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## RESEARCH ARTICLE

### MANAGEMENT OF MEDICALLY COMPROMISED PATIENTS IN ENDODONTICS

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#### ABSTRACT

Successful endodontic practice requires complete knowledge about the various medical conditions and appropriateness in planning treatment as per the need with effective safety measures. This review focuses on a number of systemic complications encountered in endodontic practice that necessitate extra knowledge and care to prevent potential complications causing otherwise unnecessary morbidity and mortality. These include diabetes, multiple drug interactions, cardiac abnormalities, respiratory disorders and infectious diseases. When the procedure is carried out in healthy individuals, it is sufficient to concentration the technical course of action, but when there is a demand to preserve the tooth for patients with systemic illness and who are under medical management, it is equally important to avoid the potential medical emergencies. The first step in managing the patient with medical problems is acquiring a thorough health history, the second step is for the clinician to fully understand the significance of the disease. Each identified condition can affect dental care in a unique manner. Hence, practitioners must be aware of common diseases, and drugs that have an impact in endodontic treatment and the management options in medically compromised patients. This review aims to highlight the clinical conditions that require special endodontic attention.

#### INTRODUCTION

A dental surgeon practicing now a days encounters plethora of patients with medical disorders in his/ her day to day practice. Assessment and management of these patients is one the major challenges faced by dental specialists (Abraham-Inpijn et al., 2008). An absolute knowledge of a patient's medical problems is vital for providing safe and appropriate dental treatment in the context of any systemic disorders, other underlying general health conditions, intake of medications, or other oral pathologies (Al-Bayat et al., 2009). Many factors can potentiate the occurrence of life threatening emergencies in dental offices such as growing trends towards longer dental appointments, increasing use and administration of drugs in dentistry. The common medical conditions encountered by the dentists in daily practice include drug allergies, cardiac abnormalities, pulmonary diseases, endocrine disorders,

infectious diseases, pregnant patient, renal disorder, psychogenic problems and patients undergoing radiation therapy (Peacock, 1995). The key to successful dental management of medically compromised patients begins with a thorough review of the medical history. This should include documentation via questionnaire as well as verbal history. Interpretation of the information collected achieves three important objectives: enables the monitoring of medical conditions and the evaluation of underlying systemic conditions of which the patient may or may not be aware; provides a basis for determining whether dental treatment might affect the systemic health of the patient; provides an initial starting point for assessing the possible influence of the patient's systemic health on the patient's oral health and/or dental treatment (Smeets, 1998). For patients having systemic diseases some modifications in treatment plan or drugs may be required in order to prevent probable interaction with their

current medications or systemic health stability (Little et al., 2002). Dental practitioners and their staff need to have appropriate skills, training and equipment available to deal with such conditions. So, prior knowledge of a patient's physical condition and nature of patient's disease, how it can impact their physiology, their response to dental management and post dental treatment healing enables the doctor to modify the treatment plan that leads to a significant reduction in occurrence of acute medical emergencies in medically compromised patients (Malamed, 2007).

**Cardiovascular disorders:** Cardiovascular diseases are one of the main causes of mortality in the developed world. Hypertension, Ischemic heart disease, cerebrovascular disease, heart failure and endocarditis are most common causes of deaths every year (Cruz-Pamplona, 2011). In patients with a history of cardiovascular disease, attention must be given on the control of pain, the reduction of stress, and the use or avoidance of a vasoconstrictor in dental anaesthesia. In turn, caution is required in relation to the antiplatelet, anticoagulant and antihypertensive medication typically used by such patients.<sup>8</sup> Therefore, a multi-disciplinary approach is required to treat these patients for preventing complications and for improving the results of treatment (Kamath, 2016).

**Hypertension:** According to Webster medical dictionary hypertension is defined as abnormally high arterial blood pressure that is usually indicated by an adult systolic blood pressure of 140 mm Hg or greater or a diastolic blood pressure of 90 mm Hg or greater, is chiefly of unknown cause but may be attributable to a pre-existing condition (as a renal or endocrine disorder). Hypertension management in dental office includes disease recognition and correct measurement, knowledge of its treatment and adverse effects, and risk assessment for dental treatment (Popescu et al., 2013).

**Endodontic considerations:** Incorporation of a vasoconstrictor to local anaesthetic provides better pain control, which in turn reduces anxiety and stress usually associated with dental treatment. But the commonly used vasoconstrictors such as epinephrine and neocobefrin can cause a rise in heart rate. Hence, the use of vasoconstrictor should be limited in individuals with cardiac disease, taking care not to exceed 0.04 mg of adrenaline (4.5ml of standard local anaesthetic solution containing 0.009mg of Adrenaline tartrate per ml). In turn, if anaesthetic reinforcement is needed, it should be provided without a vasoconstrictor (Cruz-Pamplona, 2011). It is also important to eliminate intravascular administration therefore careful aspiration before any injection is mandatory. Vasoconstrictor is an absolute contraindication in patients with unstable angina pectoris or in patients with uncontrolled hypertension, refractory arrhythmias, recent myocardial infarctions (less than 6 months), recent stroke (less than 6 months), recent coronary bypass surgery (less than 3 months), and uncontrolled congestive heart failure (Popescu et al., 2013). Patients with blood pressure greater than or equal to 180/110 (Stage III hypertension). If emergency dental treatment is necessary, medical consultation is required and vasoconstrictor amounts should be limited to one to two cartridges of 1:100,000 solution (0.018 to 0.036 mg of epinephrine). In patients with blood pressure of 160-179/100-109 (Stage II hypertension), epinephrine should be limited to three cartridges (0.054 mg) (Cruz-Pamplona, 2011; WHO, 2011).

The use of retraction cord with epinephrine and intraligamentary and intrabony injections should be avoided in these patients (Connolly, 1997).

**Ischemic Heart Disease:** Ischemic heart disease has been reported to be the main cause of death in the developed world. Coronary heart disease can manifest itself in many forms, i.e stable and unstable angina pectoris, myocardial infarction and sudden cardiac death (Kahri, 2005). Angina pectoris originates from an inadequate supply of oxygen to the myocardium which is most often due to coronary atherosclerosis. It should not be forgotten that angina pain is often felt in the mandible radiating towards neck and throat. Therefore, the patient may initially suspect the pain to be of dental origin (Jowett, 2000).

**Endodontic management:** Treatment modification considerations for patients with ischemic heart disease should include morning appointments, short appointments, oral premedication with an anxiolytic drug or nitrous oxide or oxygen sedation, limited use of vasoconstrictors, adequate pain management (during and after the dental appointment), and possible cardiac monitoring (Jowett, 2000).

#### **Cardiac Arrhythmias**

A cardiac arrhythmia can be described as an abnormality in rate, regularity, or site of origin of the cardiac impulse. In addition, conduction of the impulse within the heart may be abnormal. Symptoms that may be attributable to an arrhythmia include fatigue, dizziness, syncope, and angina. The patient may report heart palpitations occurring on a regular or irregular basis. Stress testing with monitoring commonly is used to assess an individual's cardiac status (Rhodus, 2003). Cardiac arrhythmias may be found in healthy individuals, in patients taking various medications, and in patients with certain cardiovascular conditions or with other systemic diseases.

**Endodontic Management:** Endodontic management requires evaluation of the type of heart condition and the risk of bacteremia due to the planned dental procedure. According to the recent guidelines, antibiotic prophylaxis is now recommended only for patients with valvular disease associated with the highest risk of adverse outcomes from infective endocarditis. For patients in the highest risk category, antibiotic prophylaxis is recommended for dental procedures that involve manipulation of gingival or the periapical tissue. In general, procedures associated with nonsurgical root canal-treatment such as local anesthetic injection, placement of the rubber dam, and instrumentation when contained within the canal system do not place the patient at significant risk for infective endocarditis. The incidence and magnitude of bacteremia when canal instrumentation does not extend into the periapical tissues is very low, and almost all bacteria are eliminated from the blood within 10 minutes and therefore antibiotic prophylaxis is not required.

**Endocarditis:** Bacterial endocarditis is an uncommon infection produced by the accumulation of fibrin and platelets in the form of so-called "vegetations" which are deposited on the endocardium (Blanco-Carrión, 2004).

**Prevention of endocarditis:** The most widely accepted endocarditis prevention protocols are those of the American

Heart Association (AHA) and the British Society of Antimicrobial Chemotherapy (BSAC).

SITUATION	AGENT	SINGLE DOSE 30-60 min BEFORE PROCEDURE		
		ADULTS	CHILDREN	
Standard general prophylaxis (oral)	Amoxicillin	2gr	50 mg/kg (maximum 2 gr)	
Unable to take oral medication	Ampicillin	2 gr im or iv	50 mg/kg im or iv	
	Cefazolin or Ceftriaxone	1gr im or iv	50 mg/kg im or iv	
Allergic to penicillins	Oral	Cephalexin *	50 mg/kg	
		Clindamycin	20 mg/kg	
	Unable to take oral medication	Azithromycin or Clarithromycin	500 mg	15 mg/kg
		Cefazolin or Ceftriaxone	1g im or iv	50 mg/kg im or iv
	Clindamycin	600 mg im or iv	20 mg/kg	

Figure 1.

## Endocrine Disorders

**Diabetes mellitus:** Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. A deficiency in insulin or a problem with its metabolic activity can result in an increased blood glucose level (ie, hyperglycemia) and low level of sugar, or glucose, in the blood can result in hypoglycaemia.

**Endodontic considerations:** In a diabetic patient the dentist should ascertain how well controlled the condition is. Dental appointment scheduling should take into account the importance of nutritional consistency and the avoidance of appointments that will overlap with or prevent scheduled meals, especially in patients receiving insulin, sulfonylurea or meglitinide oral therapy because of the risk of hypoglycemia. If an appointment is likely to lead to a delayed or missed meal, the diabetic regimen may have to be modified with the assistance of the patient's diabetologist. It has been well established that hyposalivation, gingivitis, periodontitis and periodontal bone loss are well associated with DM, especially when poorly controlled. Surgical procedures in well controlled diabetics do not require prophylactic antibiotics. However, when surgery is indicated in poorly controlled diabetics, antibiotic prophylaxis consisting of amoxicillin 500 mg twice daily should be considered due to the altered function of neutrophils in diabetics (Manfredi *et al.*, 2004).

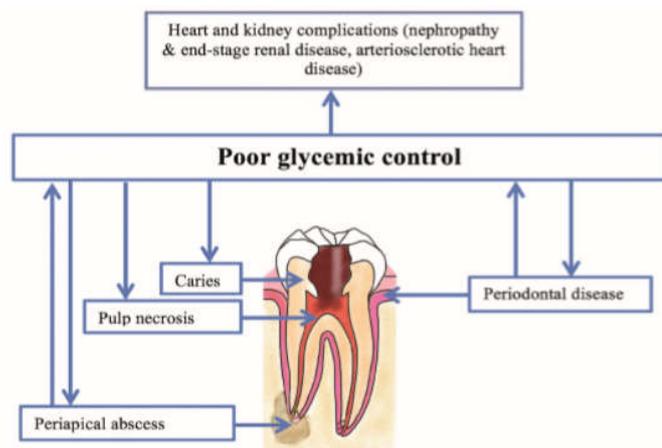


Figure 2. Pathophysiological relationship between diabetes and dental disease

**Thyroid Disorders:** Thyroid hormones play an important role in the regulation of growth, development and metabolic functions of the body.

**Thyrotoxicosis (hyperthyroidism):** Hyperthyroidism or thyrotoxicosis is defined by a decrease in thyroid hormone production and thyroid gland function.

**Hypothyroidism:** Hypothyroidism is defined by a decrease in thyroid hormone production and thyroid gland function.

**Dental Management Of Patients Who Have Thyroid Disease:** Controlling thyroid disease is defined by length of treatment, medical follow-up, thyroid hormone levels and absence of symptoms. Patients who have euthyroidism routinely are followed up at least twice a year. In patients affected by hypothyroidism, history of levothyroxine sodium dosage can be used to assess control. Following are recommendations for dental care for patients who have a known thyroid disease and are on medications. The oral health care professional should be familiar with the oral and systemic manifestations of thyroid disease so he or she can identify any complication and assess the level to which the condition is controlled. If a suspicion of thyroid disease arises for an undiagnosed patient, all elective dental treatment should be put on hold until a complete medical evaluation is performed (Pinto, 2000).

## Pregnancy

**Endodontic Considerations:** If dental caries is the source of pain or acute infection in an otherwise healthy gestational woman, a dentist should provide invasive care no matter what the patient's phase of pregnancy. Dental decay also presents an additional source of bacterial load on the patient. As previously mentioned local anesthetics are acceptable for use in pregnant women. Additionally there is no contraindication for using diagnostic procedures deemed necessary, such as appropriate radiographs, during a patient's pregnancy, as long as normal safety precautions are followed (Connolly *et al.*, 1997).

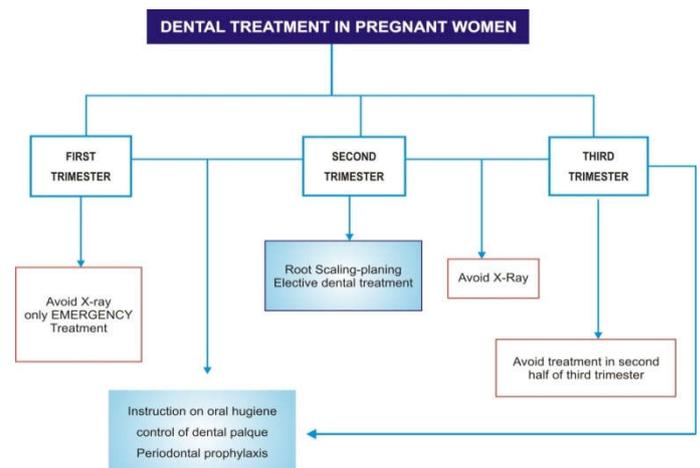


Figure 3. Algorithm for dental management in pregnant women

**Respiratory Disorders:** The respiratory system is basically responsible for O<sub>2</sub> and CO<sub>2</sub> exchange between the blood and the external environment. Maintenance of the mentioned partial pressure gradients is essential for ensuring adequate pulmonary gas exchange. This gas exchange takes place passively across partial pressure gradients within the terminal respiratory units (alveolar spaces).

**Asthma:** Asthma is a pulmonary disorder characterized by reversible stenosis or stricture of the peripheral bronchi, and is most often seen in children. Children, young adults and racial ethnic minorities living in urban areas are at the highest risk.

**Endodontic considerations:** Oral health care providers need to be aware of the potential for dental materials and products to exacerbate asthma. These items include dentifrices, fissure sealants, tooth enamel dust and methyl methacrylate. Fluoride trays and cotton rolls also have been implicated in promoting asthmatic events. The clinician should consider the need for prophylactic administration of antibiotics to prevent postoperative complications. Improper positioning of suction tips, fluoride trays or cotton rolls could trigger a hyper reactive airway response in sensitive subjects. Rubber dams should be used judiciously to avoid possible respiratory compromise. Prolonged supine positioning, bacteria-laden aerosols from plaque or carious lesions and ultrasonically nebulized water also can be asthma triggers in the dental setting.

**Chronic obstructive pulmonary disease:** Chronic obstructive pulmonary disease (COPD) is an irreversible and slowly progressing disorder characterized by a limitation of airway flow resulting from an abnormal pulmonary inflammatory reaction to harmful gases or particles – particularly tobacco smoke. Examples of COPD are chronic bronchitis and lung emphysema (Rahman *et al.*, 2000).



Figure 4.

**Bleeding disorders:** Bleeding disorders are due to altered ability of blood vessels, platelets, and coagulation factors to maintain haemostasis. Most of the bleeding disorders are iatrogenic (Little *et al.*, 2002).

**Hemophilia:** Hemophilia is an inherited X-chromosome-linked bleeding disorder caused by deficiencies of either clotting factor VIII (hemophilia A) or Factor IX (hemophilia B).

**Von willebrand disease:** Von Willebrand disease is an inherited disease marked by vWF deficiency. It is considered the most common congenital bleeding disorder, affecting 1% of the population of both sexes equally. Dental management of patients with vWD is generally similar to treatment of patients with an equivalent level of haemophilia A (Anderson *et al.*, 2017).

**Endodontic Considerations:** Endodontic treatment is generally low risk for patients with bleeding disorders. If a pulpectomy is indicated, the possibility of the tooth requiring conventional endodontic treatment must also be considered. It is important that the procedure be carried out carefully with the working length of the root canal calculated to ensure that the instruments do not pass through the apex of the root canal. The presence of bleeding in the canal is indicative of pulp tissue remaining in the canal. Sodium hypochlorite should be used for irrigation in all cases, followed by the use of calcium hydroxide paste to control the bleeding. Formaldehyde-derived substances may also be used in cases where there is persistent bleeding or even before the pulpectomy (Connolly *et al.*, 1997).

### Cerebrovascular Disorders

**Stroke:** Stroke or cerebrovascular accident is defined by WHO as clinical syndrome of rapid onset of focal (or global as in coma) cerebral deficit lasting more than 24 hours or leading to death with no apparent cause other than vascular one.

**Dental Management:** A patient with stroke in his record shall get special care during dental treatment: appointments shall be for choice in the morning, shall be short and without stress. Disabled patients shall be helped by the nurse to sit on dental chair, their airways shall be free. Dentist shall stand in front of the patient, without mask, and questions shall be simple and clear.

- History of past strokes needs to be elicited: date, seriousness, treatment, disabilities.
- Blood pressure and pain should be monitored. Emergency dental treatment is allowed six months after stroke, taking neurologist's advice and some precautions are needed, according to the specific characters of the stroke.
- If needed, dental treatment produces bleeding (teeth extraction, pulpectomy, subgingival scaling, periodontal surgery), anticoagulant systemic medication may cause serious haemorrhage, therefore anticoagulant drugs like heparin should be stopped at least 6-12 hours before treatment. Six hours after bleeding, when blood clots are built up, heparin systemic treatment can be resumed. The dentist should be ready for emergency intervention in case of local hemorrhage, with haemostatic medication and cautery.
- The minimal amount of anaesthetic solutions should be injected, concentration of added epinephrine should be very. Use of gingival retraction cord soaked with epinephrine should be avoided.
- Metronidazole and tetracycline should be avoided, since they may affect blood clotting.
- If the patient shows symptoms of stroke, he should get oxygen therapy immediately and should be referred to a hospital as soon as possible.
- Patients with poor oral hygiene, dentists advise them the use of electric toothbrushes which are easier to handle, use of dental floss, oral prophylaxis using chlorhexidine and fluoride.

**Infectious Diseases:** Cross-infection during clinical practice can occur with transmission of infectious agents between patients and health workers in a clinical environment. Transmission of dental infection can occur through infected air

droplets, blood, saliva, and instruments contaminated with secretions. In addition, some infectious diseases have prolonged incubation periods or post-infection “window period” during which antibodies can't be detected (Ibrahima *et al.*, 2016).

### Hepatitis B

Viral hepatitis is the most common liver disorder. The hepatitis B virus (HBV) is an encapsulated DNA virus that replicates within the hepatocyte. The transmission routes comprise sexual contact, intravenous drug use and blood trans-fusions. HBV is most commonly found in oral surgeons, periodontists and endodontists. If a non-immunized individual becomes exposed to HBV, immunoglobulin can be administered to afford protection after exposure.

### Hepatitis C

Hepatitis C virus (HCV) infection is the main cause of chronic liver disease. HCV is an RNA virus mainly transmitted via the parenteral route from infected blood. The sources of contagion include blood transfusion (although the risk has been minimized since donor blood tests and controls are made), percutaneous exposure through contaminated instruments, and occupational exposure to blood (Cruz-Pamplona *et al.*, 2011). The individuals at greatest risk are hemophiliacs, patients on dialysis and parenteral drug abusers. Other transmission routes are sexual contact and perinatal and idiopathic contagion.

**Dental Management:** Liver disease has important implications for patients receiving dental treatment. The most frequent problems associated with liver disease in clinical practice refer to the risk of viral contagion on the part of the dental professionals and rest of patients (cross-infection), the risk of bleeding in patients with serious liver disease, and alterations in the metabolism of certain drug substances – which increases the risk of toxicity (Fiske and Boyle, 2002). HCV has been detected on different surfaces within the dental clinic after treating patients with hepatitis C, and the virus moreover is able to remain stable at room temperature for over 5 days.

Strict sterilization measures are therefore required, since deficient sterilization can expose both the dentist and other patients to hepatitis infection (Cruz-Pamplona, 2011). The universal protective measures are applicable in order to prevent cross-infection, i.e., the use of barrier methods, with correct sterilization and disinfection measures.

PROCEDURE AFTER ACCIDENTAL INJURY	
Puncture/Cut	Mucosal surface contact
1. Careful washing of the wound, without rubbing, for several minutes with soap and water or a disinfectant.	Abundant irrigation with water or saline solution for several minutes.
2. Pressure applied beneath the level of the wound to induce bleeding.	
Determine the hepatitis antigen status of the patient	
Parenteral exposure to hepatitis virus-positive antigens ⇒ anti-hepatitis B immunoglobulin	

Figure 5. Procedure to be followed after accidental (Smith, 2001)

### HIV

HIV is a blood-borne retrovirus infection transmitted primarily by blood and bodily fluids by intimate sexual contact and parenteral route. After infection enzyme reverse transcriptase allows the virus to integrate its own DNA into the genome of an infected cell and replicate using the infected cell's ribosomes and protein synthesis. The most effective

management in the progression of HIV infection and AIDS is a Combination of antiviral agents known as highly active anti-retroviral therapies (HAART), which has significantly increased the lifespan and the quality of life of individuals infected with HIV (Connolly, 1997).

**Endodontic considerations:** Neither HIV infection nor AIDS are contraindications for endodontic treatment, including pulpotomy. Indeed, as in many other cases of immunosuppression (transplants, dialysis etc.), endodontic treatment and the retention of natural teeth offers numerous advantages for patients with HIV. Endodontic treatment does not appear to be associated with an increase in postoperative complications and does not warrant routine pre- or postprocedural antibiotics (Connolly, 1997).

**Pulmonary Tuberculosis:** Tuberculosis (TB) is one of the main causes of death throughout the world. Approximately one-third of the world population is infected with *Mycobacterium tuberculosis*. Tuberculosis can affect any body organ, though the lungs are the most common location. At first exposure to the bacterium (primary infection with the Koch bacillus), the latter induces a characteristic granulomatous reaction (tuberculous follicle or granuloma) (Lozano, 2011).

### Dental Management of tuberculosis patients (Kohn, 2003):

- Limit the use of ultrasonic scalers and highspeed handpieces in actively infected patients. High volume suction is mandatory for carrying out any procedure to minimize aerosol generation.
- Use rubber dam isolation with high vacuum suction. However, if the patient has productive cough it is better to avoid rubber dam.
- Maintenance of proper hand hygiene, personal protective equipment's like eye shields, facemasks, head caps, gloves and surgical gowns.
- Use a well constructed, soft pleated, high filtration face masks. While treating patients with symptoms of active TB, the operator should wear respirators rather than routine face masks.
- Provide dental operatories with fresh, non recirculated outdoor air to dilute the contaminated operating air.
- Cleaning and disinfecting critical and semi critical contact surfaces like Dental chair and accessories. Anti bacterial sprays may be used.
- Use of barrier techniques.
- Use of high efficacy filters or UV light in the exhaust air ducts.
- All dental settings should conduct an annual risk assessment for TB transmission.

### Renal Disorders

**Renal Failure:** Chronic renal failure is an important health care problem throughout the world. The existing management options range from simple measures based on changes in diet and life style, to different forms of dialysis (hemodialysis and peritoneal dialysis), and also kidney transplantation. Consultation with the nephrologist is essential before any dental treatment is carried out, in order to determine the condition of the patient, define the best moment for dental treatment, introduce the necessary pharmacological adjustments, or to establish other important aspects for preventing complications in the dental clinic (Cervero, 2008).

### Dental management of renal failure patients

- Consultation with the nephrologist provides information on the state of the disease, the type of treatment, the best timing of dental management, or the medical complications that may arise. Any modification of the usual medication used by the patients or of other aspects of their treatment must first be consulted with the nephrologist (Proctor, 2005).
- Close cooperation between medical and dental professionals is desirable in order to improve the oral and general health of the patient, based on the creation of a dental care program in the context of a multidisciplinary approach to the disease (Atassi, 2002).
- Prior to any invasive dental treatment, a complete blood count is to be obtained, together with coagulation tests, in view of the possible hematological alterations (Proctor, 2005).
- It is essential to eliminate any infection in the oral cavity as soon as possible, with the consideration of antibiotic prophylaxis when bleeding and/or a risk of septicemia is expected (extractions, periodontal treatments, endodontics and periapical surgery, the placement of orthodontic braces, tartrectomy, when bleeding is expected, implant surgery, and the reimplantation of avulsed teeth) (Werner, 1999).

- Blood pressure is to be monitored before and during treatment, with the administration of sedation to lessen anxiety (De Rossi, 1996).
- The metabolism and elimination of certain drugs are altered in situations of renal failure.
- The prescription of aminoglycoside antibiotics and tetracyclines is to be avoided, because of their nephrotoxicity.
- Analgesics, paracetamol is the non-narcotic analgesic of choice in application to episodic pain. Aspirin possesses antiplatelet activity, and as such should be avoided in uremic patient.
- Benzodiazepines can be prescribed without the need of dose adjustments, though excessive sedation may occur. The narcotic analgesics (codeine, morphine, fentanyl) are metabolized by the liver, and so usually do not require dose adjustment (Werner, 1999).

### Neurological Disorders

**Epilepsy:** The word “epilepsy” is derived from the Greek word “epilambanein” meaning to take or to seize. Modern medicine defines epilepsy as a chronic neurological disorder characterized by frequently recurrent seizures. Epileptic seizures are reversible and reoccur frequently (Fiske and Boyle, 2002). Seizures can be defined as the discontinuity of normal brain functions due to sudden electrical discharges

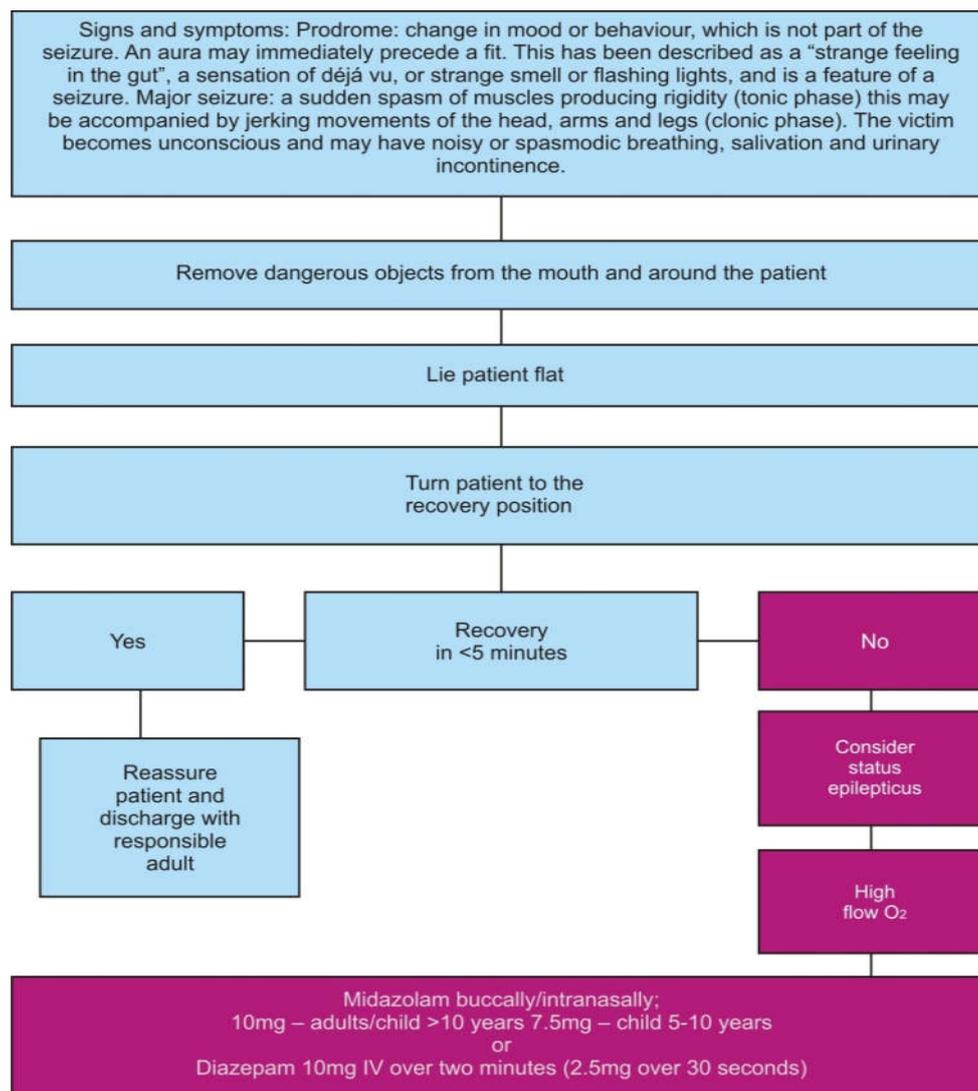


Figure 6. Algorithm for the management of seizures seen in patients with epilepsy

which may be either excessive or inadequate; these result in episodic convulsions (such as involuntary motion), disturbances in perception, or alterations in consciousness. The outcome of such excessive discharge during electrical conduction is called seizure (Mehmet *et al.*, 2012).

## Conclusion

Dental emergencies can occur at any time; however, it is important to remember that no treatment should be carried out without prior planning as this could result in additional problems. A thorough patient history can draw the practitioner's attention to potential medical emergencies that could occur. It is particularly important history to enquire about known allergies or adverse reactions to medication so that these can be avoided. Good methods of practice can prevent many emergencies, for example prompt treatment of a diabetic patient at a predictable time thereby avoiding hypoglycemia.

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