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Mini review

Customizing drug therapy based on genetic and molecular information: Review

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ABSTRACT

This comprehensive review article explores the effect of personalized medicine on patient care in clinical pharmacy. Personalized medicine tailors treatments based on genetic and molecular information, recognizing individual variability in drug responses. Pharmacogenomics, a vital subfield of genomics, reveals how an individual's genetic makeup influences their response to drugs, with practical applications in various medical conditions. This study explores the significance of customizing drug therapy based on genetic and molecular information. It provides a nuanced perspective to guide clinical pharmacists in optimizing drug regimens within this evolving paradigm. The exploration is clarified through four key sections. First, it investigates the critical role of genetic and molecular information in drug therapy, emphasizing the advantages of customizing drug therapy and acknowledging the challenges in applying personalized medicine. Second, Clinical pharmacists are essential in shaping policies, promoting accessibility, and advocating for ethical practices. Third, the future of clinical pharmacy is in genomic and molecular tools, artificial intelligence, and machine learning algorithms, providing personalized, predictive, and preventive healthcare. Fourth, Case studies and success stories highlight the benefits of incorporating genetic and molecular information into routine clinical practice, showing how tailoring drug therapy based on individual genetic factors enhances treatment efficacy and improves patient outcomes.

Keywords: Personalized Medicine, Pharmacogenomics, Genetic and Molecular Information, Customizing Drug Therapy

1. Introduction

In clinical pharmacy, personalized medicine has revolutionized patient care over the past decades (1, 2). This approach admits the diversity among individuals in their response to drug therapy and tailors treatments based on genetic and molecular information. Pharmacogenomics, a subfield of genomics, investigates how an individual's genetic makeup influences their response to drugs (3).

This approach has practical implications in diverse medical conditions, from oncology to chronic diseases, and is supported by digital tools and decision-support systems (2). While personalized medicine offers abundant promises, it also presents challenges related to ethical considerations, privacy, consent, and equitable distribution of advancements. However, it is a transformative force in clinical pharmacy, resonating at the core of patient outcomes (4).

The traditional approach to prescribing medications relied on population-based averages, leading to variations in treatment response among patients. However, genomic insights have allowed for more precise therapeutic strategies, optimizing drug regimens and enhancing treatment efficacy (3, 5).

Personalized medicine has had a deep impact in oncology, where treatments are tailored based on the unique genetic profile of each patient. Its applications extend to chronic diseases, cardiovascular conditions, neurological disorders, and other health challenges (5, 6).

1.1 Precision Oncology: Transforming Cancer Treatment Through Targeted Therapies

The integration of genomic insights into oncology has revolutionized cancer treatment, allowing for therapies tailored to individual genetic profiles. This precision approach has led to significant improvements in patient outcomes across various cancer types.

1.1.1 BRAF V600E Mutation in Melanoma

Approximately 40% of melanoma patients harbor the BRAF V600E mutation, which leads to uncontrolled cell growth (7). Vemurafenib, a BRAF inhibitor, has shown remarkable efficacy in

this subgroup. In a pivotal phase 3 trial, patients treated with vemurafenib exhibited a confirmed overall response rate of 53%, compared to 5% in those receiving dacarbazine (8). This targeted therapy significantly improved progression-free and overall survival, marking a substantial advancement in melanoma treatment .

1.1.2 BRCA Mutations in Ovarian Cancer

BRCA1 and BRCA2 mutations are present in a subset of ovarian cancer patients, rendering them particularly responsive to PARP inhibitors like olaparib. The SOLO1 trial demonstrated that maintenance therapy with olaparib extended median progression-free survival beyond four years in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation (9-11). This finding underscores the importance of genetic testing in guiding effective maintenance strategies.

1.1.3 BCR-ABL Fusion in Chronic Myeloid Leukemia (CML)

The discovery of the BCR-ABL fusion gene in CML has led to the development of tyrosine kinase inhibitors (TKIs), transforming the disease's prognosis. Imatinib, the first TKI approved for CML, has shown durable responses. In a five-year follow-up study, continuous treatment with imatinib resulted in a high proportion of patients achieving sustained responses, significantly improving overall survival rates (12).

One of the hallmarks of personalized medicine is the capacity to expect and mitigate adverse events, allowing clinical pharmacists to make decisions that minimize risks and enhance the safety of drug regimens. This tailored approach also needs patient engagement to increase adherence and improve long-term outcomes (13-15).

This study explores customizing drug therapy based on genetic and molecular information in clinical pharmacy and how it affects patients' response to drugs.

2. Genetic and molecular information in drug therapy

Genetic and molecular information play a critical role in drug therapy, providing personalized guidance for clinical pharmacists. These factors influence how drugs are metabolized, their effectiveness, and the potential for adverse reactions (16, 17).

The interplay between an individual's genetic makeup and molecular characteristics shapes drug response. Genetic factors involve gene variations responsible for drug metabolism, receptor

sensitivity, and transport mechanisms. Molecular factors control specific biomarkers and pathways that influence drug interactions within the body (18).

Genetic testing and molecular profiling are essential in understanding this complex code. Genetic testing analyzes specific genes to identify variations that may impact drug response, while molecular profiling explores the broader molecular landscape to understand unique signatures within a patient's cells (19).

Specific genes and molecules, such as CYP2D6 and TPMT, play pivotal roles in determining drug efficacy and safety. Understanding these specific genetic and molecular pathways enables pharmacists to make informed decisions, optimizing drug regimens for better patient outcomes (19, 20).

The integration of genetic and molecular information in drug therapy represents a transformative approach, shifting the paradigm from generalized prescriptions to tailored treatments. This personalized understanding empowers clinical pharmacists to augment drug response, ushering in a new era of precision in patient care (19).

3.Advantages of customizing drug therapy

Customizing drug therapy based on individual genetic and molecular characteristics is a significant advancement in treatment effectiveness. Tailoring medications to each patient's unique genetic makeup allows clinical pharmacists to optimize therapeutic outcomes. This precision approach ensures that drugs align with the individual's genetic profile, enhancing efficacy and improving the probability of a positive response. This personalized approach replaces the one-size-fits-all method, maximizing the potential for successful treatment interventions (21).

Personalized drug therapy also allows for the anticipation and prevention of adverse drug reactions and side effects. Understanding an individual's genetic predisposition to specific reactions enables clinical pharmacists to make informed decisions that minimize risks and enhance the safety of drug regimens. This proactive approach not only protects patients from potential harm but also contributes to a more positive and tolerable treatment experience, enhancing the overall safety profile of drug therapies (22).

Personalized treatment plans are advantageous as they align with the unique needs and characteristics of each patient. When patients perceive that their treatment plans are specifically

made for them, they are more likely to adhere to prescribed regimens, leading to better long-term outcomes and patient satisfaction. The cooperation between the clinical pharmacist and the patient becomes more collaborative, resulting in a more satisfied and empowered patient who recognizes the personalized nature of their care (23).

4. Challenges in implementing personalized medicine

The application of personalized medicine raises ethical concerns, especially regarding genetic testing and patient privacy. Clinical pharmacists must ensure informed consent for genetic testing and respect patient privacy. Ethical guidelines need to evolve to keep up with the changing landscape of genetic testing (24).

Despite the potential of personalized medicine, there are challenges in making genetic and molecular testing widely available. Access disparities, especially in underserved communities, need to be addressed. Clinical pharmacists are supporting ccess to personalized medicine for all patients through relationships with healthcare institutions, policymakers, and technology developers (25).

The high costs of genetic and molecular testing, as well as interpreting results, present a financial barrier to integrating personalized medicine into clinical practice. Clinical pharmacists are working to advocate for reimbursement models that recognize the long-term benefits of personalized approaches and align with the value they provide (26).

Clinical pharmacists are at the head of addressing the ethical, practical, and financial challenges of personalized medicine. They play a crucial role in shaping policies, promoting accessibility, and advocating for ethical practices to ensure the transformative potential of personalized medicine benefits all patients (27).

Single nucleotide polymorphisms (SNPs) are variations in DNA sequence that occur when one genomic nucleotide shows difference in a pair of chromosomes. A type of SNPs occurs in the coding region leading to a change in the amino acid sequence of a protein; however, other SNPs do not show an effect on the sequence of protein.

Moreover, SNPs may sometimes be related to transcription and mRNA degradation. Besides being useful for the understanding of biological functions, SNPs are helpful markers in examining the linkage to genetic polymorphisms in the area of genetics and the medical field.

Understanding SNPs helps in recognizing possible genes for certain diseases, susceptibility genes of drugs, and genes responsible for histocompatibility in cases of transplantation. Recent

researches in DNA technology enabled us to perform a more detailed analyses of DNA, leading to the appearance of the genome-wide association study (GWAS). Figure 1 shows the types of SNPs in different regions of the gene (28).

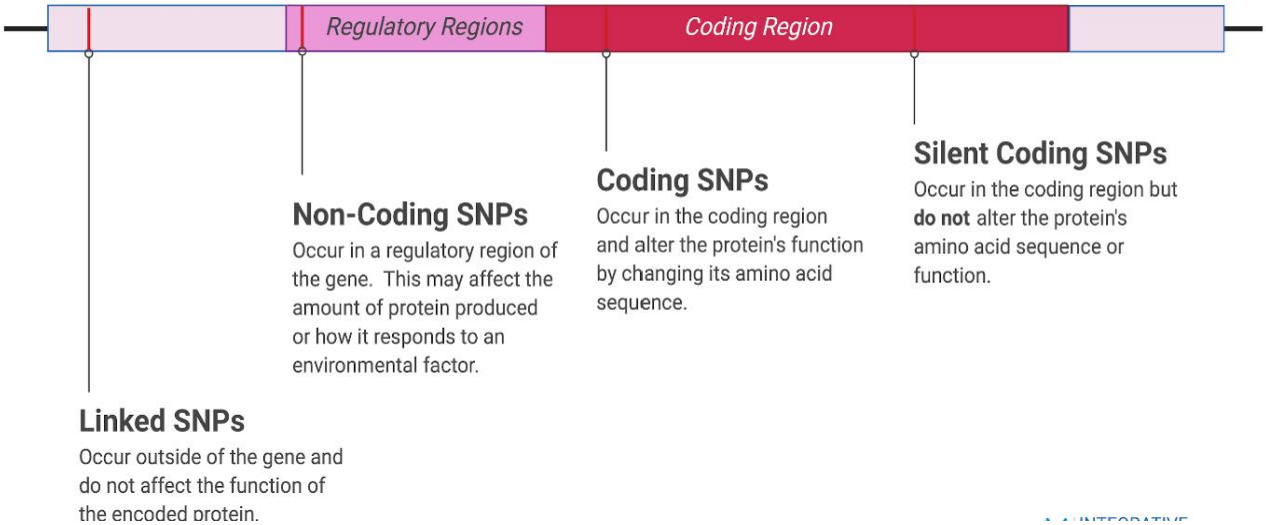

Figure 1: The types of SNPs in different regions of the gene (29).

Thus, a greater knowledge of the influence of different gene variations on an individual's health and gene function may result from the identification of these variations and an examination of their impacts. With this enhanced understanding, potentially safer, customized medications to treat the most prevalent life-threatening illnesses might be developed, as well as new, practical SNP markers for medical diagnostics. The future of medicine will be completely transformed by this. This minireview centers on data that show how genetic polymorphism affects the onset and course disorders (30).

4.1 Real-World SNP Applications in Clinical Practice

Pharmacogenomic SNP testing has moved from the bench into routine care, guiding drug selection and dosing across multiple specialties (31). Moreover, authoritative guidelines from CPIC and other bodies underscore its clinical relevance and provide dosing algorithms for key gene–drug pairs (32). Below are four illustrative examples spanning cardiology, hematology, oncology, and orthopedics.

4.1.1 Warfarin Dosing Guided by CYP2C9 & VKORC1

Genotype-guided warfarin dosing in patients undergoing elective hip or knee arthroplasty reduced the composite risk of major bleeding, excessive anticoagulation (INR ≥ 4), venous thromboembolism, or death compared with clinically guided algorithms (33). Meta-analyses of randomized trials report fewer extreme INR events in genotype-guided arms, even if time in therapeutic range findings are mixed (34).

4.1.2 CYP2C19-Guided Antiplatelet Therapy After PCI

The POPular Genetics trial (n = 2,488) showed that selecting $P2Y_{12}$ inhibitors based on CYP2C19 genotype was noninferior for thrombotic outcomes and lowered major or minor bleeding from 12.5% to 9.8% at 12 months (HR 0.78; 95% CI 0.61–0.98) (35). Real-world implementation of CYP2C19-guided de-escalation strategies in acute coronary syndrome patients confirms consistently lower bleeding without increased ischemic events (36).

4.1.3 EGFR-Mutant NSCLC and EGFR Tyrosine-Kinase Inhibitors

In the WJTOG3405 trial, patients with EGFR exon 19 deletions or L858R mutations treated with gefitinib achieved an overall response rate of 71.2% and significantly prolonged progression-free survival compared with chemotherapy in wild-type cohorts (37).

4.1.4 TPMT & NUDT15-Guided Thiopurine Dosing in Pediatric ALL

CPIC guidelines recommend starting 6-mercaptopurine at 20–50% of standard doses in intermediate TPMT or NUDT15 metabolizers, preventing up to 80% of grade 4 neutropenia episodes in pediatric acute lymphoblastic leukemia cohorts (38). Cohort studies corroborate that genotype-tailored dosing markedly reduces severe myelosuppression compared with conventional dosing (39).

5. Current developments and future prospects

The future of clinical pharmacy is marked by progressions in customizing drug therapy through the use of genomic and molecular tools. Technologies such as next-generation sequencing, CRISPR-Cas9 gene editing, and advanced diagnostic platforms allow clinical pharmacists to

tailor drug regimens with unique precision. Ongoing research in pharmacogenomics and the integration of artificial intelligence and machine learning algorithms are refining our ability to interpret vast datasets and predict individualized responses to medications (40-42).

The potential applications of personalized medicine extend far beyond the current prospect, with the promise of proactive, patient-centric approaches that prioritize prevention and targeted interventions. The ongoing synergy between research, technology, and clinical practice holds the key to unlocking the full potential of personalized medicine, paving the way for a healthcare landscape that is not only personalized but also predictive and preventive (43, 44).

6. Role of artificial intelligence (AI) in genetics

AI is a fast-growing field of study with potentially revolutionary implications for the diagnosis and treatment of many chronic disorders, including hereditary diseases. ML principles have been used to build algorithms providing predictive models for the likelihood of developing genetic illnesses or their complications (45). Time-lapse incubators and preimplantation genetic testing for aneuploidy have been created to increase the chance of a live birth, although the outcomes are still far from optimal. AI is being applied quickly in the medical field to help improve the success rates of in vitro fertilization (IVF) treatments (46). In several domains, including clinical genomics, large and complex genomic datasets are processed via a specific type of AI algorithm called as DL (47). Actually, it is the vast datasets that have rapidly amassed from electronic medical records, high-definition multi-omics (including genomics, proteomics, transcriptomics, and metagenomics), and imaging modalities (endoscopy and endomicroscopy) that have made it possible to address unmet clinical needs in genetics and uncover novel mechanistic insights. The requirement for objective prospective validation studies, along with the significant heterogeneity in AI methods, datasets, and clinical outcomes, are currently impeding the use of AI in clinical practice, even though the use of AI methods has simplified the analysis, fusion, and interpretation of large genetics datasets (48).

AI methods, such as model prediction of the presence of heart failure (HF), estimation of the HF subtype, and assessment of the severity of HF, have been used for cardiovascular illnesses in the past (49). The majority of studies on AI-assisted HF prediction to date have used clinical features and concentrated on prognostic subtype detection (50, 51), including mortality (52, 53), re-hospitalizations, and destabilizations. Furthermore, the application of AI machine-learning

techniques holds significant promise for the characterization of intricate biological processes, particularly those involving the interplay between several genetic variables and biochemical pathways that expedite the development of HF. Therefore, in order to determine the genetic variables in a high-risk group that may be linked to asymptomatic Stage B HF, we used an AI-assisted methodology in this work. Carrying this required screening for SNPs throughout the genome. To further identify the genes' possible significance in the molecular pathogenesis of HF in terms of functional connectivity and protein-protein interaction networks, we also carried out protein connectivity mapping of the genes containing the SNPs.

7. Case studies and success stories

There are some success stories that demonstrate the benefits of incorporating genetic and molecular information into routine clinical practice and show how tailoring drug therapy based on individual genetic factors could enhance treatment efficacy, reduce adverse events, and improve patient outcomes. A common illustration of genetic polymorphism is the absence of sharp classifications; instead, thereare fine grades between the extremes.

7.1. Determination of warfarin dosage for pediatric patients

A systematic review and meta-analysis [Takeuchi M. et al.2020] focused on the impact of two key genetic variations, CYP2C9 and VKORC1, on determining the appropriate warfarin dosage for pediatric patients. These genetic variations serve as markers for tailoring warfarin doses with precision, leading to better therapeutic outcomes and fewer adverse events (54).

This finding refines our understanding of how genetic variations influence personalized medicine. This case highlights the tangible effects of genetic differences on warfarin dosing, paving the way for a new era in tailored anticoagulant therapy based on each patient's unique genetic makeup.

7.2. Imatinib in Chronic Myeloid Leukemia (CML):

The PI3K-AKT pathway is a critical signaling cascade involved in cell growth, proliferation, survival, and metabolism. Dysregulation of this pathway is linked to the development and progression of various cancers, making it an attractive target for therapy. Imatinib is a tyrosine kinase inhibitor that primarily targets the BCR-ABL fusion protein, which is characteristic of chronic myeloid leukemia (CML). By inhibiting this aberrant protein, imatinib disrupts downstream signaling pathways, including the PI3K-AKT pathway, halting the uncontrolled

proliferation of leukemic cells (55). Imatinib has been successful in treating Chronic Myeloid Leukemia by targeting the BCR-ABL fusion protein, as documented in studies published in Blood (56).

In a recent review, Imatinib has significantly improved patient outcomes in CML, leading to a substantial increase in the five-year survival rate (55).

7.3. Erlotinib in locally advanced or metastatic activating epidermal growth factor receptor (EGFR) mutation-positive lung adenocarcinoma: Targeting EGFR mutations in lung cancer with drug-like erlotinib has led to improved survival rates (57).

A recent meta-analysis study shows a potential benefit for erlotinib in overall survival when used with cytotoxic chemotherapy compared to chemotherapy alone. Moreover, it reveals the clinical benefit of erlotinib in terms of progression-free survival. The hazard ratio (HR) for progression-free survival was 0.31, indicating a significant improvement with erlotinib. In the case of response rate, there was an improvement in tumor response rate with tyrosine-kinase inhibitors (TKIs) such as erlotinib. Finally, erlotinib showed improvement in health-related quality of life (58).

7.4. Genomic Profiling in Colorectal Cancer: Genomic profiling has helped identify specific mutations in colorectal cancer, guiding treatment decisions and influencing patient outcomes(59).

A recent study about the assessment of genomic profiling in patients with colorectal cancer treated in community oncology practices showed that the genomic testing rates for colorectal cancer patients increased by 61% over four years, indicating a growing recognition of the importance of genetic information in treatment decisions. They also give examples such as the identification of specific mutations and the use of circulating tumor DNA (ctDNA).

- Identification of Specific Mutations: Genomic tests identified mutations in biomarkers such as BRAF, KRAS, NRAS, NTRK, microsatellite instability (MSI), and tumor mutational burden (TMB). For example, 16% of patients had a BRAF V600E mutation, and 14% showed MSI, suggesting potential for targeted therapies.
- Use of Circulating Tumor DNA: The study found an increasing use of ctDNA, indicating its emerging role in monitoring disease progression and treatment response.

The findings highlight the importance of comprehensive genomic profiling in guiding precision medicine for CRC patients. As testing technology advances and more data becomes available, new therapeutic opportunities may emerge, improving patient outcomes (60).

7.5. Summary of Case Studies

Table 1: Case Studies.

Condition	Genetic Marker / Target	Intervention	Key Outcome	Refernces
Warfarin anticoagulation (pediatrics)	CYP2C9, VKORC1	Genotype-guided dosing	↑ Time in therapeutic INR; ↓ major bleeding events	(61)
Chronic Myeloid Leukemia (CML)	BCR-ABL fusion	Imatinib 400 mg daily	5-year overall survival > 89%	(12)
EGFR-mutant NSCLC	EGFR exon 19 del., L858R	Gefitinib (or erlotinib)	ORR ≈ 70%; PFS HR 0.30	(62)
BRAF V600E melanoma	BRAF V600E mutation	Vemurafenib	ORR ~ 48%; OS benefit at 6 months	(8)
BRCA-mutant ovarian cancer	BRCA1/2	Maintenance olaparib	PFS benefit HR 0.30; 3-yr disease-free rate + 33 pp	(63)
Thiopurine dosing in pediatric ALL	TPMT, NUDT15	6-MP dose reduction	↓ Grade 4 neutropenia by ~ 80%	(38)
Colorectal cancer genomic profiling	KRAS, BRAF, MSI, TMB	ctDNA monitoring & targeted therapy	Genomic testing rates ↑ 61%; more tailored regimens	(59)

NR: International Normalized Ratio, **CML**: Chronic Myeloid Leukemia, **NSCLC**: Non–Small Cell Lung Cancer,**ORR**: Overall Response Rate,**PFS**: Progression-Free Survival,**OS**: Overall Survival, **BRCA**: BReast CAncer gene, **ALL**: Acute Lymphoblastic Leukemia, **PARP**: Poly (ADP-ribose) Polymerase, **TPMT**: Thiopurine S-methyltransferase, **NUDT15**: Nudix Hydrolase 15, **MSI**: Microsatellite Instability, **TMB**: Tumor Mutational Burden,**ctDNA**: Circulating Tumor DNA.

8. Conclusion

This review article highlights the transformative potential of personalized medicine in clinical pharmacy. As we move into the age of personalized medicine, proactive solutions are addressing challenges and the benefits are evident in improved patient outcomes. The synergy between research, technology, and clinical practice is key to unlocking the full potential of personalized medicine, creating a healthcare landscape that is personalized, predictive, and preventive.

- **Conflict of interest**

  All authors denied any conflict of interest.

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