Paracetamol Induced Hepatotoxicity in Inpatients of a Tertiary Care Teaching Hospital

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Abstract-
Although excessive dosages of paracetamol can cause severe liver necrosis and fatal hepatic failure, it is a widely used medicine with a fair safety profile. If treated early enough, paracetamol overdose can be efficiently treated with intravenous N-acetylcysteine, but if hepatic encephalopathy develops, the risks of complications and death skyrocket. After a paracetamol overdose, orthotopic liver transplantation (OLT) is a treatment option for liver failure. The current study aimed at analyze the incidence and outcome of acute or chronic paracetamol overdosing among patients admitted in a tertiary hospital and identify the Adverse drug reactions of paracetamol. It was a prospective observational study which was carried out for a period of 1 year in vivekananda general hospital, Hubballi. When compared to deliberate paracetamol overdose, unintentional paracetamol overdose is linked to higher mortality. The paracetamol concentrations are directly linked to the reduced admission rate. Delay in presentation and/or admission and treatment, encephalopathy of various grades, coagulopathy, and renal dysfunction were the most common causes of poor outcomes

Index Terms - Paracetamol, Adverse Drug Reaction, Hepatotoxicity, N-acetylcysteine, Encephalopathy.

I. INTRODUCTION

Although excessive dosages of paracetamol can cause severe liver necrosis and fatal hepatic failure, it is a widely used medicine with a fair safety profile. If treated early enough, paracetamol overdose can be efficiently treated with intravenous N-acetylcysteine, but if hepatic encephalopathy develops, the risks of complications and death skyrocket. After a paracetamol overdose, orthotopic liver transplantation (OLT) is a treatment option for liver failure[1].

Concerns about paracetamol overdose prompted around 10% of all calls to the UK National Poisons Information Service in 1996, and 73 000 (almost 113 000 including paracetamol-containing medicines) reports to the American Association of Poison Control Centers' Toxic Exposure Surveillance Scheme. Infants and young children may be less susceptible to paracetamol toxicity after acute ingestion than adults due to age-related differences in drug metabolism and detoxification of paracetamol metabolites, but delayed presentation and treatment significantly increases the risk of clinically significant hepatocellular injury[1].

The most often used antipyretic and pain reliever is paracetamol, also known as acetaminophen, which has been available over-the-counter since 1955 as a single formulation or in combination with other substances. This medicine, according to the World Health Organization, can be used in all three stages of pain severity. It is the most commonly recommended medication for minor aches, although it can also be used to treat moderate symptoms when combined with non-steroidal analgesics. Paracetamol is used as a supplementary analgesic in combination with weak (e.g. tramadol) or strong (e.g. morphine, fentanyl) opioids when pain continues or worsens. Furthermore, it is the drug of choice in patients for whom non-steroidal anti-inflammatory drugs are contraindicated, such as in the case of gastric ulcers, aspirin hypersensitivity, blood coagulation impairments, pregnant women, nursing mothers, and children with a

disease-related elevated body temperature (fever related to illness)[2].

Although various side effects associated with medication use have been documented since its approval in the 1950s, hepatotoxicity was not discovered until 1980. During the mid-1980s, cases of fatal drug-related hepatotoxicity labelled "therapeutic misadventures" and the link between paracetamol poisoning and alcohol were first recorded[3]. One of the most common medications that youngsters inadvertently consume is paracetamol. Unlike adults, mortality and hepatotoxicity from paracetamol intoxication are extremely rare in children. Only seven deaths and fourteen cases of hepatotoxicity in children were found in a study of the literature, with the majority of the cases occurring from chronic poisoning rather than acute poisoning. Because of developmental changes in the drug's metabolism and detoxifying mechanisms, children may be less susceptible to paracetamol hepatotoxicity. Paracetamol is viewed as a medicine with a greater therapeutic index in the therapeutic setting of treating fever and pain in children, and as such, rigorous adherence to dosing regimens appears to be of little consequence. The foregoing paediatric cases of chronic paracetamol poisoning imply that the margin of safety of frequent therapeutic paracetamol dosages in newborns and young children is much smaller than previously thought. The necessity to re-evaluate the safety of paracetamol in the context of chronic therapy in newborns and young children is highlighted by this review[3].

In a significant number of cases, the patient has also overdosed on one or more other medicines; these substances may influence the outcome of the paracetamol intoxication through pharmacokinetic interaction or independent toxic or hepatoprotective effects. An increased or decreased rate of paracetamol absorption, reduced paracetamol conjugation, glutathione depletion, and suppression of cytochrome P450-mediated metabolism are suggested mechanisms of interaction (Bhattacharya et al., 2012), as well as an innate inflammatory stimulation (Roth and Ganey, 2010). Between 1994 and 2000, Schmidt and Dalhoff (2002) found that 31 percent of patients (207/671) had simultaneous drug overdose (95 percent CI 27–34 percent). The most commonly prescribed medications were benzodiazepines, opioid analgesics, acetylsalicylic acid (ASA), and nonsteroidal anti-inflammatory medicines (NSAIDs)[4]. The current study aimed at analyze the incidence and outcome of acute or chronic paracetamol overdosing among patients admitted in a tertiary hospital and identify the Adverse drug reactions of paracetamol and demographic details of study population.

II. METHODOLOGY

It was a prospective observational study which was carried out for a period of 1 year in vivekananda general hospital, Hubballi. In-patient who are admitted in vivekananda general hospital were included in the study. The study included in-patients undergoing acetaminophen therapy. The patient data was collected using patient data case sheets and laboratory investigation. The patient specific information was obtained from patients' medication profiles and case profiles. Patients' demographic details, medication history, clinical and laboratory data, progress chart, diagnosis and drugs given were reviewed and documented in a suitably designed data collection form.

III. RESULTS

Total of 20 patients were included the in the study. Out of which 11 were males and 09 were females. It showed that, Males was higher than females.

Figure 1 shows that, most of our study patients falls in the age group ranges from 41-50 years. Maximum number of toxicity population was from the age group of 41-50 followed by 51-60.

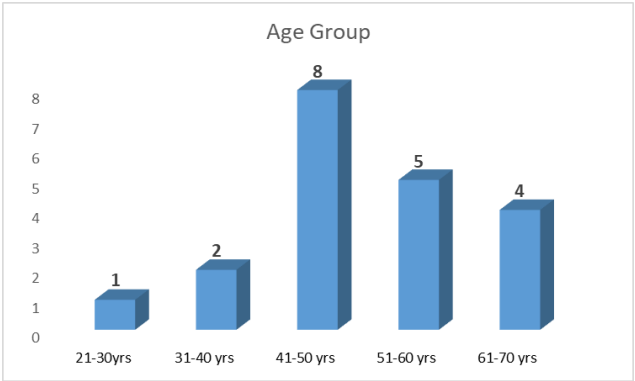

Fig No 1: Age Distribution of the Study Population

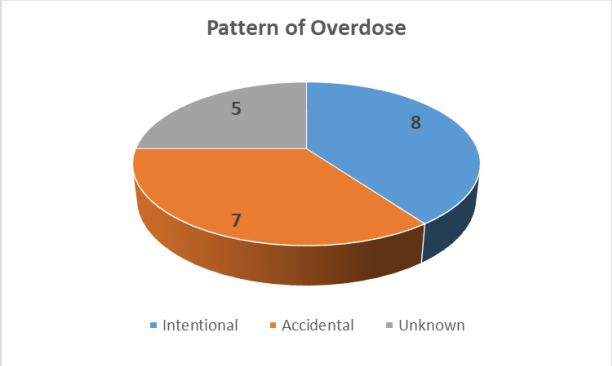

Fig No 2: Pattern of Overdose

Figure 2 shows that most of our study patients overdosed intentionally for one or another reason. The intentional overdose was seen in 08 patients and accidental in 07 patients.

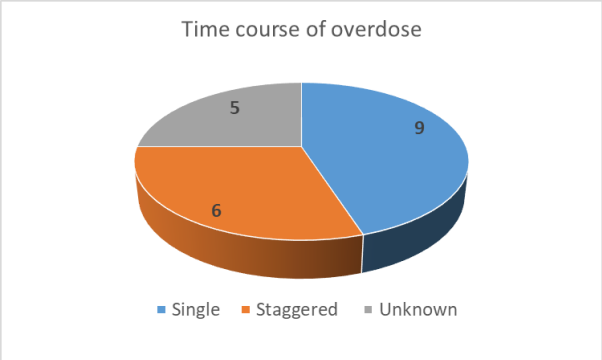

Fig No 3: Time Course of Overdose

Figure 3 shows that most of our study patients' course of overdose was single (9), staggered (6) and unknown (5).

Few of our study patients were associated alcohol with overdose. Male and women were 06 & 01 respectively. Study also showed that, that there were 07 female patients and 04 male had previous psychiatric history. It confirmed that Female were greater than male. Study also confirmed that there were 11 male patients and 03 female had active drug abuse resulting males were greater associated with active drug abuse than females. 07 female patients and 01 male had previous history of overdose. Female were greater associated than male. 03 female patients and 01 male had unemployed at time of overdose. Female were greater associated than male

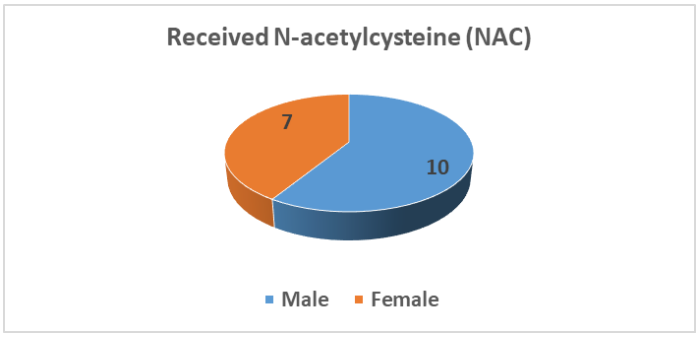

Fig No 4: Received N-acetylcysteine (NAC)

Figure 4 shows that Out of 20, there were 10 male patients and 07 female had received N-acetylcysteine (NAC) during hospital visit.

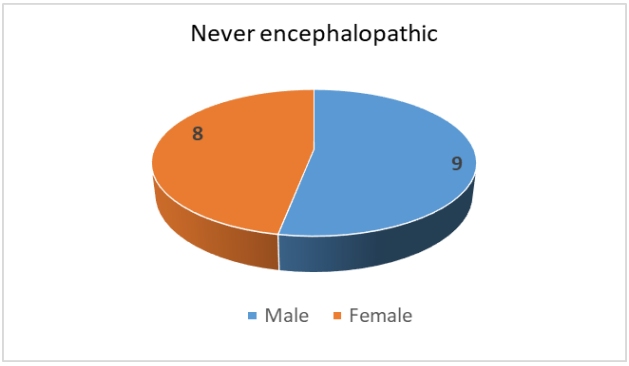

Fig No 5: Never encephalopathic

Figure 5 shows that Out of 20, there were 9 male and 08 female patients never had history of encephalopathy during hospital visit.

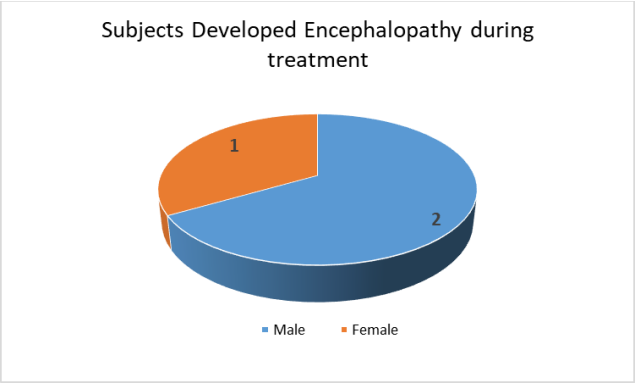

Fig No 6: Subjects Developed Encephalopathy during treatment

Figure 6 shows that there were 02 male patients and 01 female had developed encephalopathy during treatment.

Study shows that, all the 20 patients survived concludes that the survival rate is higher than death rate after proper treatment.

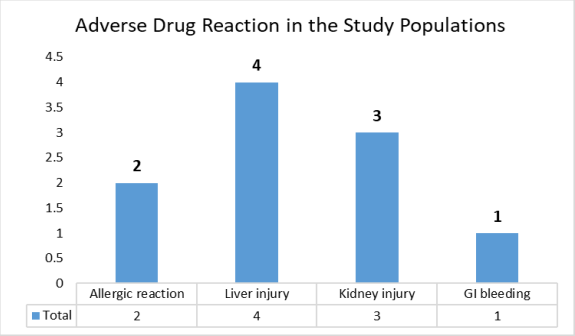

Fig No 7: Subjects Developed Encephalopathy during treatment

Figure 7 shows that, there were total 10 ADR's found in the study. The most common ADR found was liver injury (4) followed by kidney injury (3), allergic reaction (2) and GI bleeding (1).

IV. DISCUSIONS

In children, overdosing on paracetamol produces toxic liver damage and encephalopathy less frequently than in adults, although it can still be fatal [(1)]. We looked at the impact of suicidal ideation on patient outcome in this small observational research of paracetamol-induced acute or chronic severe liver injury. The most common pattern of paracetamol ingestion was intentional (suicidal) overdose, which accounted for more than half of all paracetamol cases. Individuals who overdosed unintentionally had a shorter survival rate than those who overdosed intentionally, despite having lower admission paracetamol and ALT readings[5]. The study's limitations include the small number of patients, the fact that it was conducted at a single centre, and the lack of established overdose criteria. Previous research has connected accidental paracetamol overdose to an increased risk of death. More cohort studies of paracetamol hepatotoxicity, on the other hand, have not consistently revealed a worse outcome [5-6]. Previous research has discovered that nephrotoxicity (8.9%) and oliguric renal failure occur in 1–2% of all cases and 11% of severely poisoned patients [1].

V. CONCLUSION

When compared to deliberate paracetamol overdose, unintentional paracetamol overdose is linked to higher mortality. The paracetamol concentrations are directly linked to the reduced admission rate. Overdosing on paracetamol can cause acute or chronic liver damage in both adults and children. Delay in presentation and/or admission and treatment, encephalopathy of various grades, coagulopathy, and renal dysfunction were the most common causes of poor outcomes. To corroborate these findings, a larger multicentric prospective observational study may be needed.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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