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Contemporary Pharmaco-Kinetics and -Dynamics of Drugs in Oro-Dentistry and Surgery

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Précis– To simplify, oro-dental pharmacology is the study of drugs used in the treatment of oral and dental diseases. Hence, pharmacokinetics and pharmacodynamics are two essential concepts in/for the understanding of the behavior of drugs in the body. While pharmacokinetics refers to the process by which drugs are absorbed, distributed, metabolized, and excreted from the body, pharmacodynamics refers to the study of the relationship between drug concentration and its effects on the body. The absorption of drugs in the oral cavity depends on various factors, such as the physico-chemical properties of the drug, the formulation, and the oral health status of the patient. The effectiveness of a drug in treating oral and dental diseases depends on its ability to reach the target site and produce the desired effect. Therefore, efficacy and safety of a drug depend on its pharmacodynamic properties, such as its potency, selectivity, and duration of action. And so, the understanding of pharmacokinetics and pharmacodynamics is crucial in the effective use of drugs in dental therapy and oral surgery. The appropriate selection of drugs and dosages can improve treatment outcomes and reduce the risk of adverse effects. Such would require a comprehensive understanding of the principles of drug(s) action, patient-specific factors, and the specific disease or condition being treated.

Sir William Osler (1849-1919), a Canadian physician and one of the "Big Four" founding professors of Johns Hopkins Hospital, known as the father of modern medicine, once said, "The desire to take medicine is perhaps the greatest feature which distinguishes man from animals." Pharmacology can be considered today as one of the few bio-medical sciences that bridges the gap between basic science(s) and applied clinical practise. Pharmaco-therapeutics, therefore, can be described as the proper selection of a bio-agent whose biologic effect on a living organism is most appropriate to manage or treat a particular disease state2. Hence, it requires a careful consideration, amongst

others, of dose and concentration, therapy duration, and adverse/side effects of any drug treatment.

Pharmacology[1], in general, is an extensive applied science dealing with drugs or pharmaceuticals and understanding the drug action on the body. Further, it is the study of the metabolism of drugs by the body. Hence, pharmacology plays a critical and key role in dentistry and oral surgery. Herein, in education and training, the aim of dental pharmacology is for the student and clinician to understand the scientific aspects of how medicaments, pharmaceutics, compounds, and drugs applied in dentistry, act within various body systems[2]. Briefly, pharmacology comprises [3] main facets of drug metabolism – pharmacokinetics and pharmacodynamics. Basically, while pharmacokinetics deals with drug absorption, distribution, metabolism, and excretion; pharmacodynamics deals with drug efficacy, safety, potency (receptor occupancy), and drug interactions. Hence, knowledge of such aspects drug is deemed essential and vital to safely and effectively manage or treat an oro-dental condition. Indeed, while the most common classes or types of drugs used by a dentist or an oral surgeon are analgesics (e.g., Acetaminophen or Paracetamol), anesthetics (e.g., Lidocaine, Articaine, Bupivacaine, Prilocaine, Mepivacaine, Propofol, Nitrous Oxide and/or Benzocaine), antibiotics (e.g., Penicillin, Amoxicillin, Metronidazole or Clindamycin) and anti-inflammatory drugs (e.g., NSAIDs, such as Aspirin, Ibuprofen, Naproxen, Celecoxib or Celebrex), each drug functions differently and distinctively; and so, it is essential to keep such allots on mind; for the occupied clinician or surgeon, to not neglect. Use of nitrous oxide or intra-venous sedation requires caution. Recently, Gabapentin[4], an inexpensive anti-seizure drug that is often prescribed for epilepsy and anxiety and by us for neuropathic/nerve pain to help manage chronic oro-facial pain, including pain related to temporo-mandibular disorders (even if as an adjuvant), and despite its availability (off-label) in the United States since 1993, has been increasingly associated with mis-use and drug abuse, both alone and in combination with other substances (typically, opioids). Toxicology5, an aspect of pharmacology dealing with poisons, actions, detection, and the treatment or remedy of any consequences, is, thus, another essential issue to consider.

By definition, pharmacokinetics studies the movement and fate of drugs, and pharmaco-dynamics studies the molecular, biochemical, and physiologic effects and/or actions of a drug2. In particular, pharmacokinetics deals with understanding the ability of the drug(s) to move from the site of administration to the site of action. Nevertheless, pharmacokinetics also helps us determine the ideal or correct dosing (concentration at target site) and route of administration of a given drug or drugs[2]. On the other hand, the pharmacodynamic parameters would relate those pharmaco-kinetic factors for the ability of a particular drug, pharmaceutical or compound to distribute and have a therapeutic effect. Therefore, pharmaco-dynamics deals with the effect of the drug in relation to its concentration in the body: drug absorption (the drug movement from the site of administration to the site of action), bio-distribution (the drug journey through the bloodstream to the various tissues of the body), metabolism (the drug break-down process) and excretion (the removal of the drug from the body)[5, 6, 7, 8, 9]. To simplify, when considering or thinking about pharmacokinetics, it is 'what the body does to the drug' whereas, for pharmacodynamics, it is 'what the drug or drugs does/do to the body'.

Consider yourself when administering a routine local anaesthetic: do you feel that such factors are of no or little importance, since the drug is injected directly near the nerve to block? Wouldn't achieving effective anaesthesia in an area where there is significant inflammation, much more difficult, challenging and/or frustrating, when compared to a non-inflamed tissue? Well, if you do, then such can be potential explained via understanding basic pharmaco-kinetics and -dynamics. Indeed, for example, a wide-spread fallacy is that the "half-life" of a drug can be used to predict the effect duration upon injection or administration. In dentistry and oral surgery, such applies to analgesics, anaesthetics and/or sedation. Try to remember that although the drug continues to be present in the blood and body for several half-lives, this does not identify the point at which the concentration falls below that required level to sustain a bio-effect. The "distribution half-life" of a drug can be used to predict the action duration, more precisely.

Here are some ways to optimize pharmaco-kinetics and -dynamics in oro-dental therapy:

- **Choose the Right Drug:** The selection of the drug should be based on the specific disease or condition being treated, taking into consideration the pharmacodynamic and pharmacokinetic properties of the drug(s). The choice of drug(s) should also consider any allergies, medical conditions, as well as other drugs/medications that the patient is taking.

- **Administer the Drug Properly:** The route (and fate) of drug administration, timing, and dosing are critical factors in the effectiveness and safety of the chosen or prescribed drug. Proper administration can improve the pharmacokinetic profile of the drug and enhance its therapeutic effects while minimizing any potential adverse effects and/or complications.

- **Monitor Patient Response:** Is essential to evaluate the effectiveness of the administered drug, assess adverse effects, and adjust the dosing as needed. Monitoring should be done regularly to ensure the drug is having the desired effect and not causing any harm.

- **Consider Patient-Specific Factors:** Age, weight, gender, and medical history, amongst others, can affect drug pharmacokinetics and pharmacodynamics. Consideration of these factors can help in determining the optimal dosing and administration of the chosen drug.

- **Educate the Patient:** Educating about the effects, dosing, and potential adverse effects of the drug can enhance (a) patient compliance with the treatment plan and (b) outcomes.

- **Personalize Treatment:** Personalizing treatment to the unique characteristics of each patient can further optimize pharmacokinetics and pharmacodynamics. Indeed, individualized treatment plans that consider age, weight, gender, medical history, and drug interactions can help achieve better therapeutic outcomes with fewer complications.

- **Consider Drug Interactions:** Many drugs used in dental therapy and oral surgery can interact with other medications that the patient may be taking for other indications and/or underlying diseases. Understanding the potential drug interactions and adjusting the treatment plan accordingly can help avoid adverse/side reactions and improve outcomes.

- **Utilize Technology:** Technology can help optimize pharmacokinetics and pharmacodynamics in dentistry and oral surgery. Tools such as electronic prescribing, clinical decision support systems, and medication management software can help stream-line (timely) medication management, reduce errors, and enhance patient safety.

- **Stay Informed:** Staying up-to-date with the latest developments in pharmacokinetics and pharmacodynamics can help dental professionals deliver the most effective and safe treatment. Continuing education and professional development can help us stay informed of the latest research, innovation, and the best practices in drug/medication management.

In summary, to better optimize, control and predict the pharmacokinetics and pharmacodynamics in dentistry and oral surgery, it is essential to perform a thorough pre-operative evaluation, choose the right/appropriate drug (and timing selection), administer it properly, monitor the patient's response, consider patient-specific factors, and educate the patient[4, 10]. Also, as mentioned earlier, consider personalizing treatment, drug(s) interactions, utilizing modern technology, and staying informed/updated of the latest RDI and best practices. Using evidence-based medicine, considering alternative therapies, monitoring adverse effects, and collaborating with other healthcare providers, in addition to addressing compliance issues or barriers, can be beneficial too. Hence, by taking a comprehensive approach to medication management, dental and surgical professionals can optimize treatment outcomes and improve patient safety, preferences, and satisfaction (implementation of quality assurance programs into/within your routine clinical practise, as guided by the American Dental Association and the American Association of Oral and Maxillofacial Surgeons)[?].

This is an open call for our young dentists and surgeons to better consider a comprehensive understanding of drugs affecting patient care and practise more concern about the pharmaceutics a patient is already taking, or the drugs prescribed for treatment; to reduce risk and provide patients with the safest and most effective oral and dental care.

Dentists and oral surgeons must have a solid understanding of pharmacology in order to make informed decisions about drug therapy

and to identify and manage potential complications. They should also be familiar with the principles of drug-drug interactions and be able to recognize any potential adverse effects or drug allergies in their patients. Incorporating pharmacology courses into the dental and oral surgery curriculum (topics such as drug interactions, drug metabolism, and drug toxicity), providing hands-on training and using case-based learning, can help ensure that students have the knowledge and skills necessary to provide safe and effective drug therapy to their patients. These should be up-to-date, evidence-based, and accessible to all our students.

1 | ENHANCING DRUG DELIVERY AND RX EFFICACY/OUTCOME VIA INTEGRATING NANOTECH AND AI

Briefly, nano-technology and -biotechnology can/do have potential applications in dentistry and oral surgery[6, 7]. While nanotechnology involves the design, synthesis, and manipulation of materials at the nano-scale level (typically in the range of 1 to 100 nanometers), nanobiotechnology is focused specifically on the application of nanotechnology to biological and biomedical systems. In the dental context, both could be used to improve drug delivery and treatment efficacy, as well as to develop new materials for restorative and regenerative dentistry. However, the use of nanotechnology in dentistry (nanoDentistry[?]) is still to be considered a relatively new and emerging field, despite significant advancements in the development of novel drug delivery systems and pharmacotherapeutics for oro-dental care, in recent years. For example, one area of active RDI is the employment of nanoparticles and nanostructured materials to enhance the bioavailability and therapeutic outcomes of anti-microbial and -fungal drugs, while also reducing or diminishing side effects. Another area of active research is the development of regenerative therapies for dental soft and hard tissue injuries and defects. Researchers are exploring the use of stem cells, growth factors, and other regenerative biomaterials to promote in situ tissue regeneration and repair in the oral and dental environment. Furthermore, there is growing interest in the emerging personalized medicine approaches, which involve tailoring treatments to individual patient needs based on their genetic and epigenetic profiles, as well as other factors such as life-style and environmental exposures. Overall, such accruing advancements do hold a great promise for further improving the quality of targeted oral and dental health care, preventive measures and treatment outcomes for our patients.

In parallel, while there is still much work to be done in developing and implementing AI (Artificial Intelligence) tools for pharmacology education and training in dentistry and oral surgery, the potential benefits are expected to be significant. Here are some ways in which AI could be beneficial, given the growing zeal about the likely AI uses in dentistry:

- **Personalized learning:** AI-powered adaptive learning systems can help customize our learning, training and routine practise experiences based on the individual needs, interests, learning and practise style. This can also help dental students learn more efficiently and effectively, via providing tailored learning content that cater to the individual strengths and weaknesses (i.e. adjusted level of content difficulty matching the skill level).

- **Simulation and virtual training:** AI-powered simulation and virtual training systems can provide a safe and controlled environment for us and students to practice administering drugs and monitoring their effects (mimicking the unique conditions/profile of the patient). This can help develop skills needed to apply pharmacology principles in clinical practice.

- **Data analytics:** AI algorithms can analyze large amounts of data to identify patterns, trends, and insights that can inform drug therapy decisions. This can help us make more informed decisions about drug therapy, treatment plan and so, improve patient outcomes.

- **RDI (research and development and innovation):** AI can help accelerate drug discovery and development by analyzing large datasets and predicting the efficacy and safety of new drug candidates. This can help bring new drugs to the market faster and more

efficiently. Herein, AI can also help us discover new clinical knowledge and insights from large amounts of the dental data, such as dental images and patient records. This can help identify patterns and trends that may not be visible to the human eye and help us diagnose conditions earlier, plan treatments more effectively, and lead to new discoveries and innovations in dentistry.

- **Stream-lined workflows and practice management:** AI can automate many of our routine tasks, such as appointment scheduling and billing thereby freeing up staff time for more complex tasks; i.e. aid clinical practices operate more efficiently and cost-effectively.

- **Predictive analytics:** AI algorithms can analyze patient data to identify risk factors, as mentioned earlier, however also for dental conditions, such as cavities and gum disease. This can help us develop preventative strategies to lower disease incidence and severity.

2 | COMMENTARY

To add, incorporating AI into dental education and training programs can help our students stay up-to-date with the latest developments in dental technology and prepare them for a future in which AI is likely to play an increasingly important role (exposure to emerging technologies). Learning how to use AI-powered tools and systems (early on) can also help our dental students develop enhanced critical thinking skills and learn to evaluate and interpret complex data sets. Dental schools could (should?) quickly adapt and consider offering courses or modules on AI and its applications in dentistry. This could include both theoretical and practical components, such as lectures, workshops, and hands-on training with AI-powered tools and systems. It is worth noting that while incorporating AI into dental education and training would require substantial investment in new resources and infrastructure, such as AI-powered dental imaging systems and software, one can, however, advocate that the potential benefits in terms of improved education outcomes and better-prepared dental professionals could make it a worthwhile investment; and is likely to become more widespread in the coming years (some dental schools are already using AI-powered dental imaging software to teach students how to analyze dental images and develop treatment plans and AI-powered virtual reality simulations to help students practice surgical procedures; such as the Los Angeles and the San Francisco Schools of Dentistry at the University of California, the School of Dentistry at the University of Michigan and at the University of Sao Paulo and Universidad de Buenos Aires) as the technology continues to develop and become much more accessible. Hence, as AI continues to transform the field of dentistry, it is indisputably important for Chilean dental schools to prioritize the integration (and succeed in the rapidly evolving field) of AI into their curriculum and research programs to ensure that, both, students and faculty are at the forefront of the latest advancements in dentistry and oral surgery, equipped with the adaptive knowledge and vital skills (and functioning infrastructure), really needed to meet the challenges and opportunities of the 21st century.

The Chilean government can also support the integration of AI into dental education and practice via not only providing funding and resources for research and development of AI applications in dentistry and pharmaceutics, yet also through establishing partnerships between universities and AI companies to facilitate the transfer of technology and expertise, developing policies and regulations that encourage the responsible and ethical use of AI in dentistry, providing incentives for dental schools to adopt AI into their curricula, such as grants or tax credits, offering training and continuing education programs for dental professionals to learn about AI applications, and prioritizing the development of infrastructure to support the implementation of AI in clinics and practices. By taking these actions, the Chilean government can perhaps play a very critical role in supporting and boosting the integration of AI into dental education and practice, which, as aforesaid, can have significant benefits for the dental profession and for public health.

3 | ACKNOWLEDGMENTS

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