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On Transdermal Pharmacology and Toxicology

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Abstract

Objective: To evaluate the underlying pharmacology, safety, and misuse/abuse of transdermal fentanyl, one of the cornerstone pharmacotherapies for patients with chronic pain.

Methods: Literature was identified through searches of Medline (PubMed) and several textbooks in the areas of pharmacology, toxicology, and pain management. A bibliographical review of articles identified by these searches was also performed. Search terms included combinations of the following: fentanyl, transdermal, patch, pharmacology, kinetics, toxicity, and poisoning. All pertinent clinical trials, retrospective studies, and case reports relevant to fentanyl pharmacology and transdermal fentanyl administered by any route and published in English were identified. Each was reviewed for data regarding the clinical pharmacology, abuse, misuse, and safety of transdermal fentanyl. Data from these studies and information from review articles and pharmaceutical prescribing information were included in this review.

Results: Fentanyl is a high-potency opioid that has many uses in the treatment of both acute and chronic pain. Intentional or unintentional misuse, as well as abuse, may lead to significant clinical consequences, including death. Both the US Food and Drug Administration (FDA) and Health Canada have warned of potential pitfalls associated with transdermal fentanyl, although these have not been completely effective in preventing life-threatening adverse events and fatalities related to its inappropriate use. Conclusions: Clinically consequential adverse effects may occur unexpectedly with normal use of transdermal fentanyl, or if misused or abused. Misuse and therapeutic error may be largely preventable through better education at all levels for both the prescriber and patient. The prevention of intentional misuse or abuse may require regulatory intervention.

Keywords: Fentanyl; Transdermal; Pharmacology; Toxicology; Poisoning; Opioid

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Presentation

Torment influences all individuals. Torment might be intense (e.g., injury), long winded (e.g., migraines), or constant (e.g., sciatic torment); no matter what its tendency it diminishes a patient's personal satisfaction. The yearly cultural expense because of lost efficiency from torment is safely assessed at north of 60 billion bucks in the United States. The typical specialist experiencing a problem related with torment loses 4 days of work consistently contrasted with a half day for a laborer without an aggravation condition. Subsequently, as well as working on personal satisfaction, satisfactory torment control could bring about billions of dollars of saved productivity. This article surveys the pharmacology and toxicology of transdermal fentanyl, one of the foundation pharmacotherapies for patients with ongoing agony. At the point when utilized as coordinated and in a protected way, this long-acting type of a profoundly powerful medicine [1].

History and Background

Fentanyl, a timetable II prescription, was acquainted in 1960 with substitute morphine and other narcotics for use in heart medical procedure because of its higher power (roughly 75-to 100-overlay contrasted with morphine). It is additionally connected with less

unfavourable cardiovascular impacts than morphine and triggers considerably less receptor discharge. A flexible pain relieving, fentanyl is presently utilized as often as possible for patients with one or the other intense or constant torment disorders. Intense and constant agony are hard to characterize explicitly, and may coincide. By and large, intense agony starts suddenly, is extreme, and is supposed to endure for no longer than a few days. It generally diminishes in power during this period. Ongoing torment is regularly lower in power than intense torment, consistent in force with some variety, and endures longer than seven days frequently years [2].

Unfavourable Events Reports of Transdermal Fentanyl

Sales of Johnson and Johnson's (Janssen) Duragesic transdermal gadgets have consistently expanded since its presentation, and had outperformed 4 million solutions and almost 2 billion bucks in 2004; however deals have fallen with the presentation of generics. Of course, there has been a corresponding expansion in unfavourable occasions and crisis division (ED) visits connected with the transdermal fentanyl gadget. The purposes behind this are indistinct and reasonable multifactorial. In 2004, the Drug Abuse Warning Network (DAWN), a public observation data set, detailed north of 8,000 ED visits in the United States because of the abuse of transdermal fentanyl. This number is probable an underrate, because of the degree of dependability in coding for the different narcotics and to the specific and will ful nature of emergency clinic cooperation in DAWN [3].

Clinical Pharmacology of Transdermal Fentanyl Patches

Fentanyl possesses many of the physicochemical properties essential for transdermal use. The molecular weight of fentanyl base is 337 Da within the maximum molecular weight considered suitable for skin permeation (< 1000 Da). Fentanyl, unlike morphine and other opioids, is highly potent, and produces desired clinical effects following the systemic absorption of a fraction of a milligram in no tolerant individuals [4].

Transdermal Delivery Systems

There are two general types of transdermal delivery systems currently in clinical use (Figure 3). The original transdermal therapeutic system (TTS), also called the reservoir transdermal device (made by Jannsen and generics by Sandoz, Watson, Pricara, and Actavis) consists of four functional layers and a protective peel strip [5].

Pharmacokinetics of the Transdermal Fentanyl Device

Fentanyl becomes detectable in the serum within 1–2 hours of application of a transdermal fentanyl device. However, therapeutic serum fentanyl concentrations are not achieved until approximately 12–16 hours after transdermal device application [6].

Therapeutic Considerations

The maintenance of a relatively steady serum concentration with transdermal fentanyl, which is particularly difficult for drugs with short half-lives, results in reduced side effects and improved efficacy. This improves therapeutic compliance, which is perhaps less of an issue with analgesics than with other trans dermally-administered drugs (e.g., oestrogens, clonidine). However, in patients with chronic pain, the substitution of transdermal fentanyl for other opioids is often considered as much for convenience (e.g., reduced dosing frequency, covert use) as for any specific analgesic benefit. This highlights the importance of weighing the overall therapeutic benefit of a drug and its delivery system against its overall safety aspects in the associated risk-benefit analysis [7].

Clinical Effects

The clinical effects of fentanyl, regardless of route of administration, are similar to those of other opioids, and are similarly dependent on both the dose and the degree of patient tolerance. At serum fentanyl concentrations of 0.63–1.5 ng/mL, postoperative analgesia is produced in most opioid-naïve patients [15]. Hypoventilation begins to manifest at concentrations >1.5 ng/mL,a sub therapeutic serum concentration for some.

Conclusion

Fentanyl is a very powerful narcotic conveying critical pain relieving benefit, yet fit for really hurting. Moreover, transdermal organization of fentanyl expands large numbers of the medication's remedial advantages, yet additionally adds interesting variables that might muddle the medication's wellbeing. There are many purposes behind the improved poisonousness, including unseemly solution and inappropriate use. As a powerful narcotic pain relieving in a concentrated transdermal gadget framework, its maltreatment potential is very high and conveys a high gamble of dreariness or mortality. Doctor training and mindfulness concerning the various and frequently creative ways with which transdermal fentanyl might be abused or mishandled ideally will bring about less unfortunate results and eventually save lives.

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