PRACTICE

5

VERIFIABLE CPD PAPER

IN BRIEF

- Liver disorders are important to the dentist due to a potential bleeding tendency, intolerance to drugs eg general anaesthetics, benzodiazepines and the possibility of underlying infective causes for the liver dysfunction.
- Signs of liver disease include jaundice, spider naevi, leuconychia, finger clubbing, palmar erythema, Dupuytren's contracture, sialosis and gynaecomastia.
- The general anaesthetic agent halothane (now used infrequently) should not be given twice to the same patient within 3 months. A 'halothane hepatitis' is likely to result.
- Dental sedation should only be performed in specialist units for patients with significant liver disease as small doses can lead to coma.

General medicine and surgery for dental practitioners Part 5: Liver disease

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The liver has a number of important functions. It metabolises drugs and endogenous substances and contributes to their excretion by the body. Plasma proteins are synthesised in the liver which also acts as a storage organ for glycogen and vitamin B_{12}. The liver is also important in the production of clotting factors for normal haemostatic function.

GENERAL MEDICINE AND SURGERY FOR DENTAL PRACTITIONERS:

1. Cardiovascular system
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POINTS IN THE HISTORY

The history may reveal evidence of liver disease. This is important in terms of potential **drug toxicity, bleeding tendency** and the possibility of **viral hepatitis.** Chronic liver disease (defined as liver disease present for more than 6 months) can enter an acute phase if unrecognised eg after the administration of sedation. Acute liver failure itself may be precipitated by any type of viral hepatitis, the anaesthetic agent halothane, paracetamol overdose or Reye's Syndrome (*see* later).

Viral hepatitis is clearly of importance to the dentist.[1] Indeed, dental students must show satisfactory immunisation against hepatitis B in order to undergo clinical training in the United Kingdom.[2] **Hepatitis A** is transmitted via the faeco-oral route and has a 3-week incubation period. There is no known carrier state. **Hepatitis B** may be transmitted by blood-to-blood contact eg via contaminated sharps, and droplet infection. It has an incubation period of 6 weeks to 6 months. A small proportion of patients will progress to a hepatitis B carrier state associated with chronic active hepatitis and eventually cirrhosis. The presence of Hepatitis B Surface Antigen (HBsAg) is the first manifestation of infection. The presence of antibody to HBs is associated with protection from infection. Hepatitis B Core Antigen (HBcAg) is detected by the development of an antibody to it. It may persist for 1 to 2 years signifying donor infectivity if HBsAg negative but HBcAg positive. Hepatitis B e Antigen is only found in HBsAg positive sera and appears during the incubation period. It is an index of infectivity. DNA polymerase is first detected when the level of HBsAg is increasing, and indicates the presence of virions in the serum and is associated with replication. A summary of serological markers for hepatitis B is given in Table 1.

Table 1 Serological markers for Hepatitis B

Hepatitis B Surface Antigen – first manifestation of infection
Antibody to Hepatitis B Surface Antigen – associated with protection from infection
Hepatitis B Core Antigen – detected by development of antibody and signifies donor infectivity if surface antigen negative but core antigen positive
Hepatitis B e Antigen – only found if HBs Antigen positive (an index of infectivity)

Hepatitis C can be contracted from a contaminated blood transfusion. **Hepatitis D** (or delta) is a viral RNA associated with hepatitis B and demonstrated in association with HBcAg. Other viral causes of a hepatitis include Cytomegalovirus, Herpes Simplex, Epstein Barr Virus and Coxsackie B Virus.

Efficient cross infection control[3] should minimise the risk of contracting the infective types of hepatitis. There is an adjunct in the form of a **hepatitis B vaccine** (Engerix B). This vaccine is injected into the deltoid muscle of the upper arm and is repeated at 1 and 6 months after the original dose. Serology is used to time boosters and identify none or poor responders. Poor responders tend to be members of the older population, smokers and male. An anti-HBs level of less than

Table 2 Points in the history in a patient with liver disease

- Hepatitis
- History of jaundice
- Bleeding tendency
- Cirrhosis
- Liver tumours
- Reaction to medications
- Liver surgery eg transplants
- Familial disorders

Table 3 Possible signs of liver disease on clinical examination

- Dupuytren's contracture
- Palmar erythema
- Finger clubbing
- Leuconychia
- Parotid enlargement
- Jaundice
- Spider naevi
- Gynaecomastia
- Ascites/ankle oedema
- Scratch marks (itching)

Haemostasis

Liver disorders can interfere with haemostasis after surgery due to interference with the production of clotting factors

one hundred is not enough to confer protection and in such cases a booster is required and a further level checked a month later. Even with a good response it is not until 6 weeks after the first injection that protection is achieved and therefore a specific anti-hepatitis B immunoglobulin is required for individuals exposed to the virus during this time.

A history of **jaundice** may be obtained. This does not necessarily imply liver disease eg bile duct obstruction due to gallstones or malignant disease may also cause jaundice. Jaundice at birth is common and is usually of no significance. Normally, bilirubin (a breakdown product of haemoglobin) is conjugated in the liver where it becomes water soluble and is excreted in the bile which colours the faeces. If the bilirubin is not conjugated eg due to parenchymal liver disease, it colours the skin and mucous membrane ('jaundice'). In obstructive jaundice, bile does not reach the gut leading to pale faeces but there is increased urinary bilirubin, the urine therefore is dark. Dark urine and pale faeces are a hallmark of obstructive jaundice.

It is important to suspect and enquire about any **bleeding tendency** (and testing of clotting is required). Poor absorption of fat soluble vitamin K occurs with its attendant effects on clotting and there is also decreased synthesis of clotting factors.

Obstruction to blood flow in the liver (portal circulation) leads to an increase in portal blood pressure with formation of enlarged blood vessels (varices) at the base of the oesophagus (one place where systemic and portal circulations meet) with consequent risk of gastrointestinal haemorrhage. Chronic bleeding may lead to anaemia.

In **cirrhosis** of the liver, the architecture is irreversibly destroyed by fibrosis and regenerating nodules of hepatocytes. The cause is often unknown but a quarter of cases are alcohol related. Hepatitis B or C, and the chemotherapy drug methotrexate can all be implicated. Primary biliary cirrhosis (PBC) is a disease primarily of females thought to be autoimmune in origin. It can be associated with Sjogren's Syndrome or oral lichen planus.[4]

The most common liver tumours are **metastases.** These signal advanced disease and the outlook depends on the extent and nature of the primary tumour. Recent advances in surgery have meant that in certain situations resection of metastases is possible and chemotherapy may be appropriate. Jaundice, if present at all, is a late sign. Hepatocellular cancer may occur after hepatitis B or C infection and cirrhosis of the primary biliary type.

The patient may give a history of liver problems after certain **medications.** Likely to be of interest to the dentist are aspirin, carbamazepine, erythromycin estolate, tetracycline and halothane.[5] Halothane is discussed later. Aspirin is not indicated in children due to the risk of Reye's Syndrome which comprises liver damage and encephalopathy occurring after aspirin ingestion.

Patients may be encountered who have undergone a **liver transplant** – the most common indication for which is end-stage liver disease. Management considerations are discussed later.

Familial conditions may occur eg Gilbert's Syndrome in which the bilirubin level increases but is not conjugated and therefore does not enter the urine. It generally presents as mild jaundice. Many patients have no symptoms but some have episodes of malaise, anorexia and upper abdominal pain with jaundice. These episodes may be related to infection, fatigue or fasting.

A summary of the main areas of enquiry in a patient with liver disease is given in Table 2.

EXAMINATION

There may be significant clues to the presence of liver disease that are discernible from a patient sitting in a dental chair, (Table 3).

The hands may show a **Dupuytren's contracture** (a condition in which the ring and little fingers are held flexed when the hand is held passive due to thickened palmar fascial tissue) or there may be **palmar erythema.** The fingers may be clubbed, and the fingernails may have a whitish colouration (**leuconychia**). If the hands are held outstretched in front of the patient a marked flapping tremor may be noted – 'liver flap' in severe liver decompensation.

Oedema (secondary to hypoproteinaemia) may lead to ascites (fluid in the abdomen leading to distension) or ankle oedema. The commonest cause of the latter however is likely to be cardiovascular. **Itching** may produce scratch marks on the skin. The itching occurs due to deposition of bile salts in the skin. The patient may be jaundiced. **Gynaecomastia** (enlarged breast tissue in the male) may occur due to increased circulating oestrogen levels. This is also said to be responsible for the palmar erythema mentioned earlier. **Spider naevi** (numerous thin, tortuous blood vessels emanating from a central arteriole) may occur on the face, neck, upper chest and back (said to be within the distribution of the superior vena cava). Parotid enlargement (**sialosis**)[6] may be seen in cases of cirrhosis but this is due to the associated alcohol intake rather than the cirrhosis itself.

FACTORS AFFECTING DENTAL TREATMENT UNDER GA/LA AND SEDATION

Agents such as sedatives and general anaesthetics are potentially dangerous in liver disease mainly due to impairment of detoxification. In the case of halothane, a hepatitis may follow its use especially in the obese, in smokers and in middle aged females and if a halothane anaesthetic has been given in the last 3 months. The precise mechanism is not known. The hepatitis tends to develop after about a week and comprises jaundice, malaise and anorexia. The newer agents eg enflurane, sevoflurane are less hepatotoxic and as a result the use of halothane has waned.

A patient with a history or signs suggestive of a liver disorder or a high alcohol intake which might potentially cause liver damage should have blood taken for liver function tests (LFT's) and clotting studies. These should be carried out prior to GA or surgery. Severe bleeding can occur after dental extractions in patients with chronic liver disease[7] so the clotting status must be tested. There are many different types of LFT but the commonest involve measurement of aspartate transaminase (AST) and alanine transaminase (ALT). ALT may also be raised in cardiac or skeletal muscle damage and is therefore not specific for liver disease. Gamma glutamyl transferase (γGT), when it is raised, usually reflects alcoholic liver disease. Alkaline phosphatase levels may be raised in obstructive jaundice but this is not a specific marker. The level of alpha fetoprotein may be raised in hepatocellular cancer. In cirrhosis, treatment should only be carried out in conjunction with the patient's physician. Relative analgesia is preferred to sedation with a benzodiazepine. A specialist anaesthetist is required even if GA is acceptable.

In many liver diseases brain metabolism is altered and it therefore becomes more sensitive to certain drugs. Encephalopathy can be triggered by sedatives or opiates. In obstructive jaundice, the main risk is bleeding due to vitamin K malabsorption. If surgery is required in such patients, intravenous vitamin K may be required for several days beforehand to correct any bleeding tendency. Any patient with jaundice has an increased risk of bleeding excessively following any surgical procedure including dental extractions. A peri-operative infusion of fresh frozen plasma will often be required. If the patient is severely jaundiced a GA may precipitate renal failure, the **Hepato-Renal Syndrome.** The risk is decreased if the patient is well hydrated with intravenous fluids and given the osmotic diuretic mannitol to ensure a good urine flow pre, per and post-operatively.

Local anaesthesia is not entirely safe in patients with hepatic impairment. Most of the amide local anaesthetics used in dental practice undergo biotransformation in the liver. Articaine is metabolized partly in plasma[8] and prilocaine receives some metabolism in the lungs.[9] However, the liver is the main site of metabolic activity. All of an injected dose of local anaesthetic will eventually reach the circulation and if metabolism is affected the concentration in plasma will slowly increase. Only about 2% of the drug will be excreted unchanged. This may lead to signs of CNS toxicity with relatively low doses of the anaesthetic, as little as two cartridges in an adult patient may be too much if liver disease is severe.

If possible a full dental assessment should be carried out prior to a liver transplant particularly since post-operatively the patient will be immunosuppressed. Invasive dental treatment should only be carried out after consultation with the patient's physician. After transplantation no elective dental treatment should be carried out for the first three months. GA, if needed, must be carried out in units with the required expertise.

Dental sedation should only be performed in specialist units for patients with significant liver disease as small doses can lead to coma.

PRESCRIBING FOR PATIENTS WITH LIVER DISEASE

The use of any drug in a patient with severe liver disease should be discussed with the patient's physician. Hepatic impairment will lead to failure of metabolism of many drugs that can result in toxicity. In some cases dose reduction is required, other drugs should be avoided completely. The anti-fungal drug miconazole is contra-indicated if there is hepatic impairment and fluconazole requires dose reduction. Erythromycin, metronidazole and tetracyclines should be avoided.

Non-steroidal anti-inflammatory drugs increase the risk of gastro-intestinal bleeding and interfere with fluid balance and are best avoided. Paracetamol doses should be reduced as at high doses this drug is hepatotoxic.

SUMMARY

Knowledge of liver disorders is important for the safe delivery of dental care. A thorough history will usually alert the clinician to potential problems. Haemostasis may be affected and this should be particularly borne in mind.

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Pain and anxiety control

Liver disease impacts on the provision of local anaesthesia, intravenous sedation and anaesthesia in dentistry