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Original Research Paper

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OUTCOME OF PARACETAMOL(ACETAMINOPHEN) POISONING CASES AT TERTIARY CARE HOSPITAL-A RECORD BASED RETROSPECTIVE STUDY

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ABSTRACT Paracetamol (PCM, Acetaminophen) is one of the most widely used drug in the world. It is an effective mild analgesic, antipyretic agent which is inexpensive and mostly sold as an over the counter drug. Paracetamol or acetaminophen overdose is a common means of self poisoning worldwide due to its wide availability and accessibility.A record based retrospective study was conducted at a tertiary care hospital to determine the demographic profile of paracetamol poisoning cases and to record the outcome of paracetamol poisoning cases .Primary outcome in terms of development of hepatotoxity and days of hospitalization and Secondary outcome in terms of recovery status as either survived or expired. Datas of 70 patients admitted with history of paracetamol poisoning in the past year was obtained and analysed for demodraphic and clinical features.It was observed that most predominance of paracetamol overdose in young age with median age of 26 with female preponderance and Hepatotoxicity was seen in only six cases of all paracetamol overdose with no mortalities.This study concluded that Paracetamol poisoning is frequently seen in young females attempting suicide. In India the rate of hepatic toxicity tends to be low. Mortality and Morbidity were not seen despite high doses of paracetamol ingestion.

KEYWORDS : Overdose, paracetamol, toxicity

INTRODUCTION AND NEED FOR STUDY

Paracetamol (PCM, Acetaminophen) is one of the most widely used drug in the world. It is an effective mild analgesic, antipyretic agent which is inexpensive and mostly sold as an over the counter drug. It is generally safe for use at recommended doses (1000 mg per single dose and up to 4000 mg/ day for adults and 2000 mg/day for alcoholics).[1,2] Paracetamol or acetaminophen overdose is a common means of self poisoning worldwide due to its wide availability and accessibility.It is a major public health problem in the Western world mainly Europe and United States of America.[3] However this is becoming one of the public health problem in our country as well especially among youngsters in urban areas.[4] To cause toxicity, an acute overdose must total be more than or equal to 150 mg/kg (about 7.5 gram in adults) within 24 hours.[5,6] Its overdose can cause mild hepatotoxicity to severe hepatic centrilobular necrosis and even liver failure.

MECHANISM OF TOXICITY

In therapeutic doses 60-90% of the drug is metabolized by conjugation to form paracetamol glucuronide and sulphate.5-10% is oxidized by mixed function oxidase enzymes (principally CYP2E1) to form highly reactive N-acetyl-p-benzoquinoneimine(NAPQI),which is immediately conjugated with glutathione and excreted as cysteine and mercapturate conjugates.

In overdose larger amounts of paracetamol are metabolized by oxidation to NAPQI because other conjugation pathways are saturated. As a result liver glutathione stores become depleted and the liver is unable to detoxify NAPQI which can then bind to key cellular enzymes,this results in oxidative stress, mitochondrial injury, hepatocyte death by necrosis(and to lesser extent apoptosis),inflammation and if severe acute liver failure leading to multiorgan failure(particularly encephalopathy and acute kidney injury)[7].Hepatotoxicity was defined by a peak serum alanine transaminase (ALT)LEVEL>1000IU/L, in accordance with previous accepted nomenclature in the literature.[8] ALF was defined as the presence of coagulopathy(INR>1.5)together with hepatic encephalopathy within 8-26 weeks of onset of symptoms in a patients without any prior liver disease.[9]

The estimated serum Paracetaol concentration in relation to the post ingestion time is interpreted using the nomogram. The standard nomogram recommends estimation of serum Paracetaol level every four hours, which is plotted in a graph. This guides for general line of management whether the case falls within standard treatment line or high risk treatment line and it also provides clinicians a method to predict whether patients would develop hepatic toxicity following an initial serum level after an overdose of Paracetamol.

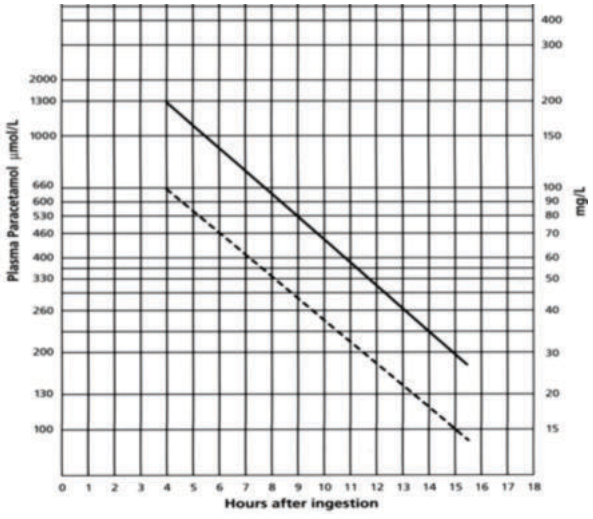

Figure 1-Rumack-Matthew Nomogram

1) Upper solid line (commencing 1300 µmol/L) All cases above this line must be treated
2) Lower dotted line (commencing 660 µmol/L)

– acetylcysteine (NAC) is the standard recommended antidote for Paracetamol poisoning that acts by repletion of Glutathione. It is available in both oral and intravenous (IV) forms.[10]The approved therapeutic duration for oral NAC is 72 hours (140 mg/kg body weight stat followed by 17 doses of 70 mg/kg every 4 hours with a total dose of 1330 mg/kg over 72

hours) and IV NAC is 20 hours (150 mg/kg in 200 ml of 5% Dextrose over 15 minutes followed by 50 mg/kg in 500 ml of 5% Dextrose over next 4 hours and then 100 mg/kg in one liter of 5% Dextrose over next 16 hours with a total dose of 300 mg/kg given over 20 hours).[11,12] Available formulations of NAC in our market are Tablet NACFIL 600 mg: Fourt's India Ltd, Tamil Nadu, India; Injection Mucomix 20%: Samarth Life Sciences Pvt Ltd, Himanchal Pradesh, India. Many researches have shown that both formulations are equally effective and some comparative studies have even shown that oral forms have better outcomes in those who present late for treatment in hospitals.[13,14]

Our aim in this study was to measure the Paracetamol poisoning outcome. Primary outcome in terms of development of hepatotoxity and days of hospitalization and Secondary outcome in terms of recovery status as either survived or expired.

AIMS AND OBJECTIVES

1. To determine the demographic profile of paracetamol poisoning cases admitted at General medicine department of a tertiary care hospital mandya.
2. To record the outcome of paracetamol poisoning cases

METHODOLOGY

This was a record based retrospective cross-sectional study conducted by collecting datas of patients admitted with history of Paracetamol poisoning to the General Medicine department, Mandya Institute of Medical Sciences, Mandya during a period January 2021 to December 2021. Records of 70 subjects who are of age more than 18 years were obtained and analysed for demographic features like age and sex, estimation of the amount of paracetamol ingested, development of hepatotoxicity, the use of N-acetylcysteine, duration of hospital stay and in-hospital mortality.

RESULTS

In this study it was observed that most of the subjects belonged to the age group of 21-30 years, followed by 31-40 years. Paracetamol poisoning was least found in the age group more than 40 years.

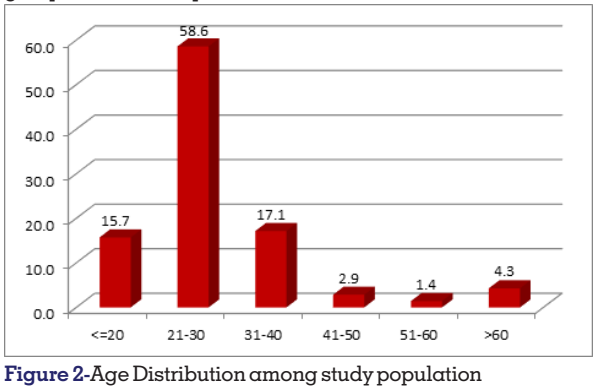

Figure 2-Age Distribution among study population

We also found a female preponderance in Paracetamol poisoning cases with a male : female ratio of 3:2.

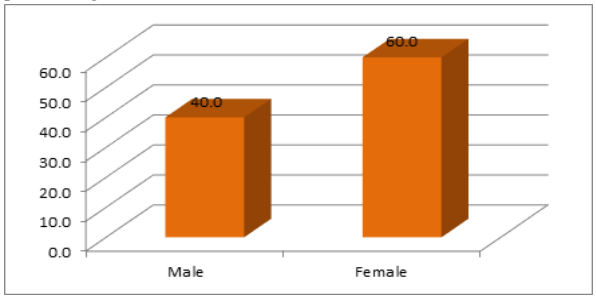

Figure 3- Sex Distribution among study population

Avarage dose of paracetamol ingested (mg) is 9.1+-4.1,and 22 patients had ingested >10g of paracetamol.

Table 1-Dose (gm) of paracetamol ingested

Dose (gm)	Count	Percentage
<=10 gm	48	68.6
>10 gm	22	31.4
Total	70	

	Mean ± SD	Median	Min - Max
Dose (gm)	9.1 ± 4.1	7.2	2.6 - 19.5

N-acetylcysteine was given to all 22 patients who has consumed >10gm paracetamol dose.

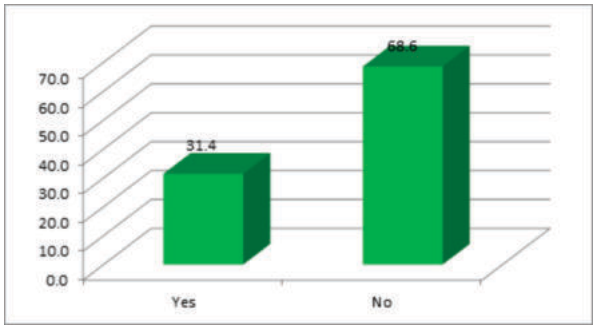

Figure 4-NAC Administerd among study population

Only six cases met the definition of hepatic toxicity.

Table 2-Outcome of patients

HEPATOTOXICITY	Count	Percentage
Yes	6	8.6
No	64	91.4
Total	70	

the remaining 64 patients had normal liver function tests.22 patients had ingested >10g of paracetamol,but only 6 developed hepatotoxicity but none of the patients with hepatotoxicity developed acute liver failure.All 70 patients with paracetamol poisoning were discharged well following hospitalization.There were no mortalities as a result of paracetamol overdose in our database.

The average hospital stay was 2.3 ± 1.3 days.

Table 3-Average Hospital Stay (In Days)

	Mean ± SD	Median	Min - Max
Hospital Stay (Days)	2.3 ± 1.3	2.0	1 - 7

DISCUSSION

We conducted this study among 70 Paracetamol poisoning cases to explore the demographic profile and Outcome. In our study the predominance of paracetamol overdose in young age with median age of 26 which matches the similar study conducted by Almansori et al ,24 and marzilawati et al ,23 to 28. [15,16] We also found a female preponderance, 60% patients were young females which matches the similar study done by Almansori et al,70%and marzilawati et al, 82%[15,16] and this observation can imply a social problem and the need for a cultural program aimed at improving health, especially since a recent study has shown that family conflicts were the common cause of suicide attempts[17] while the mean dose of paracetamol ingested in our sample was about 9.1gm, which matches the similar study done by Almansori et al, and Marzilawati et al is 8.2g and 10g respectively.[15,16] Hepatic toxicity has been associated with doses >10 g , Hepatotoxicity was seen in only six cases of all paracetamol overdose accounting for 8.6%,where as study conducted by Almansori et al,is 2.3% .[15] this low rate (8.6%) of hepatotoxicity in Asian patients with paracetamol overdose suggested that ethnic differences in paracetamol metabolism may contribute to hepatic toxicity .Another possible explanation for the lower

rate of paracetamol-induced hepatic toxicity is related to the dose ingested. The outcome of acetaminophen intoxication is almost always good as long with timely administration of N Acetyl cysteine,particularly when given within the first 10 hours.Fulminant hepatic failure and death from acetaminophen poisoning result from inability to recognize poisoning or delayed initiation of management. N-acetylcysteine is the antidote for paracetamol overdose as it prevents paracetamol-induced hepatic injury by restoring hepatic glutathione level, especially when administered within 8 h of the overdose. In our study 31.4% of the patients received N-acetylcysteine (all 31.4% received the intravenous form of the medicine), 79.3% and 56% patients received nac in study done by Marzilawati et al,and Almansori et al,respectively.[15,16]N-acetylcysteine was given to those who are consumed toxic dose was calculated according to body weight (as no facilities available to assess serum concentration of acetaminophen in our hospital Rumack and Matthew normogram was not used to calculate the toxic dose). These calculations NAC administration are based on information obtained from western countries and may not be accurate when applied to different populations. Since people in the west tend to have higher body weights our patients might have been given excessive doses of N-acetylcysteine This could have lowered the rate of hepatic toxicity seen in our sample.none of the patients with hepatotoxicity developed acute liver failure.All 70 patients with paracetamol overdose were discharged well following hospitalization and There were no mortalities,which is similar to study done by Almansori et al and Marzilawati et al.[15,16].The average hospital stay was 2.3 ± 1.3days in our study where as study done by Almansori et al ,is 4.8+-4.9.[15]

CONCLUSION

Paracetamol poisoning is frequently seen in young females attempting suicide. In India the rate of hepatic toxicity tends to be low. Mortality and Morbidity were non-existent despite high doses of paracetamol ingestion.

LIMITATIONS

1. The first being its retrospective nature, the small sample size and a single-center study
2. Our sample had no information on the time lapse between ingestion and presentation.

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