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Review Article

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A BRIEF REPORT ON PARACETAMOL AND ITS TOXICITY

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ABSTRACT
Paracetamol is common analgesic as well as antipyretic drug. It is one of the most available OTC drug almost in every medical stores of our country. The continuous exposure and addiction of this medicine is affecting the human health and results in mild to severe toxic effects on human health. A brief report regarding its toxicity is described in the article.

KEYWORDS: Paracetamol, toxicity, Analgesics.

INTRODUCTION

The world is at present time facing the health crisis in form of Covid-19, since last 3 years. It seems that everything is just stopped abruptly.

Our daily life routine, busiest schedule all of the activities related to our livelihood have changed all of sudden.

It feels that now the time have come to think about our own selves and about our own health. We must draw attention towards the fact that, what we are consuming to make our health fit and what are the elements which are causing the adverse effect on our health. As for example – In minor health problem, We become totally dependent on medicines specially on analgesics, antipyretics etc. We prefer the practice of self-medication and blindly trust the OTC drugs like paracetamol. Paracetamol is one of the most commonly used analgesics as well as antipyretics drug. It is available in every medical stores with numerous brand names. Due to its effectiveness in giving immediate relief from pain and fever with its safety profile, People are using this medicine and have totally become addiction to this medicine.

PARACETAMOL FORMULATIONS

Paracetamol can be taken in number of ways and can be bought in many different formulation.

- Common ones are tablets (500)mg, Fazy dispersible tablets 500mg and 650mg.
- Pediatric Oral Solution 120mg.
- Oral suspension 250mg.

It is also sold in capsules and works in synergy when combined with number of other agents including IBUPROFEN, CODEINE, TRAMADOL and CAFEEINE improving analgesic efficacy whilst minimizing side effect of the adjunct agent.

MECHANISM OF ACTION OF PARACETAMOL

Paracetamol produce its therapeutic effect through inhibition of prostaglandin synthesis by inhibiting the conversion of Arachidonic Acid (AA) into prostaglantin H- synthese (PGHS) or Cycloxygenase (COX)

METABOLISM OF PARACETAMOL

The metabolic pathway of paracetamol involves three different orgens.

1. Liver
2. Instestine
3. Kidney

In liver Biotransformation process occur. It includes two different phases Phase I and Phase II. Phase – II involves the conjugation and sulfonation process. In conjugation there in addition of UDP-Glucolonic Acid which form paracetamol Glucouronide (50-55%). Sulfation requires addition of sulfate group to form paracetamol sulfate (30-40%) excreted in form of urine.

Whereas Phase-I includes involvement of Cyto-Chr P450 where. Small percentage of paracetamol (5%) is oxidized by Cyt-chr P450 isozyme system in the liver this oxidation process results into the production of N-acetyl-P-benzoquinone imine (NAPQI). It is very toxic intermediate metabolic. It can induce severe acute hepatic necrosis, fortunately the glutathione molecule in a liver rapidily conjugate NAPQI molecule to produce non-toxic metabolic that can be peacefully excreted by kidney.

OVERDOSE

Paracetamol conjugation machinery can safely process the flooding of paracetamol molecules.

As result paracetamol molecules directed towards CyP450 system which leads to massive production of NAPQI, as a result Glutathione try its maximum effort neutralize the NAPQ, but unfortunately due to limited production of glutathione results in accumulation of NAPQ molecule in liver which causes the serious toxic effect, and results into acute hepatic necrosis. The sulfhydryl donor N-acetyl cysteine (NAC), a precursor for glutathione, speeds the detoxification of NAPQI.

REPORTED TOXIC EFFECTS OF PARACETAMOL ON VARIOUS ORGAN SYSTEM

1. Liver injury:- Liver injury induced by paracetamol is the most common form of drug induced liver injury (in human which came as a leading cause of about 50% of the cases of acute liver failure around the world (Lee, 2012)
2. Renal Failure:- Its overdose have been reported to cause renal failure due to increase in lipid peroxide levels and depletion of glutathione (Abraham 2005)
3. Disruption of ETC Electron transport chain and ROS Formation:- Several studies on mice, have reveal the report that paracetamol metabolite protein adducts seems to cause disruption of electron transport chain and thus formation of reactive oxygen species in mitochondria (Jaeschke etal., 2012)
4. Pulmonary Toxicity:- findings in animal and in micro studies showed that paracetamol may deplete the level of glutathione" Epidemiological data are strongly suggesting that frequent paracetamol usage may be a direct risk factor for wheezing, rhinitis and asthama morbity in adults and children (Eneli, 2005)
5. Genotoxic Effect:- some reports are available about genotoxic effect of paracetamol (Ying and Yi 2000, Arun and Robeth, 2010) and also genotoxicity in mice sperm cells have also been reported (verma and kumari, 2020).

CONCLUSION

The available reports and collected information suggest that paracetamol posses mild to Severe hazardous effect on health.

Its addiction is trapping major mass of human beings. So, some major steps should be taken to control its uncontrolled uses.

1. Before taking its dose we must consult to the physican.
2. Reduce its dependency by adopting physical exercise, Yoga etc.
3. Use antioxidants rich medical herbs in diet so that it can combat its toxic effect.

The above measures can be taken to reduce its toxicity.

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