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OFF LABEL DRUGS IN DENTAL PRACTICE

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Abstract

Whenever a drug is used in a different way from what the regulatory body has approved it is said to be 'off label use'. The drug may be given for different use other than its original use or may be of different dosage or may be given for different age group or may be given in different route. Off label usage may lead to Adverse Drug Events. With continuous increase in patients seeking multiple practitioners for the same problem off label usage has become a routine practice. Off label usage is not clinically unacceptable. Lack of guidelines regarding off-label use has left its use at discretion of the prescriber.

Keywords: Off Label Usage, Analgesics, Regulatory Body Guidelines, Drug Dosage.

INRODUCTION

Off-label drug use refers to **prescribing a drug for a different purpose than what the regulatory body has approved**. This practice is called "off-label" because the drug is being used in a different way other than on its package.[1] Recent evidences show that increase in polypharmacy and the drugs available on the market make off-label drug usage very common in clinical practice.[2] Dentists frequently prescribe opioid analgesics for pain. The patients may misuse the prescription & become a regular opioid user.[3]

The clinical practice of dentistry is regulated by laws and regulations. Dentists should be aware of all such regulations including REMS. Risk, Evaluation, and Mitigation Strategies (REMS) to ensure that the benefits outweigh the risks for a particular drug. Standard of care changes from time to time due to the data & experience acquired with that drug. Sometimes off-label use becomes standard of care.[4]

Rationale Behind Off Label Drug Usage

Continuous post extraction pain following third molar surgical impactions, gingival flap surgeries.

When NSAIDs becomes resistant to pain

Polypharmacy

Apprehensive patients

Delayed dental care due to COVID-19 pandemic has greatly influenced Off-label usage.

Migration of patients in pandemic

Commonly Prescribed Off Label Drugs In Dentistry

Anticonvulsant Gabapentin is commonly prescribed off-label to treat chronic nonspecific & NSAIDs resisant pain

Tricyclic antidepressants amitriptyline and nortriptyline, used in the treatment are depression are prescribed for TMDs.[5]

Botulinumtoxin A (Botox) neuromuscular blocking agent used in spasticity strabismus cervical dystonia overactive bladder & migraines. It is used off-label in dentistry for treating pathologic clenching, masseter muscle hypertrophy, bruxism dysphagia, hypersalivation and TMDs. It is also to treat gummy smile.[6,7,8]

Fluoride varnish used in the treatment of hypersensitivity seals dentinal tubules in cavity or applied as a liner in sensitive root surfaces. Now dentists use it for caries prevention[9]

Dental products containing amorphous calcium phosphate and casein phosphopeptide is approved for treating dentinal hypersensitivity during dental procedures. Its Off-label use is utilized in the treatment of xerostomia and remineralizing subsurface lesions.[10]

Silver diamine fluoride (SDF) was approved to treat dentinal hypersensitivity, now used off-label for arresting caries. FDA in 2016 approved SDF for arresting caries in pediatric age group and adults. Off label usage are not clinically inappropriate. This product now is considered standard of care.

Chlorhexidine gluconate 0.12% is an antimicrobial rinse used to reduce periodontal pocket depths in gingivitis & periodontitis. Off-label used to treat caries.[11]

Povidone iodine is an approved external antiseptic agent. Off label it is used for subgingival irrigation during SRP procedures[12,13,14,15]

Pentoxifylline is an approved agent in the management of the peripheral vascular disease. Offlabel used in the management of Oral submucus fibrosis & Recurrent apthous stomatitis[16,17,18,19]

DRUG	INDICATION	OFF LABEL USE
Gabapentin	Anticonvulsant	Chronic nonspecific & NSAIDs resisant pain
Tricyclic antidepressants (TCAs)	Depression	TMDs.
Botulinumtoxin A (Botox)	overactive bladder, migraines, spasticity, cervical dystonia, and strabismus	TMDs.Smile correction
Fluoride varnish	Hypersensitivity, sealing of dentinal tubules during cavity preparations or on sensitive root surface as liner	Dental caries
Caseinphosphopeptide/Amorphous calcium phosphate	dentinal hypersensitivity	xerostomia, and remineralizing of subsurface lesions.[10]
Silver diamine fluoride (SDF)	dentinal hypersensitivity	Dental caries
Chlorhexidine gluconate	Gingivitis & Periodontal pocket	Dental caries
Povidone iodine	External antiseptic	Subgingival irrigation & early childhood caries
Pentoxifylline	Peripheral vascular disease	OSMF,RAS

Implications

A thorough knowledge on patient's medical history and medications is essential for accurate diagnosis and safe treatment. This helps clinicians to consider adverse drug reactions or noncompliance issues.

Ethics Of Off-Label Drug Use

Off-label use pose a great threat to increase in the risk of adverse drug reactions. Drug safety & continuous monitoring are the two key factors that determines outcome of off label usage. The most ethical & safe practice should be based on relevant scientific evidence, after weighing the potential risks associated with each treatment option. Clinical decisions lacking sufficient scientific evidence can increase the risk of adverse reactions.

Legal Considerations

Legal claims have been made against clinicians for adverse drug reactions related to off-label usage.While using drugs or medical devices in research institutional review board approval,ethical approval are required. No such review are done for off label usage.

Further Research tests hypotheses, draws conclusions and adds to a knowledge base, while practice aims to diagnose, prevent, or treat. Informed consent is mandatory in research whereas no such things are practised in offlabel usage. Till now there are no regulations to streamline offlabel usage. As a result scientific evidences cannot be traced because of offlabel usage.It still remains a mystery whether to allow or not practice offlabel usage.As long as regualtions are not made for offlabel usage the clinician may not be liable for adverse drug reactions & medical negligence following offlabel usage.

DISCUSSION

National Disease and Therapeutic Index (NDTI) 2001 says 21% of commonly prescribed medications were offlabel and 15% lacked scientific evidence of its therapeutic efficacy.[20] In a 2006 study of clinic-based physicians nearly 21% of their prescriptions were off-label & 27% of those had strong scientific evidence. A 2016 Canadian study of primary care clinics found overall rate of 12% of prescriptions for off-label uses. The percentage varied by therapeutic class, ranging from 5% for ENT medications, 25% for CNS medications ,50% oncology drug use is off-label.[21,22,23]

Results from various studies show an overall lack of knowledge concerning off-label drugs and their use regardless of clinicians level of education and years of experience. No educational programme discuss about offlabel drug usage in detail. There is no literature appraising off-label drug use and polypharmacy in the medical & dental discipline.

CONCLUSION

Off-label uses have not been formally evaluated and evidence drawn from one clinical situation may not apply to others. As a result off-label use provides contradictory results among various stakeholders including physicians and consumers. The Physicians freedom to prescribe drugs off-label carries has greater advantages, it permits innovation in clinical practice particularly when approved treatments have

failed. It allows physicians to adopt new practices based on emerging evidence. Off-label prescriptions should be allowed for good patient care and to explore various therapeutic options but such prescriptions should be controlled by regulatory agencies using well-defined frameworks for innovations in treatment & patient well being.

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