

The Mystery of Anticancer Drug Dosing: Why Can't Everyone Take the Same Dose?

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Abstract. When we fall ill and visit a hospital, doctors typically determine medication dosages based on a patient's body weight. For example, if the standard dose is "a certain number of milligrams per kilogram of body weight," then a heavier person will receive more medication. This approach seems reasonable and precise. However, for some very expensive targeted anticancer drugs, scientists are vigorously debating whether to continue calculating doses precisely by body weight or prescribe a uniform fixed dose for all adult patients. Traditionally, drug dosages have been calculated based on a patient's body weight to ensure stable blood drug concentrations. However, in recent years, fixed-dose regimens have attracted much attention due to their ease of administration and lower cost. This paper explores the question of equivalence between fixed-dose and body weight-based dosing by analyzing the case of panitumumab. The study finds that there is no significant difference in efficacy and safety between the two regimens, while the fixed-dose regimen offers distinct practical advantages. This paper concludes that, given equivalent therapeutic effects, fixed-dose medication serves as a viable alternative to weight-based dosing. This conclusion reveals the balance between precision and practicality in pharmaceutical practice.

Keywords: Panitumumab, Anticancer Drugs, Dosing Regimen, Fixed Dose, Body Weight-Based Dosing

1. Introduction

The design of dosing regimens for targeted anticancer drugs is a hot topic in clinical pharmacy. Traditionally, drug dosages are calculated based on a patient's body weight to ensure stable blood drug concentrations. However, recent studies have found that for monoclonal antibody-targeted drugs, fixed-dose regimens deliver equivalent therapeutic efficacy to conventional weight-based dosing schemes, offering advantages such as ease of administration and lower cost [1, 2]. Currently, debate continues over the pros and cons of these two regimens, and a unified dosing standard is lacking, particularly for drugs like panitumumab [3].

This paper investigates the question of equivalence between fixed-dose and body weight-based dosing for targeted anticancer drugs. Specifically, it seeks to answer: On the condition that efficacy and safety remain comparable, can fixed-dose administration serve as a reasonable alternative to body weight-based dosing? Can its clinical practical advantages compensate for its theoretical lack of precision? This paper employs a method combining literature review and case analysis. This

study helps clarify the core logic of dosing regimen design, provides a reference for clinical decision-making, and illustrates the trade-off between accuracy and practicality in clinical medication

2. Germination period: the empirical accumulation of ancient pharmacy (ancient times—16th century AD)

In ancient times, drug discovery relied largely on serendipity and repeated trial and error, a process full of hardship and uncertainty.

2.1. The courage and wisdom of "tasting a hundred herbs"

Stories of ancestors trying herbal remedies are found in ancient civilizations worldwide. China has the legend of "Shennong Tasted a Hundred Herbs and Encountered Seventy Poisons in a Single Day." Ancient Egypt's Ebers Papyrus records 877 prescriptions. Hippocrates in ancient Greece began attempting to attribute the causes of disease to natural factors rather than divine punishment.

The outcomes of these early explorations proved remarkable. Ancient people found chewing willow bark and placing it on wounds could alleviate pain. (later found to be due to salicylic acid, a precursor to aspirin). Applying moldy tofu to wounds helped with healing (ancients inadvertently used a primitive antibiotic). These discoveries were invaluable, but ancient knowledge remained at the "what" level—they knew willow bark worked, but had no idea "why" it worked. This led to highly unstable drug effects: willow bark collected today might work, but a batch collected tomorrow might not; a physician's prescription might be effective, but the same prescription from another physician might fail.

2.2. Alchemy: the misunderstood pioneer of pharmacy

Mentioning alchemy conjures images of smoke-filled labs, mysterious-looking alchemists, and the "elixirs of immortality" that poisoned emperors. These impressions are correct, but alchemy has another side.

Both Chinese alchemy and Western alchemy involved practitioners who, through long-term practice, did three things with profound influence on later generations:

First, they invented and improved chemical instruments. To complete complex alchemical processes, they developed devices including distillers, sublimators, condensers and grinders which remain basic tools in chemical laboratories today.

Second, they discovered and recorded numerous chemical reactions. Ge Hong, a Jin Dynasty alchemist and physician, detailed in his Baopuzi chemical reactions such as the thermal decomposition of cinnabar, namely mercury sulfide, that generates metallic mercury, and the reduction of lead powder by carbon to produce lead. This represents humanity's first active observation and recording of material transformations.

Third, they accumulated empirical knowledge of mineral drugs. Alchemists experimented with diverse minerals such as cinnabar, realgar and saltpeter in human trials. Although this often led to poisoning tragedies, it accidentally uncovered some effective drugs. For example, calomel (mercurous chloride) was once used to treat scabies, and arsenic trioxide was later found to be effective against certain types of leukemia.

Ge Hong himself, an alchemist and physician, recorded a method for treating malaria using *Artemisia annua* (sweet wormwood) in his Handbook of Prescriptions for Emergencies: "Take a

handful of *Artemisia annua*, soak it in two pints of water, wring out the juice, and drink it all." Nearly two millennia later, this record inspired Tu Youyou's discovery of artemisinin, for which she won the Nobel Prize. This age-old legacy vividly demonstrates the subtle yet tangible link between alchemy and contemporary pharmacy.

However, it must be acknowledged that the core methods of alchemy were "trial and error" and "analogical reasoning." It relied on individual luck and experience, lacked systematic theoretical guidance, was non-reproducible, and difficult to popularize. It was more like a "craft" secretly passed down within a family than a science that could be openly learned and verified.

3. Maturity period: the establishment of modern pharmaceutical evaluation systems

To understand the panitumumab dosing debate, it is necessary to revisit the formation of contemporary pharmaceutical assessment frameworks. Before the mid-20th century, judging drug efficacy relied primarily on physicians' personal experience and patients' subjective feelings, both of which had significant bias [4].

British statistician Bradford Hill designed the randomized double-blind controlled trial in the 1950s [5]. The core elements of this method include: ① random assignment of patients to experimental and control groups; ② use of a placebo in the control group; ③ blinding of both patients and physicians to group assignment ("double-blind"); ④ final comparison of treatment outcomes between groups. This design effectively eliminates the interference of the placebo effect and observer bias, providing an objective standard for drug evaluation.

For anticancer drugs, the traditional dose-finding principle was the "maximum tolerated dose." This principle was reasonable during the era of cytotoxic chemotherapy, as the efficacy of these drugs was positively correlated with dose [6]. Nevertheless, the emergence of targeted therapies has challenged this established paradigm. The mechanism of action for targeted drugs is "occupancy-based"—once the drug occupies enough targets, efficacy reaches saturation, and higher doses bring no further benefit. This property is known as "target-mediated drug disposition" [7]. Therefore, dose determination for targeted drugs no longer needs to pursue the maximum tolerated dose; exceeding the "minimum effective concentration" is sufficient.

In the panitumumab case, the study by Liao et al. reported the coefficient of variation in plasma drug concentration stood at 29% for the body weight-based dosing group and 34% for the fixed-dose group [3]. From a traditional perspective, a higher coefficient of variation implies "less precision." However, Hendriks et al. pointed out that blood drug concentrations in both groups were far above the minimum effective concentration, meaning all patients had achieved effective drug exposure levels [8]. Under this premise, the difference in coefficients of variation loses clinical significance. This view reflects a significant shift in modern pharmaceutical evaluation: evaluating a dosing regimen requires looking not only at theoretical precision but also at whether clinical outcomes meet the standard.

4. Frontier period: dosing strategies in the era of precision medicine

Entering the 21st century, pharmacy is undergoing a profound shift from "broad-spectrum therapy" to "precision medicine" [9]. However, the panitumumab dosing debate shows that precision medicine does not mean "tailoring" the dose for every patient—sometimes, "simplification" is the more precise choice.

The core of precision medicine is "the right dose for the right patient at the right time" [10]. In oncology, this concept is chiefly reflected in screening eligible populations by biomarkers and

individualizing dose adjustments based on therapeutic drug monitoring. However, the necessity of therapeutic drug monitoring has been questioned for drugs like panitumumab. Studies show that once plasma drug concentration surpasses the minimum effective level, further dose increases do not improve efficacy [8]. Given limited healthcare resources, excessive pursuit of "individualization" can lead to waste.

In recent years, a growing number of monoclonal antibody drugs have been approved for fixed-dose administration. For example, nivolumab and pembrolizumab have both received approval from the US FDA and the European EMA for fixed-dose administration [11, 12]. Clinical data show no significant difference in efficacy and safety between fixed-dose and body weight-based dose groups, yet the former boasts prominent strengths in administration simplicity and cost efficiency.

The advantages of fixed-dose regimens can be summarized as follows: ① Simplified administration, reducing the risk of dosing errors; ② Cost reduction effectively cuts down unnecessary drug wastage; ③ Patient convenience, improving the treatment experience; ④ Global accessibility, easier to implement in regions with limited healthcare resources [8].

From a health economics perspective, fixed-dose regimens tend to deliver superior cost-effectiveness. One simulation study showed that adopting a fixed-dose regimen for 1,000 patients can cut annual drug expenses by roughly 15% and labor expenditures by around 10% [13].

In the future, with the application of real-world data and artificial intelligence technologies, dose optimization will become more intelligent. Machine learning-driven pharmacokinetic models can forecast individual drug exposure levels of patients, allowing the selection of the simplest possible dosing regimen while ensuring efficacy [7]. We are likely to see more hybrid strategies of "primarily fixed-dose, supplemented by individualized adjustment."

5. Conclusion

Reviewing the millennia-long evolution of pharmacy, a clear thread emerges: humanity's exploration of drugs has gradually shifted from reliance on chance, experience, and authority towards observation, experimentation, and data. What has made drugs more effective and safer is not a more advanced alchemist's furnace, but more advanced ways of thinking—the spirit of skepticism, the method of experimentation, the logic of statistics, and the attitude of seeking truth.

The debate over panitumumab dosing reflects the complexity of contemporary clinical pharmaceutical decision-making. The two dosing regimens show no significant difference in efficacy and safety, but the fixed-dose regimen has a distinct practical advantage. This conclusion suggests that pharmaceutical decisions should not prioritize "precision" alone but seek the best balance between scientific evidence and clinical practice.

From a broader perspective, this debate also reflects the internal logic of pharmaceutical development – from a "craft" reliant on individual experience, to a "science" based on rigorous experimentation, and further to a "decision-making art" that balances multiple factors. Every refinement of dosing regimens embodies efforts to maximize patient benefits. In the future, with the further application of pharmacokinetic models and real-world data, the design of dosing regimens will become more scientific and flexible, but the core goal remains unchanged: to ensure every patient receives the most appropriate treatment.

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