Assessment of drug-related problems in depressive patients

Background: Drug-related problems (DRPs) frequently occur in modern medical practice, increasing the morbidity and mortality as well as increasing cost of care. Objective: The study is to evaluate the incidence of DRPs in patients admitted to a psychiatric department. Materials and Methods: A prospective observational study was conducted for a period of 4 months at Baliga psychiatric hospital. All prescriptions of the study population were screened for DRPs such as adverse drug reactions (ADRs) and potential drug-drug interactions (pDDIs) by using computerized database system. Results: Out of 120 patients, 19 patients had observed 26 DRPs. Out of 33 patients, 19 patients had observed 26 ADRs and 14 patients had observed 24 pDDIs. The overall incidence of DRPs was 15.83%. Female patients outnumbered the male patients, in which 12 women constitute 10% followed by men 7 (5.83%). The common ADRs observed were hyponatremia and headache. Considering the outcomes, 20 (76.9%) cases recovered from ADRs and 20 (76.9%) of the ADRs were definitely preventable. Majority of ADRs were probable and were found to be mild to moderately severe. Conclusions: Age, female gender and polypharmacy were the risk factors for the developing DRPs. Key words: Depression, drug-related problems, psychiatric

INTRODUCTION

Drug-related problems (DRPs) are events involving drug therapy that actually or potentially interfere with desired health outcomes. DRPs are prevalent and cause considerable patient morbidity and mortality, as well as increased healthcare costs. Antidepressants are the third ranked therapeutic class in global pharmaceutical sales,
totaling USD 17.1 billion and growing at a rate of 5% annually. In addition to treating depressive disorders, antidepressant drugs are increasingly used to treat other illnesses, including anxiety disorders, chronic pain, and eating disorders. In many cases, antidepressant drugs are used concurrently with other medications, thus exposing patients to potential harm owing to adverse drug reactions (ADRs). Patients with depressive disorder are particularly vulnerable to drug-drug interactions (DDIs) and ADRs due to their advanced age, polypharmacy, and the influence of psychiatric disease on drug metabolism. ADRs appear to be, between the fourth and sixth leading cause of death in India and the United States and they lead to an additional USD 4 billion in direct hospital costs per year. Limited data were available on antidepressants and ADRs in the medically ill Indian patients. Hence, there is a need for the development of a uniform, prospective, well-defined monitoring program to enhance awareness and promote research in depressive patients. The objective of the study is to analyze the incidence of DRPs in patients admitted to a psychiatric department.

MATERIALS AND METHODS

A prospective observational study was conducted for a period of 4 months at Baliga psychiatric hospital, Udupi. Ethical approval was obtained from the hospital ethics committee prior to the initiation of the study. Informed consent was obtained from the patient/patient’s party for enrollment in the study. Patients admitted consecutively to the psychiatric department, who were taking at least two drugs and had a hospital stay of at least 24 hours, were included in the study. Patients referred to the psychiatric unit for evaluation, patients visiting on outpatient basis and patients who died during hospital stay were excluded from the study. Demographic information, number of drugs taken, duration of hospital stay and laboratory investigations were obtained from the patients’ and clinical records. Certain demographic characteristics were studied to find out the risk factors for DRPs such as patient characteristics [gender, age (more than 18 years old), concurrent morbidities and duration of stay], drug characteristic (number of drugs) and laboratory investigations. All the prescriptions were screened for potential drug-drug interactions (pDDIs) by using computerized database system (Drug Reax-Micromedex, 2008) and ADRs are identified from volunteered symptoms or observed signs from patients. For determining the DRPs, both the medications added as well as discontinued were considered.

Causality assessment was done by using Naranjo’s ADR probability scale. The Naranjo algorithm or Naranjo Scale is a questionnaire designed by Naranjo et al., for determining the likelihood of whether ADRs are actually due to the drug or the result of other factors. Severity, preventability and the presence of predisposing factors for the reaction was analyzed. Preventability of ADRs were categorized by using the criteria of Schumock and Thornton modified. Further, any possible relationship between the patient characteristics and the characteristics of the reaction was assessed. Management strategies were employed for the management of ADRs and categorized as drug withdrawal, dose reduction, additional treatment for ADR, and no change in regimen with any additional treatment. Further, categorization of the outcome of ADRs was done for response after dechallenge and rechallenge as well as the outcomes of the event.

Statistical analysis

Frequencies with percentage were used to summarize age, gender, number of drugs taken, number of diseases, frequency of ADRs, drugs involved in the ADRs and severity of ADRs. Mean and standard deviation was used to summarize age and number of drugs taken. Median and range was used to summarize number of diseases. Chi square test was used to find the association between age, gender, number of drugs, number of diseases and DRPs. A P < 0.05 was considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences software (SPSS version 18).

RESULTS

Out of 120 patients, 33 patients had observed a minimum of one ADR and pDDI and maximum of two ADRs and pDDIs. Among 33 patients, 19 patients had observed 26 ADRs and 14 patients had observed 24 pDDIs. Although the pDDIs were not observed during the study, healthcare professionals should be aware of this during their prescription as it had the potential to occur. The overall incidence of DRPs in the present study was 15.83% (n = 19). Among the 19 patients, one patient developed a minimum of one DRP and maximum of two DRPs. Female patients outnumbered the male patients, of which 12 women constitute 10% followed by men 7 (5.83%), the age group of 40-60 years had 9 (7.5%), followed by other age groups. Most of the DRPs were developed in 12 (10%) patients with a length of their stay in hospital of >7 days, followed by 7 (5.83%) with <7 days. Patient characteristics and statistically significant of the results were summarized in the Table 1.

In the present study, sertraline 6 (23.07%), amitriptyline 4 (15.38%) and lithium 4 (15.38%) were the most commonly observed drugs involved and the common
ADRs observed were hyponatremia 9 (34.61%) and headache 4 (15.38%). Incidence of individual suspected drugs with their ADRs results were summarized in the Table 2. All the ADRs were confirmed to have the possible causality by using Naranjo algorithm. The suspected drugs were withdrawn in 3 cases (11.53%) and dose was altered in 3 cases (11.53%). Six (23.07%) patients improved after dechallenge was done. Rechallenge was done in 6 patients and no recurrences of symptoms were observed. These adverse drug interactions were classified into mild, moderate and severe, in which, 20 (76.92%) were mild followed by 6 (23.07%) were moderate. Predictability and preventability were as depicted in management, outcome and analysis of ADRs, which were summarized in the Table 3.

DISCUSSION

Our study revealed that the overall incidence of DRPs in the study population were 15.83% which is low, compared to similar studies. Our findings showed that the patterns of incidence of DRPs are positively associated with patient’s age, gender and number of drugs prescribed. A higher rate of DRPs was present in female patients and particularly in the age group of 40-60 years. These results are in accordance with the observations of similar reported studies.

It is important to recognize that the absence of reported ADRs is no evidence but may reflect many antidepressants have not

Table 1: Patient characteristics

| Patient demographics | Number of patients with DRPs (%) |
|----------------------|----------------------------------|
| Age (years)          |                                  |
| Mean±SD              | 44.9±14.15                      |
| 20-40                | 4 (3.33%)                        |
| 40-60                | 9 (7.5%)                         |
| >60                  | 6 (5%)                           |
| Gender group (%)     |                                  |
| Male                 | 7 (5.83)                         |
| Female               | 12 (10)                          |
| No of diseases       |                                  |
| Median (range)       | 2 (1-4)                          |
| 1-2                  | 6 (5%)                           |
| >3                   | 13 (10.83%)                      |
| No of drugs taken    |                                  |
| Mean±SD              | 6.2±1.51                         |
| <5                   | 8 (6.66%)                        |
| >5d                  | 11 (9.16%)                       |

1. χ² = 27.73, df = 2 P < 0.001; 2. χ² = 3.8 P = 0.05; 3. χ² = 6.89, df = 2 P = 0.045; 4. χ² = 5.52 P < 0.000, SD: Standard deviation, DRP: Drug-related problem

Table 2: Suspected drug with their adverse drug reactions

| Suspected drug | Adverse outcome | Number of ADRs (%), (N=26) |
|----------------|-----------------|-----------------------------|
| Sertraline     | Hyponatremia    | 5 (19.23)                   |
|                | Increased       | 1 (3.84)                    |
| Lithium        | Hyperkalemia    | 3 (11.53)                   |
|                | Hypercalcemia   | 1 (3.84)                    |
| Fluoxetine     | Hyponatremia    | 3 (11.53)                   |
|                | Loss of appetite| 1 (3.84)                    |
| Amitriptyline  | Seizure         | 2 (7.69)                    |
|                | Confusion       | 1 (3.84)                    |
|                | Headache        | 1 (3.84)                    |
| Escitalopram   | Headache        | 3 (11.53)                   |
| Clonazapine    | Seizure         | 1 (3.84)                    |
|                | Weight gain     | 1 (3.84)                    |
| Olanzapine     | Weight gain     | 1 (3.84)                    |
| Zolpidem       | Abnormal dreams | 1 (3.84)                    |

ADR: Adverse drug reactions

Table 3: Management, outcome and analysis of ADRs

| Parameters                        | Number of ADRs (%), (N=26) |
|-----------------------------------|----------------------------|
| Management                        |                            |
| Drug withdrawn                    | 3 (11.53)                  |
| Dose altered                      | 3 (11.53)                  |
| No change                         | 20 (76.92)                 |
| Treatment given                   |                            |
| Specific                          | 6 (23.07)                  |
| Symptomatic                       |                            |
| Nil                               | 20 (76.92)                 |
| Outcome                           |                            |
| After dechallenge                 |                            |
| Definite improvement              | 6 (23.07)                  |
| No improvement                    |                            |
| Unknown                           |                            |
| After rechallenge                 |                            |
| Recurrence of symptoms            |                            |
| No recurrence of symptoms         | 6 (23.07)                  |
| Unknown                           |                            |
| Final outcome                     |                            |
| Fatal                             |                            |
| Recovery                          | 20 (76.92)                 |
| Continuing                        | 6 (23.07)                  |
| Unknown                           |                            |
| Severity                          |                            |
| Mild                              | 20 (76.92)                 |
| Moderate                          | 6 (23.07)                  |
| Severe                            |                            |
| Predictability                    |                            |
| Predictable                       | 26 (100)                   |
| Non-predictable                   |                            |
| Preventability                    |                            |
| Definitely preventable            | 20 (76.92)                 |
| Probable preventable              | 6 (23.07)                  |
| Not preventable                   |                            |

ADR: Adverse drug reactions
been properly evaluated for ADRs. Sertraline 6 (23.07%), amitriptyline 4 (15.38%) and lithium 4 (15.38%) were the most commonly observed drugs involved in the present study and the common ADRs observed was hyponatremia 9 (34.61%), headache 4 (15.38%) and followed by others. These results were supported by similar studies.[6,13,14]

LIMITATIONS AND FUTURE DIRECTIONS

The duration of this study was only for 4 months and the patients were monitored from the date of their admission till the date of their discharge. The sample required for this study was not computed. Intervventional studies should be performed to investigate whether good clinical management of DRPs can reduce drug-related morbidity or mortality by providing pharmaceutical care. Identification of DRPs with resolution is one of the prime objectives of pharmaceutical care.

CONCLUSIONS

Our study results conclude that age, female gender and polypharmacy were the risk factors to develop the DRPs. Over time, ongoing program to monitor and report DRPs may help to measure the economic impact of pDDIs and ADRs prevented, as manifested through reduced hospitalization, efficient and economical drug use, and minimize organizational liability and entail the safety of the patient. The challenges for the pharmacist are to identify the DRPs and search for comparable therapy and convince the physician regarding the preference of the idea, which can resolve the DRPs. Hence, there is an imperative need of the pharmacist to improve the patient care and safe use of medicines.

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