

HEPATOPROTECTIVE AGENTS



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ACETAMINOPHEN HEPATOTOXICITY



❑ APAP (N-acetyl para aminophenol) is leading cause of acute liver failure. NAPQI (N-acetyl-p-benzoquinone imine) is main metabolite of APAP which is main reason of liver failure.

❑ Signs and Symptoms:-

❑ APAP toxicity include nausea, vomiting, anorexia, right upper quadrant pain, elevated ALT and AST, elevation of bilirubin and finally may lead to multiple organ failure.

Treatment

- ❑ Activated charcoal is given less than 4 hours after ingestion dose (1g/kg by mouth)
- ❑ N-acetylcysteine is given as antidote in APAP poisoning. dose (loading dose 140mg/kg, then 70mg/kg po every 4 hours for total of 17 doses)
- ❑ Intravenous (iv) dosing prepare the infusion by adding 30g of 20% NaC solution (150ml) to 1LD5W this will result in a final concentration of 30mg/ml.

Hepatitis

❑ Hepatitis is inflammation of the liver tissue

Is caused by

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D, E and F



Hepatitis A

Hepatitis A is a highly contagious liver infection caused by the hepatitis A virus

symptoms:-

Fatigue

Sudden nausea and vomiting

Abdominal pain or discomfort, especially on the upper right side beneath your lower ribs (by your liver)

Clay-colored bowel movements

Loss of appetite

Low-grade fever

Dark urine

Joint pain

Yellowing of the skin and the whites of your eyes (jaundice)

Intense itching

TREATMENT

No specific treatment exists for hepatitis A. Your body will clear the hepatitis A virus on its own. In most cases of hepatitis A, the liver heals within six months with no lasting damage.

- Avoid alcohol and use medications with care.
- Manage nausea
- Rest.



HEPATITIS B

- Hepatitis B
- Hepatitis B is a serious liver infection caused by the hepatitis B virus (HBV). For some people, hepatitis B infection becomes chronic, meaning it lasts more than six months. Having chronic hepatitis B increases your risk of developing liver failure, liver cancer or cirrhosis — a condition that permanently scars of the liver.

- prevention includes vaccination with hepatitis B vaccine.
- Treatment
- For Acute form, no medicine available
- For chronic form following treatment is required

- **Antiviral medications.**
- **Interferon injections.**
- **Liver transplant.**



Chronic Hepatitis B

Approved drugs

Interferons



- Conventional IFN- α
- Peg-IFN α -2a (*Pegasys*)

Combined antiviral and immunomodulatory effect

Nucleoside/nucleotide analogues



- Lamivudine (*Zeffix*)
- Adefovir (*Hepsera*)
- Entecavir (*Baraclude*)
- Telbivudine (*Sebivo*)
- Tenofovir (*Viread*)

Direct antiviral effect

Lamivudine:

- Mechanism of action:
 - Inhibits HBV DNA polymerase
 - It must be phosphorylated by host cellular enzymes to triphosphate (active) form.
- Pharmacokinetics:
 - Orally absorbed
 - Widely distributed
 - 9 hours plasma half life
 - 70% excreted unchanged



Adefovir

- A nucleotide analog that is phosphorylated adefovir diphosphate, which is then incorporated into viral DNA.
- Terminates further DNA synthesis and prevents DNA replication.
- **Pharmacokinetics:**
 - Administered once a day
 - Excreted in urine
 - 45% excretion as active compound.
 - Should be used cautiously in patients with renal dysfunction.



Entecavir:

- ❑ Guanosine analog
- ❑ Competes with natural substrate, deoxyguanosine triphosphate for viral reverse transcriptase.
- ❑ Effective against lamivudine resistant HBV
- ❑ Need to be given once a day
- ❑ Renal excretion



Telbivudine

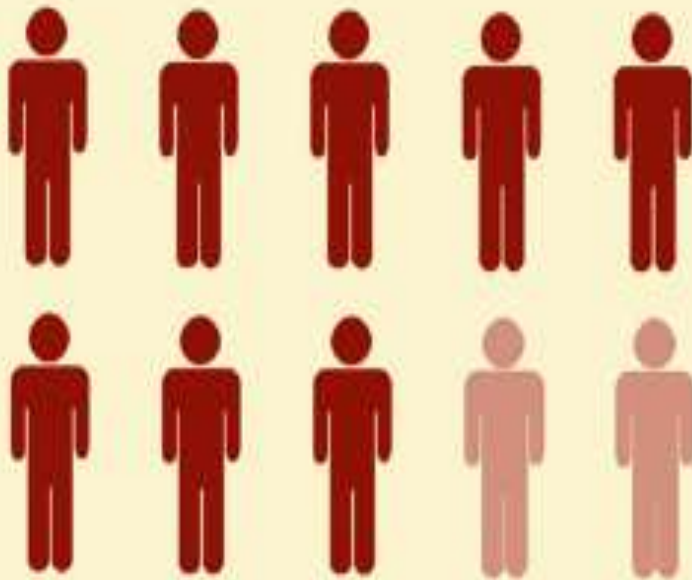
- ❑ Thymidine analog
- ❑ Phosphorylates intracellularly to triphosphate
- ❑ Can either compete with endogenous thymidine triphosphate or can be incorporated in viral DNA.
- ❑ Administered orally once a day
- ❑ Eliminated unchanged by glomerulus filtration

Hepatitis C

- Hepatitis C is a virus that can infect the liver. If left untreated, it can sometimes cause serious and potentially life-threatening damage to the liver over many years.
- However, with modern treatments it's often possible to cure the infection and most people with it will have a normal life expectancy.
- It's estimated that around 215,000 people in the UK have hepatitis C.

Symptoms

70-80%
of people with hep C
don't show any symptoms



Symptoms can include:



Yellowing skin
and eyes



Dark urine



Light-colored
stools



Nausea and
vomiting



Loss of
appetite



Extreme
fatigue

TREATMENT

- Medication stops multiplication of virus and it needs to be taken for several months.
Treatment is not initiated in an acute infection rather it is recommended for chronic infection.
- Commonly used drug
- Pegylated interferon Injection
- Ribavirin

Newer medication

- Treatment for hepatitis C depends upon viral strain(its genotypes); there are many new effective drugs available now a days used alone or in combination with others. These all agents are given orally (P.O). They are more efficacious and safer as compared to IFN- RBV. In clinical studies commonly reported Side effects are headache, tiredness and weakness.

Newer medication

- Ledipasvir–Sofosbuvir (Harvoni)
- Daclatasvir
- Sofosbuvir

