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Review Article

Drugs and dentistry: A review

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ABSTRACT

A drug is defined as a chemical substance which alters functions of living organisms. These are used as a medication for the diagnosis, prevention, control or for treatment of a disease. Drugs effects depend on various factors such as body size, general health of individual, amount and strength of medication and whether one drug is taken or two are taken at same time. Dentists also use certain medications for management of some health conditions which affect oral cavity. Medications used in dentistry may be used for management of pain, prevention of diseases or fight against infections. These can also be used before or after any dental procedure to reduce pain or discomfort and also to prevent complications associated with dental procedure. These drugs may also develop variable adverse effects such as headache, skin rashes, nausea, sweating, lack of appetite etc depending on type, and dose of drug taken. Medications used in dentistry include anaesthetics, pain killers, antibiotics, antiviral drugs and antifungal etc. This paper provides an insight to the various medications, their role in dentistry & how they can help a dentist.

1. Introduction

Pharmacology is the study of interaction of drugs with living organisms along with history, source, physicochemical properties, dosage forms, and methods of administration, absorption, distribution, mechanism of action, biotransformation, excretion, clinical uses and adverse effects of drugs.[1] A drug is defined as a chemical substance which alters functions of living organisms. These are used as a medication for the diagnosis, prevention, control or for treatment of a disease. Drugs are used to reduce abnormal effects, pain and other symptoms associated with various diseases.[1] Drugs can be obtained from minerals, animals, plants, prepared from synthetic sources, micro organisms and from genetic engineering.[1] There are various mechanisms in which drugs act and generate pharmacological effects. These mechanisms include: action via a receptor, action via direct change of the effect of an endogenous agonist, action via inhibition of transport process, via enzyme inhibition or activation of enzymatic activity and via some other ways like chelating agents, osmotic diuretics and replacement drugs.[2]

The chemical substance in the drug which affects physiological functions in body is called as active

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ingredient. For most of drugs, the quantity needed to generate an effect is very less, often as less as five micrograms. So this quantity is too small to handle and package and these chemicals are costly and giving out small amounts will cause most of drug to be lost and wasted. So inactive ingredients which produce no effect on functioning of body, are added to drug to fill out the drug. The inactive ingredients include lactose, dyes and gluten. For the drugs to be taken orally, the inactive ingredients act to binder and also provide lubrication for easy swallowing of drug. Therefore inactive ingredients are categorized as fillers, binders and lubricants.[3]

A drug can act either as an agonist or an antagonist. An agonist drug acts as an activator, or promoter of an activity of a specific regulatory system of body. An antagonist drug acts as an inhibitor and has opposite effect as that of agonist. These drugs act on a regulatory molecule, called as a receptor, which receives the agonist or antagonist drug, and further sends the signal to the body system it regulates, activate or inhibit according to type of drug molecule used whether agonist or antagonist.[4]

A drug must have some features which makes it suitable for interacting with a receptor. As receptors are specific in nature and only respond to a very specific drug.

1.1. Thus, drugs must have the following characteristics in order to be an effective pharmacological drug

1. The drug must possess specific size, shape, atomic configuration and electrical charge so that it can interact with the receptor.
2. A drug must have the appropriate features to travel to its site of action or receptor from its site of administration in the body.
3. A dug should have such composition that it can be easily inactivated or excreted from the body of patient after it has been used for its purpose.[4]

1.2. Drugs used in dentistry

There are several medications which are used to manage various types of conditions associated to the oral cavity. Following medications are used commonly:

1. Anaesthetics
2. Analgesics (Pain killers)
3. Antibiotics
4. Antifungal
5. Antiviral
6. Astringents and Gingival Displacement Products
7. Desensitizing Agents
8. Medical Emergency Drug Kit

1.3. Local anaesthetics

Local anaesthesia is given mostly by the operating dentist using various infiltrative techniques and nerve blocks. These may be combined, if needed, with conscious sedation or topical anaesthesia.[5] Modern local anaesthetics are categorized based on chemical structure. Most commonly local anaesthetic agents used in dentistry are amide type. These include lidocaine, mepivacaine, bupivacaine and prilocaine. The other type of local anaesthetic agents consist of an additional ester linkage. Both these types of local anaesthetic agents have same mechanism of action but slightly different metabolism. Ester type agents are rarely used in dentistry for local anaesthesia. They are used as topical agent prior to injection to reduce patient discomfort which may occur from needle.[6]

1.3.1. Indications

Dental treatment procedures can be associated with mechanical, thermal, or chemical stimuli, resulting in a painful response. These procedures include oral surgery, periodontal, endodontic, prosthetic, and restorative treatments. Local anesthesia is used to manage these pain responses during treatment as they produce temporary sensory loss so that treatment procedure can be completed without any patient discomfort.

1.3.2. Contraindications

Local anaesthetic agents are contraindicated in patients who have known allergic history. Allergy is the only absolute contraindication to local anesthesia. However, some anesthetic agents or techniques should be avoided or used with caution in some individuals. Toxicity and interactions with other medications should also be considered while using these agents.[7]

1.4. Anaesthetic agents used in dentistry are

1.4.1. Lidocaine 2% plain

Used for blocks and infiltrations. It produces analgesia for brief duration. Maximum safe dose for adults is 4 X 2.2 ml cartridges or 3 mg kg^{-1}. Its effectiveness can be increased by the addition of 1:80 000 epinephrine and maximum adult safe dose to 10 X 2.2 ml cartridges.

1.4.2. Prilocaine 3% with felypressin 0.03 IU ml^{-1}

Used for blocks and infiltrations and have effective analgesia for longer duration that is over 90 minutes. Maximum adult safe dose 9 X 2.2 ml cartridges or 6 mg kg^{-1}.

1.4.3. Articaine 4% with epinephrine (1:100 000)

Currently recommended for infiltration only. It has rapid onset and ideal where blocks are contraindicated. Maximum safe adult dose 7 mg kg^{-1}.

1.4.4. Bupivacaine 0.25–0.5% plain

Used for blocks and infiltrations where up to 8 h of anaesthesia is required. Maximum safe dose 2 mg kg^{-1}.[5]

2. Analgesics (Pain killers)

Numerous analgesics are available for pain management. These are categorized into two types that are opioid and non-opioid analgesics. Non steroidal anti inflammatory drugs fall in non opioid category. These are further divided into nonselective traditional Non-steroidal anti-inflammatory drugs (tNSAID) and selective cyclooxygenase (COX)-2 inhibitors.[8]

2.1. Opioid analgesics

These are often prescribed by dental professionals for managing dental pain. Morphine is the main alkaloid in opium. It is effective analgesic which can diminish even pain. Pain suppression with opium is selective in nature without any effect on other sensations.[9] The opioids used in dentistry are: hydrocodone, codeine, oxycodone and tramadol.[8] The standard dose used in dentistry is 30-60 mg for codeine, 5-10 mg for hydrocodone and oxycodone.[9] In literature it has been thought that potency and efficacy of non-opioid analgesics is less than opioids, but clinical studies have repeatedly reported that non-opioid analgesics are more effective than opioids in reducing postoperative dental pain. If in any condition non-opioid analgesics fail to manage pain, an opioid analgesic may be administered along with non-opioid analgesics to provide synergistic effect for pain relief. In dentistry, opioid analgesics are commonly prescribed in conjunction with acetaminophen or NSAIDs to increase the analgesic effect rather than using them alone.

There are numerous side effects caused by these analgesics including nausea, vomiting, respiratory depression, constipation, disturbance in sleep pattern of individual, development of dependence and addiction for drug.[8]

2.2. Non Opioid analgesics

NSAIDs reduce the synthesis of prostaglandins which result from inhibition of action of COX. tNSAIDs prevent activity of both COX 1 and COX 2 to variable level. These drugs have anti inflammatory action, analgesic and anti pyretic actions, which are primarily due to inhibition of COX 2 activities and its expression is induced by inflammation. But COX 1 inhibition is responsible for NSAID induced gastropathy, nephropathy and increased bleeding time.[10]

Among the NSAIDs, aspirin remains a gold standard to which other analgesics are compared. It is rapidly changed in the body to salicylic acid,that is responsible for its actions. Aspirin inhibits COX-1 irreversibly by acetylating it and return of COX activity depends on production of new enzyme. Various clinical studies reported that, NSAIDs are effective for treatment of moderate to severe dental pain. There is need to clearly understand the mechanism of action of these drugs for their appropriate use. It also must be taken into consideration that analgesic only provide symptomatic relief from pain and has no effect on the causative factor of the pain, so removal of cause of infection must be the first line of treatment.[9]

3. Antibiotics

Dental infections are usually show symptoms of pain and swelling in the oral area. These infections of oral area should be managed as soon as possible, because they may result in severe and irrecoverable consequences such as osteomyelitis, brain abscess, airway obstruction, carotid infection, sinusitis, septicemia, meningitis, cavernous sinus thrombosis, orbital abscess, and loss of vision.[11] It has been reported that the most commonly occurring feature of orofacial infections are dentoalveolar abscess.[12]

Antibiotics are typically used by dental professionals for the following purposes:

1. For treatment of acute odontogenic infections.
2. For treatment of non-odontogenic infections.
3. These drugs are used for prophylaxis against focal infection in patients at risk (endocarditis and joint prostheses).
4. Also used for prophylaxis against local infection and systemic spread in oral surgery.[13]

Infections in dental origincan be treated by surgical interventions, endodontic treatment, and by giving antibiotic therapy.[14] In dentistry most commonly used antibiotics are Amoxicillin and Clindamycin. Amoxicillin is used for treatment of bacterial infections such as abscess, sinusitis, pericoronitis and acute necrotizing ulcerative gingivitis. Side effects of this drug include nausea, vomiting or diarrhea. Severe allergic reaction to this drug rarely occurs.[15] Amoxicillin and penicillin V are the safest drugs and the most common drugs used during pregnancy. Tetracycline and Doxycycline when given during pregnancy affect teeth and bone development. Animal studies reported arthopathy and congenital cartilage defects with use of Ciprofloxacin but there is no sufficient evidence among human studies.[16]

Clindamycin is used in cases of penicillin allergy and it is substitute for penicillin resistant bacteria. Similar to other antibiotics, it may cause overgrowth of harmful bacteria in large intestine which may result in mild diarrhea or life threatening condition called as colitis.[15] Use of broad spectrum antibiotics may disturb the normal ecological balance of micro flora in oral cavity which may result in development of candidiasis.[17]

3.1. Antifungal agents

An antifungal drug is used to treat fungal infections. Fungal infections may produce superficial infestations which affect the skin or mucous membrane and there may be systemic infections affecting various organs of body. Superficial fungal infections are primarily caused by Candida albicans fungus usually found in oral cavity. These infections are usually indicator of serious systemic conditions such as immunodeficiency.

Systemic infections are categorized into two groups on the basis of status of the patient and the type of organism causing infection. Opportunistic infection occurs in weakened and immunocompromised patients and also occurs in patients who are taking immunosuppressive agents. Endemic infection is caused by variety of pathogens distributed unevenly in the environment.[18] The perfect fungi, dividing by sexual reproduction are rarely seen in oral cavity. But occasionally isolated perfect fungi in patients with acquired immunodeficiency syndrome. These include Aspergillus, Geotrichium and Mucor species. The imperfect yeasts like Candida species, divide by sexual reproduction are isolated from oral cavity.[19] This species form the largest proportion of fungal microflora in human oral cavity and 30% to 50% individuals carry this organism. It is isolated from 60% of old patients wearing dentures over age of 60 years.[20]

Antifungal drugs are classified as following types:[21]

1. Antibiotics: [polyene]
   Amphotericin, Nystatin, Hamycin and Natamycin.
2. Heterocyclic benzofuran
   Griseofulvin.
3. Antimetabolites
   Flucytosine
4. Azoles
   Topical: Clotrimazole and Econazole.
   Systemic: Ketoconazole.
5. Triazoles
   Systemic: Fluconazole and Itraconazole.
   Allylamine: Terbinafine
6. Other topical agents

Tolnaftate, Undecylenic acid, Benzoic acid, Cyclopiroxolamine, Quiniodochlor, andSodium thiosulfate.[21]

Commonly used antifungal drugs in dentistry are: Amphotercin B, Nystatin, clotrimazole, ketoconazole, miconazole and griseofluvin.[18]

4. Astringents and Gingival Displacement Products

The main aim of Prosthodontic treatment is to restore esthetics and occlusal functions after loss of teeth.[22]Fixed prostheses are used as most common treatment modality to replace the lost teeth. During taking impressions tissue or gingival management is critical step to reproduce marginal details precisely in fixed restorations. Gingival displacement is deflection of marginal gingiva away from the tooth. It was reported that the optimum gingival displacement is approximately 0.2 mm. Impressions taken without gingival displacement, results in higher chances of voids, tearing of impression materials, and less marginal accuracy.[23,24]

Astringents are the substances used for management of bleeding during gingival retraction. They also help in enhancing the gingival resistance against infections. They precipitate proteins, without penetrating into cells, therefore affecting the superficial layer of mucosa only. They make the surface mechanically stronger to toughen it and reduce exudation. The word came from the Latin word adstringere which meaning "to bind fast". They have relatively less cell permeability, and they act generally as irritants in moderate concentrations and caustics in high concentrations.[25]

In dentistry they are applied to gingival tissues before taking impressions, placing Class V restorations or root surface restorations. The most common procedure for the displacement of soft tissues surrounding the abutment is based on the placing the cord which is commonly pre-impregnated with liquids for maintaining haemostasis. Astringents may be administered by use of retraction cords which are impregnated with the agent or by applying them to cotton pellets. Varieties of astringents are available such as alum, aluminum chloride, zinc chloride (8-20%) and tannic acid. Styptics are the concentrated form of astringents. They produce superficial and local coagulation and these are ferric chloride and ferric sulfate, Aluminium chloride and Ferrous sulfate are mostly preferred in prosthodontic procedures as they produce very less tissue damage.[26]

5. Desensitizing Agents

Dentin desensitizing agents are used for treating dentin hypersensitivity. Dentin hypersensitivity (DH) is a painful response in the exposed dentin to stimuli that are thermal, evaporative, tactile, osmotic, or chemical.[27] It is a challenging condition in dental practice, and is popular dental problem in the world population. Incidence of DH occurrence is found to be about 35% of the population worldwide and occurs mainly between 20 and 50 years of age. It is more common in females than males in an age range from 30 to 40 years old.[28]

There are two common methods to treat tooth sensitivity, these are passive and active. The passive method is a non-drug infusion approach, where subjects experiencing mild tooth sensitivity while conducting tooth whitening can follow this regimen by reducing treatment time, alternating days or even holding treatment until the sensitivity resolves. Active treatment of sensitivity makes use of desensitizing agents, and is more concerned with the management of moderate to severe tooth sensitivity. These desensitizing agents either act via dentinal tubule occlusion

or nerve depolarization. Several agents are used to occlude dentinal tubules such as strontium ions, sodium fluoride, stannous fluoride, and sodium mono fluorophosphate.[29]

5.1. Various desensitizing agents used in dentistry are classified as

1. Mode of administration
   (a) At home desensitizing agents
   (b) In-office treatment
2. On the basis of mechanism of action
   (a) Nerve desensitization: Potassium nitrate
   (b) Protein precipitation: Gluteraldehyde, Silver nitrate, Zinc chloride and Strontium chloride hexahydrate
   (c) Plugging dentinal tubules: Sodium fluoride, Stannous fluoride, Strontium chloride, Potassium oxalate, Calcium phosphate, Calcium carbonate and Bio active glasses (SiO_2 –P_2O_5 –CaO–Na_2O)
   (d) Dentine adhesive sealers: Fluoride varnishes, Oxalic acid and resin, Glass ionomer cements, Composites and Dentin bonding agents
   (e) **L**asers: Neodymium: yttrium aluminum garnet (Nd-YAG) laser, GaAlAs (galium-aluminium-arsenide laser), Erbium-YAG laser
   (f) Homeopathic medication: Propolis[30]

5.2. Antiviral drugs

Antiviral drugs are medications that help the body to fight against some viruses that can cause disease. These drugs also act as preventive measures and can protect the humans from getting viral infections or spreading a virus to others. These medications work in different ways depending on type of drug and virus. These drugs can:

1. Cause blockage of receptors so that virus can't bind to receptor and unable to enter into cells.
2. These drugs can boost immune system of body and help body to fight against viral infections.
3. Antiviral drugs lower the viral load in the body.[31]

Acyclovir and valacyclovir are purine nucleoside analogues antiviral drugs and both of these drugs act against herpes simplex 1 infections, varicella zoster (shingles and chicken pox), and the Epstein-Barr virus. Neither acyclovir nor valacyclovir cures the viral infection, but these drugs reduce the symptoms and signs associated with the viral infection. These drugs can be taken with or without food, and it is best to take the drug around the same time every day. For the old patients dose of each drug should be reduced as compared other patient.

These drugs have impact on viral growth as they inhibit replication of the viral DNA. More drug is absorbed by virus-infected cells as compared to the normal cells. Thus, the active form of the drug remains available for long time where it is needed, increasing the efficacy of the drugs.[32]

Other antiviral drugs available include Famciclovir, Ganciclovir, Zidovudine, Didanosine, Stavudine and Lamivudine.

Side effects are variable depending on type of drug and its dose used. Adverse effects caused by antiviral agents are:

1. When applied topically may cause stinging and burning sensation after each application.
2. Orally taken drugs may result in, headache, nausea, malaise and some CNS effects
3. Anaemia and neutropenia are the most important side effects.
4. Nausea, anorexia, abdominal pain, headache, insomnia and myalgia
5. Myopathy, lactic acidosis, hepatomegaly, convulsions and encephalopathy are infrequent.[18]

6. Medical Emergency Drug Kit

Medical emergencies can occur in the dental office and emergency drugs in the dental practice have been designed to help dental care professionals to manage these medical emergencies effectively and safely.[33] There is list of Medicines and equipments which are required in any Dental Emergency Kit to manage any medical emergency in dental clinic. Along with these medicines, Staff in dental clinic should the know CPR or Cardio Pulmonary Resuscitation.

6.1. Medical emergency drug kit consists of following drugs and equipments

1. Oxygen Can (Portable 5L): It is used to provide Oxygen to patients who are having difficulty in breathing which can be resulted from various reasons on the dental chair like allergy, underlying heart conditions etc.
2. Oxygen Mask: This is to supply Oxygen to the patient
3. BP Apparatus**:** It may be digital or manual. This is useful to monitor the blood pressure of the patient.
4. Stethoscope: For evaluating heart rate and Blood Pressure of patient
5. Glucometer with Strips: To check Blood Sugar of patient as low blood sugar of a patient can result in coma if not attended immediately.
6. Pulse Oximeter: To monitor the pulse of the patient in case of a dental emergency
7. AMBU Bag: Also referred as Artificial Manual Breathing Unit. It is used for helping the patient to breathe properly as it pumps air into the lungs forcefully. This is used as a part of CPR or Cardio Pulmonary Resuscitation.
8. Inj. Adrenaline/Epinephrine: In patients having severe low blood pressure, this drug helps in increasing the

heart rate to counter low blood pressure.

9. Inj. Atropine: This is used to control or decrease heart rate in patients with High BP or in patients who have hyper salivation as it reduces the production of saliva and hence prevents aspiration of saliva in any dental emergency.
10. Inj. Avil: It consists of pheniramine maleate which is used for managing allergic conditions resulted from dental materials used during the dental treatment procedure.
11. Inj. Valium 2mg or 5mg**:** It is used for treating anxiety and also as a short-term treatment option for seizures.
12. Inj. Hydrocortisone: It is also used for management of allergic reactions which may result in dental emergencies. It decreases Inflammation to replace the function of corticosteroids in the body.
13. Tab. Prednisolone 5mg: It is primarily used as an Immunosuppressant or anti-inflammatory medication to counter any Auto Immune conditions which result in inflammation.
14. Inj. Phenytoin: It is an Anti-epileptic drug, used to treat or prevent seizures. It must be given prior to treatment procedure in patients with history of seizures or in conditions when seizures occur during dental procedure.
15. Inj. Deriphyllin 2ml: It is an emergency drug for asthma attack or COPD. It should be given to patient who suffers from an asthma attack during any dental procedure.
16. Salbutamol Inhaler: Also used in case of Asthma attack
17. Tab. Sorbitrate: It is a nitrate drug which causes widening of blood vessels and relaxing the vessels to increase the flow of blood to the heart. It is given in patients complaining of chest pain – Angina or patients who have a history of Coronary heart disease etc. This helps in increasing the flow of blood to the heart muscles and prevents a heart attack.
18. Tab. Asprin 75mg: This is used in patients who have a history of heart disease – angina, stroke, heart attack etc due to its antiplatelet effect. It has to be remembered that this drug delays formation of a clot and lead to increased bleeding in case of any surgical treatment in patients.
19. I/V fluid D25 100ml
20. Gel Foam Dental Sponge: In patients having High BP and on antiplatelet drugs, there may be problem in controlling bleeding from extraction socket, so in such condition gel foam dental sponge is used which helps in controlling bleeding and also helps in the formation of Blood Clot faster.
21. Glucose Powder: For providing immediate energy and increase blood glucose levels in patients suffering from low sugar.
22. Electrol: Used for replacing salts in cases of low BP
23. Drug Expiry Chart: Expiry dates of all the medicines in the Kit should be checked. For that expiry chart should be there so that expired drugs can be replaced.[34]

7. Conclusion

It is well said by Leonardo Da Vinci that "A physician who practices without knowledge of science is like a sailor who sails a ship without a compass. He is never sure of where he is going." Therefore a dentist should have appropriate knowledge of various types of drugs along with dental procedures which he/ she can use for benefit of patients. Dental professionals should have proper knowledge about the drugs including their mechanism of action, dose to be used, drug interactions and also side effects of drugs. Dentist should be ready to handle any medical emergency which can occur during any dental procedure. It can be best managed if a dentist keeps dental emergency kit ready in clinic and know how to use its all equipments and drugs.

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9. Conflict of Interest

None.

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