC Causality Assessment Scale.

Results

Total 35 ADRs were reported in 34 patients. Most common ADRs observed were EPS and dry mouth in 6 (17.14%) patients each, followed by dizziness, sedation, weight gain and constipation in 4 (11.43%) each, nausea in 3(8.57%) each, headache, postural hypotension, somnolence and tremors were observed in 1 (2.86%) patient each. Out of 34 patients who experienced ADRs , males were 67.60 percent and females 32.40 percent . No significant association was seen among gender and adverse drug reactions (p=0.786). On average , there were 1.02 ADRs per patient. Naranjo algorithm causality assessment scale reported maximum ADRs reported fell in possible category with 57.14 percent in number, 40.00 percent were in were in probable category , 2.86 percent were in doubtful category and none were reported in definite category. WHO UMC causality assessment scale reported maximum of 45.71 percent were in possible category, 31.43 percent in probable category , 22.86 percent were in unlikely category and none were reported in unassessable, conditional and certain category .

Conclusion :

Awareness and early detection of ADRs will help the consulting psychiatrist to make necessary alterations in the drugs prescribed or addition of newer drugs to reduce the symptoms of ADRs . This will ultimately help to improve patient care and compliance.

Keywords: adr, naranjo algorithm, who umc causality assessment scale

Introduction

WHO defined health as “A state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”. Mental health is said to be absolutely fine when a person is able to deal with the normal stressful situations of life, work productively and can contribute to community work (1).Psychiatric medications combined with other means such as psychotherapy and social rehabilitation are used to manage psychiatric disorders. These medications cause a wide range of potential adverse drug reactions thus leading to decrease in the quality of life, increased morbidity, increasing the cost of healthcare thus leading to discontinuation of therapy and subsequent loss to follow-up (2). So, it is important for psychiatrists to be aware of the processes involved in identifying and reporting Adverse Drug Reactions (ADRs) for these drugs. The processes involved form the basis for pharmacovigilance. Pharmacovigilance has been defined by the WHO as “The science and activities related to the detection, assessment, understanding and prevention of adverse drug effects” (3). The role of

pharmacovigilance in recognising, reporting and preventing ADRs in a psychiatry unit holds paramount importance as it can protect the patients from preventable harm and appraise the physicians regarding the feasibility of those events in the near future (4). ADRs may occur due to a single dose of a drug, prolonged administration of a drug or a combination therapy of two or more drugs. One of the leading causes of adverse drug reactions in psychiatric patients is polypharmacy (5). Patients with psychiatric illnesses require lifelong psychotropic medication therapy which puts them at risk for a variety of ADRs (6). Tremors, tardive dyskinesia, weight gain and somnolence are some of the typical side effects of psychiatric medications. Antipsychotics and mood stabilisers are the psychiatric medications most frequently linked to ADRs, according to studies (7). Theoretically, algorithms used to assess ADRs should be able to determine causation with greater certainty because they are organised systems created specifically for the identification of an ADRs. Monitoring of Adverse drug reactions helps to develop suitable strategies for intervention to manage, prevent and minimize the risk of developing ADRs and thereby cost of care can be reduced (8). So, in this study, we evaluated the various ADRs to antipsychotic drugs used in psychiatry patients, estimated the incidence of ADRs, assessed the causality of documented Adverse drug reactions to antipsychotic drugs in Psychiatry department of our hospital. We used Naranjo algorithm and the WHO-UMC criterion, two most commonly used pharmacovigilance techniques for the same.

Materials & Methods

The present study was conducted in the Department of Psychiatry, Guru Gobind Singh Medical College and Hospital, Faridkot. It was a one year study. Subjects aged between 18 and above, registering as OPD/IPD patients, fulfilling the inclusion and exclusion criteria were included in the study. The diagnosis was confirmed by consultant of the department . An informed consent was taken from the patient and caregiver. Prescriptions of the patients visiting the OPD were collected on the first day of visit. The prescription of the patients admitted in ward under IPD were noted and they were monitored for any adverse drug reaction throughout their duration of stay in the hospital. Both OPD and IPD patients were also followed up for 6 months during subsequent visits to the hospital in the OPD .The patient's sociodemographic profile , illness related variables like history of illness , past history, any known drug allergy and Psychiatric prescription were documented in the structured Performa. The record of each follow up of patient was maintained on follow up performa. Routine investigations (CBC, blood sugar levels, blood urea, serum creatinine and electrolytes, liver function tests, viral markers- HIV, HCV, HBsAg) were done as required. In case during follow up visit , any patient reported ADRs it was documented on the Suspected Adverse Drug Reaction Reporting Form and reported to the Pharmacovigilance Center of the institute in the Pharmacology Department. Suitable scales (Naranjo Algorithm and WHO UPC Causality assessment scale) were applied on those patients in which ADRs were reported . Most of the ADRs reported in the study were sought by active surveillance rather than passive reporting . This study was conducted up to a period of 1 year. The follow-ups will be done every 15 days for a period of 6 months**.**

Statistical Analysis

The data pertaining to socio-demographic and other clinical variables was entered as a data matrix in Microsoft® Excel® and analysed using IBM SPSS version 26, in the light of suitable statistical tests. Data were described in terms of range ; mean±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi square (X2) test was performed and exact test was used when the expected frequency is less than 5. A probability value *(p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 26 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

Results

Total 173 patients who were on antipsychotics and who fulfilled the inclusion and exclusion criteria were included in the study. 22 patients had loss to follow up, thus the final sample population consisted of 151 patients of which 90 cases were from the OPD while 61 patients were admitted in ward under IPD. Majority of patients in the present study were in age group 31-40 years with 43 (28.5%) patients. Least number of patients were present in age group =>60 with 6 (4%) patients. The mean age of the patients was 37.89±12.1 years. Males dominated in the present study population being 69.5 percent and females were 30.5 percent. Total 35 ADRs were reported in 34 patients. Most common ADR observed were EPS and dry mouth in 6 (17.14%) patients each , followed by dizziness, sedation , weight gain and constipation in 4 (11.43%) each , nausea in 3(8. 57%) each , headache, postural hypotension, somnolence and tremors were observed in 1 (2.86%) patient each. Naranjo algorithm causality assessment scale reported maximum ADRs fell in possible category with 57.14 percent, 40.00 percent were in were in probable category, 2.86 percent was in doubtful

category and none were reported in definite category. WHO UMC causality assessment scale reported maximum of 45.71 percent were in possible category, 31.43 percent in probable category , 22.86 percent were in unlikely category and none were reported in unassessable, conditional and certain category . Maximum ADRs were seen with Risperidone being 12 in number ,second most common being 11 with Quetiapine ,10 with Olanzapine, 4 each with Amisulpride and Haloperidol and 2 each with Aripiprazole, Clozapine and Trifluperazine respectively. 35 ADRs were observed in a total 34 patients. According to Naranjo Algorithm, maximum ADRs were under possible (20, 57.14 %) category, probable were 14 (40.00%), doubtful was 1(2.86 %) and none was under definite category. As per WHO UMC causality assessment scale 16 (45.71%) were under possible category, 11 (31.43 %) were under probable category, 8 (22.86%) were unlikely, none were under conditional/unclassified, unassessable/unclassifiable and certain category. Maximum of 19 (12.6%) ADRs were reported during first follow up at 15 days, 4 (2.6%) ADRs were reported each at 30 and 45 days, 1 (0.7 %) was reported at 60 days , 2 (1.3 %) each were reported at 2.5 months and 3 months , none were reported at 3.5 and 4 months ,1 (0.7 %) was reported at 4.5 months ,none were reported at 5 and 5.5 months and 1 (0.7 %) was seen at 6 months . Maximum ADRs were reported during first 3 months of follow up, being total 33 (94.26 %) out of 35 reported during these months.

Table 1: Distribution of patients according to incidence and number of adverse drug reactions

ADVERSE DRUGS REACTIONS	FREQUENCY	NO OF ADRs	PERCENT
ABSENT	117	0	77.5
PRESENT	34	35	22.5
TOTAL	151	35	100

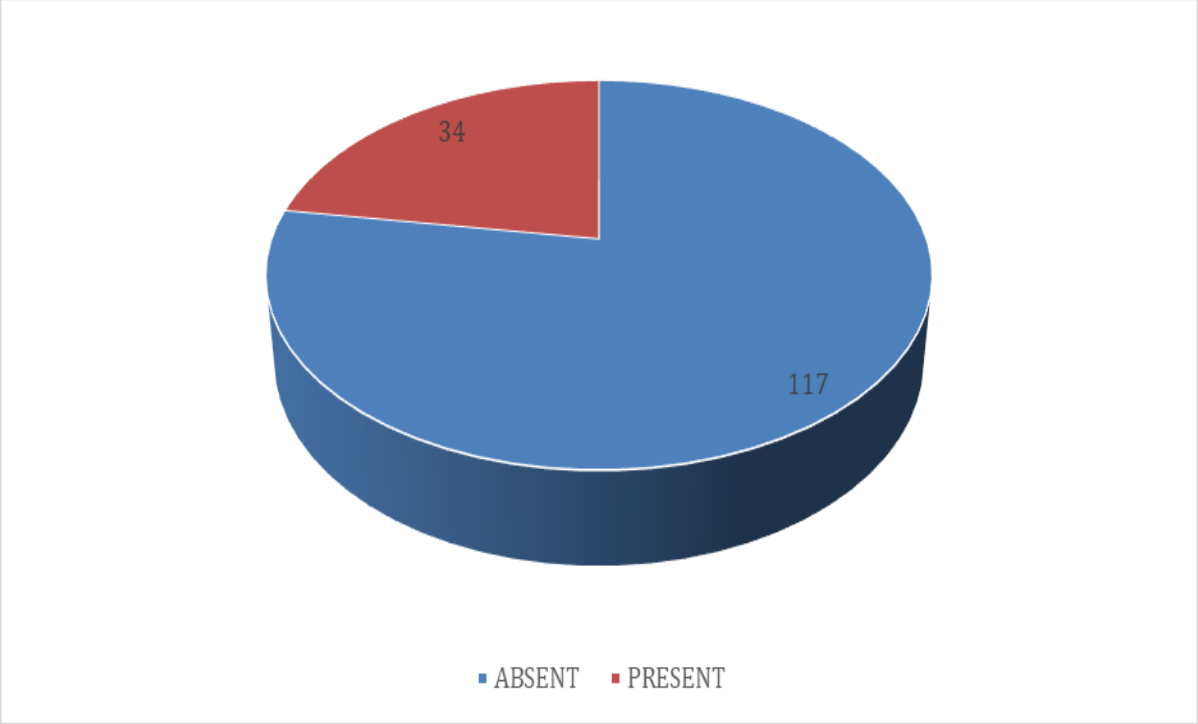


Table 2: Total ADRs reported in the study

ADR	Frequency	Percentage
EPS	6	17.14%
DRY MOUTH	6	17.14%
DIZZINESS	4	11.43%
SEDATION	4	11.43%
WEIGHT GAIN	4	11.43%
CONSTIPATION	4	11.43%
NAUSEA	3	8.57%
HEADACHE	1	2.86%
POSTURAL HYPOTENSION	1	2.86%
SOMNOLENCE	1	2.86%
TREMORS	1	2.86%
TOTAL	35	100.00%

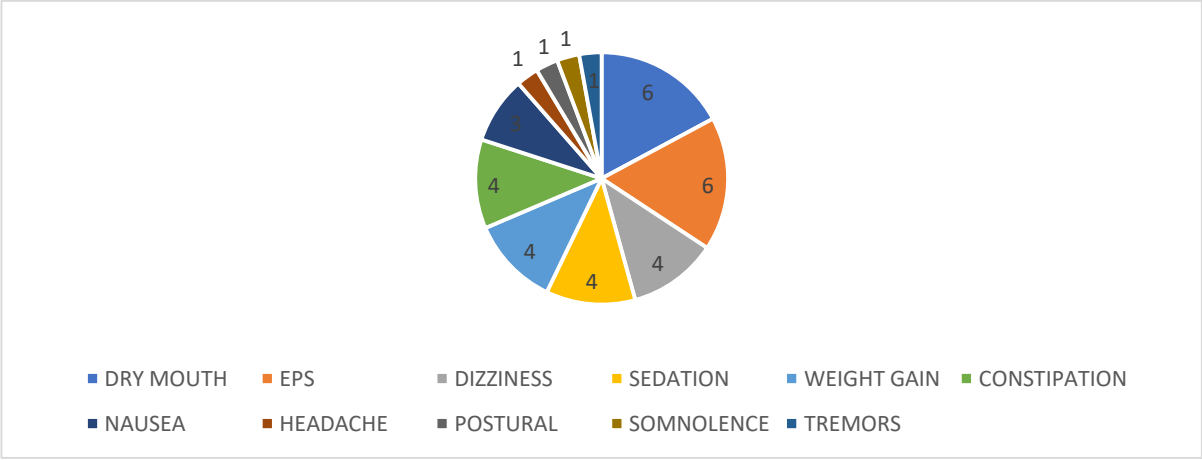


Table 3: NARANJO ALGORITHM

CATEGORY	FREQUENCY	PERCENT
DOUBTFUL	1	2.86%
POSSIBLE	20	57.14%
PROBABLE	14	40.00%
DEFINITE	0	0.00%

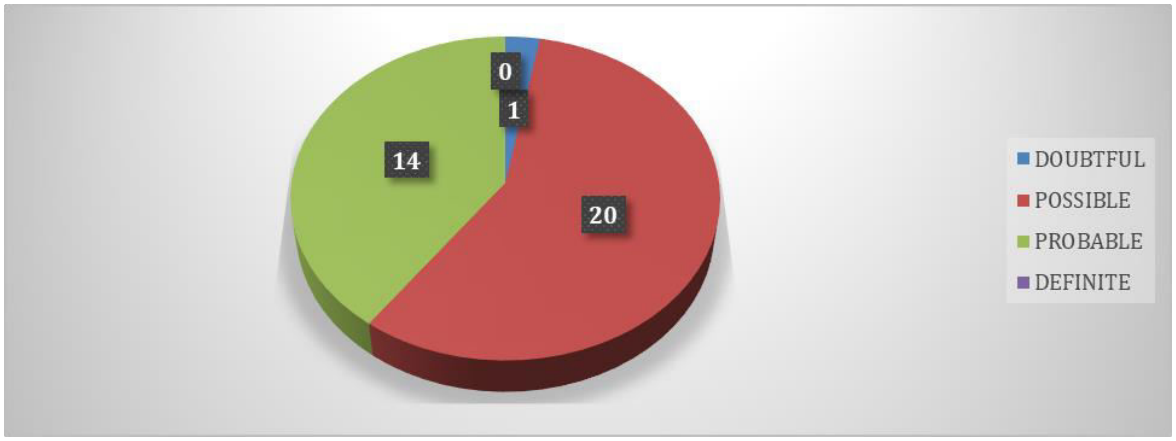
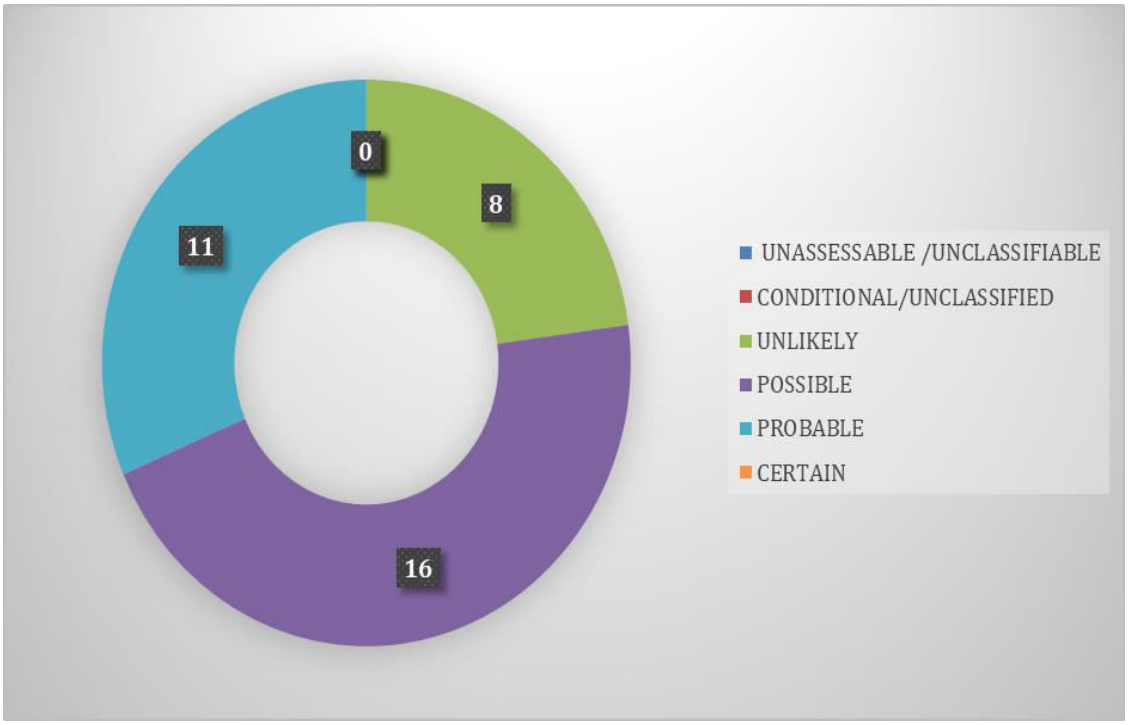


Table 4: WHO UMC CAUSALITY ASSESSMENT SCALE

WHO UMC CAUSALITY ASSESSMENT SCALE	FREQUENCY	PERCENT
UNASSESSABLE /UNCLASSIFIABLE	0	0
CONDITIONAL/UNCLASSIFIED	0	0
UNLIKELY	8	22.86%
POSSIBLE	16	45.71%
PROBABLE	11	31.43%
CERTAIN	0	0
TOTAL	35	100%



Discussion

Adverse drug reactions pose a significant impact on the quality of life and affect compliance and adherence of treatment .So it is essential that clinician should be well versed with these adverse affects .Majority of patients in this study belonged to age group 31-40 years with 43 (28.5%) patients . Similarly in a study by Chawla et al. majority of the patients belonged to the age group of 31–40 years (31.4%) .The mean age of the patients was 37.89±12.1 years (9). In this study, maximum patients were on olanzapine (49,32.5%) followed by quetiapine (39,25.8%), risperidone (37,24.5%), trifluoperazine (21,13.9%), haloperidol (17,11.3%), clozapine (11,7.3%), amisulpride (9,6%), fluphenazine (1,0.7%), ziprasidone (1,0.7%). In 113 (74.8%) patients atypical drugs were used , in 13(8.6%) typical drugs were used and in 25 (16.6%) patients both typical as well as atypical drugs were used.

No significant association was seen in this study among age group and ADRs. However it was seen that that ADRs were more in age group >41-50 years being 12(35.30%) in number, but it was not statistically significant(p=0.08). Angadi et al (10) in their study showed no statistically significant relationship of ADRs with age or gender of the study population which was in accordance to this study.In this study , it was observed that out of total 151 patients enrolled , ADRs were absent in 117 patients (77.5%) while they were present in 34 (22.5%) patients. In a study by Hemendra et al. ADRs were seen in 15.5% patients on antipsychotic drugs. Chawla et al. (8) in their study reported incidence of ADR to be 16.96% , as total 67 adverse drug reactions were found in 61/250 (24.4%) patients. Angadi et al.,(10) in their study reported the overall prevalence of ADRs in patients with antipsychotics to be 51.9%. Also in a study by Ahmed et al.(11) with the utilization of antipsychotics, the prevalence of ADRs was as high 43.5%. On basis of above studies, the rate of ADRs with antipsychotics varies between 15.5 to 51.9%. In present study the prevalence of ADRs with antipsychotics is 22.5% which is within the range of above mentioned previously conducted studies. Hemendra et al.,(12) in their study showed that among the antipsychotic drugs, Risperidone (41,36.6%) was the most commonly implicated drug in causing ADRs followed by Olanzapine (26 ,23.2%).The findings in our study are similar to this study with maximum ADRs in the study population seen with Risperidone being 12 (25.53 %) in number ,followed by 11(23.40 %) in Quetiapine , 10 (21.27 %) in Olanzapine, 4 (8.51%) each in Amisulpride and Haloperidol and 2 (4.26%) each in Aripiprazole ,Clozapine and Trifluoperazine respectively In our study, in 34 patients total 35 ADRs were reported. Most common ADRs observed were extrapyramidal symptoms and dry mouth (6,17.14% each), followed by dizziness, sedation, weight gain and constipation (4,11.43% each), nausea (3,8.57%) , headache, postural hypotension , somnolence and tremors were observed in 1(2.86%) patient each . Study of Munoli S et al.,(13) also reported maximum ADRs to be extrapyramidal symptoms (15) followed by anticholinergic side effects (10) and weight gain seen in

8 patients. Most of the adverse effects in the study for e.g.dry mouth and constipation were managed conservatively with interventions like intake of more fluids and dietary changes , some required treatment with Trihexyphenidyl , in some patients dose of the drug was reduced or either the drug was replaced with alternative drug.In our study, according to Naranjo algorithm, in 1(2.86%) ADR was doubtful, in 20(57.14 %) they were possible and in 14(40 %) they fell under probable category . According to WHO causality assessment scale, in 8(22.86%) the ADRs were unlikely, in 16 (45.71 %) they were possible and 11(31.43%) were reported in probable category. None of the ADRs were under certain, unclassifiable and conditional category. Rechallenge test was not attempted with the offending drug in our study. Maximum ADRs reported were in possible category according to both Naranjo algorithm (57.14%) and WHO UMC assessment scale (45.71%). Sridhar et al.,(14) conducted a study on 714 patients and observed total 112 ADRs. Naranjo causality assessment showed 10(9%) ADR to be definite, 38 34%) to be probable, 60(53.5%) to be possible and 4(3.5%) to be doubtful. In WHO UMC causality assessment scale 16(14.3%) were certain, 39(34.9%) to be probable, 51(45.5%) to be possible, 1(0.9%) to be unclassifiable, 2(1.8%) to be unlikely and 3(2.7%) to be conditional. The findings of our study are similar to the findings of the above mentioned study directed by Sridhar et al. In our study maximum ADRs were reported during first 3 months of follow up being total 33 (94.26 %) out of 35 during these 6 months. Similarly study done by Guo et al.,(15) also showed maximum ADRs reported in first 3 months (97.26 %). In his study cumulative reporting proportion was 6.99 % one the same day, within a week it was 36.52 %, and 78.56 % within a month.There are potential limitations to our study. Being majority of the adverse drug reactions reported by active surveillance by the healthcare staff on follow up visits and less of reporting by patients themselves, it is likely that we might have missed ADRs that were transient or too mild that the patient would not have reported the same.The size of the study population does not allow the observation of rare adverse effects that occurs in one patient out of thousand.

Conclusion

In this study , adverse drug reactions to various antipsychotics were assessed prospectively in psychiatry department of a tertiary care hospital. The study concluded that incidence of adverse drug reactions was 22.5 percent. A considerable number of patients who developed ADRs were on atypical antipsychotics. Extrapyramidal symptoms and dry mouth were the most commonly occurring ADRs. Risperidone was prescribed in maximum study patients having adverse drug reactions. No statistically significant association was seen with ADRs based on sociodemographic profile of the patients. An in depth knowledge about the ADRs and the causative drugs helps in proper selection of the drugs for the patient. Awareness and early detection of ADRs will help the consulting psychiatrist to make necessary alterations in the drugs prescribed or addition of newer drugs to reduce the symptoms of ADRs. ADRs can perhaps be reduced by using less medication and with adequate knowledge of drug interactions. This will ultimately help to improve patient care and compliance.

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