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Genetic Predictors of Adverse Drug Reactions in Common Medications Prescribed in Family and Dental Practice

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Abstract

Adverse drug reactions (ADRs) pose a significant challenge in both family and dental practices, leading to patient harm, reduced treatment compliance, and increased healthcare costs. This systematic review explores the role of genetic predictors in influencing ADRs to commonly prescribed medications, including opioids, NSAIDs, antibiotics, anticoagulants, and local anesthetics. The review analyzes 24 high-quality studies published between 2009 and 2025, identifying key pharmacogenetic markers—such as CYP2D6, CYP2C9, VKORC1, HLA-B*57:01, and RYR1—that significantly affect drug metabolism and safety. The findings emphasize that genetic polymorphisms can predict individual drug responses and reduce adverse outcomes through personalized therapy. However, the implementation of pharmacogenetic testing remains limited due to cost, awareness, and infrastructural barriers. The review recommends integrating genetic screening into high-risk prescribing, enhancing provider education, and linking genetic data to clinical decision support systems to promote safer and more effective care in primary and dental settings.

Keywords:

Pharmacogenetics, Adverse Drug Reactions, Genetic Polymorphism, Family Medicine, Dental Practice, Personalized Medicine, CYP2D6, VKORC1, HLA Alleles

Introduction

Adverse drug reactions (ADRs) remain a significant concern in both family and dental practice, contributing to patient morbidity, noncompliance, and increased healthcare costs. Although most medications are generally considered safe, individual variability in drug response poses a challenge to achieving optimal therapeutic outcomes. One of the critical

factors influencing this variability is genetic makeup, which affects drug metabolism, efficacy, and safety (Pirmohamed et al., 2004). Pharmacogenetics, the study of how genetic variation influences an individual's response to drugs, has gained increasing attention as a tool for predicting and preventing ADRs.

Family medicine and dental practice frequently involve the prescription of medications such as antibiotics, analgesics, local anesthetics, anticoagulants, and antihypertensives. These drugs, while commonly used, are also frequently implicated in ADRs. For instance, polymorphisms in the CYP2C9 and VKORC1 genes can alter warfarin sensitivity, while variations in CYP2D6 influence the metabolism of codeine, leading to either insufficient pain control or opioid toxicity (Crews et al., 2012). In dental settings, genetic variants such as SCN9A and RYR1 have also been linked to altered pain perception and risk of malignant hyperthermia following anesthetic administration (López-López et al., 2012).

Understanding the genetic underpinnings of drug response can guide personalized treatment strategies, minimize risks, and improve therapeutic efficacy. In clinical practice, however, the implementation of pharmacogenetic testing remains limited due to cost, awareness, and infrastructure constraints (Relling & Evans, 2015). Nonetheless, emerging evidence suggests that integrating genetic information into prescribing practices could revolutionize patient safety in primary care and dentistry.

This review aims to explore the genetic predictors of ADRs associated with commonly prescribed medications in family and dental practice. By identifying the most clinically relevant gene-drug interactions, the paper highlights the potential of pharmacogenetic approaches in advancing precision medicine and improving patient outcomes in frontline healthcare settings.

Objectives and Scope of the Review

The primary objective of this systematic review is to examine the genetic predictors associated with adverse drug reactions (ADRs) to commonly prescribed medications in family and dental practices. Given the widespread use of pharmacological therapies in both domains, a thorough understanding of how genetic variations affect drug response is crucial for enhancing patient safety and individualizing treatment.

Specific Objectives:

1. **Identify Commonly Prescribed Drugs:** To catalog the most frequently used medications in family and dental practices that are known to be associated with ADRs (e.g., antibiotics, analgesics, anticoagulants, anesthetics).
2. **Determine Relevant Genetic Markers:** To highlight specific gene polymorphisms (e.g., CYP450 variants, HLA alleles, ABC transporters) that have been scientifically linked to altered drug metabolism or heightened risk of ADRs.
3. **Assess Clinical Evidence:** To synthesize existing clinical and pharmacogenetic studies that establish associations between genetic variants and drug-related adverse outcomes.

4. **Evaluate Implementation in Practice:** To evaluate the current state of pharmacogenetic testing implementation in primary healthcare and dental settings and identify barriers to its broader adoption.

Scope of the Review:

This review will include peer-reviewed studies published in English over the past 15 years that focus on adult populations in outpatient settings. Both observational and interventional studies will be considered, as well as systematic reviews and meta-analyses. Emphasis will be placed on genetic testing that can inform prescribing decisions for medications commonly used in:

- **Family Practice:** including antihypertensives, statins, anticoagulants, and antidepressants.
- **Dental Practice:** including NSAIDs, local anesthetics, antibiotics, and opioids.

Methodology

This systematic review follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparent, comprehensive, and replicable reporting of the search, selection, and synthesis of relevant literature.

1. Search Strategy

A systematic search was conducted across the following electronic databases:

- **PubMed/MEDLINE**
- **Embase**
- **Scopus**
- **Cochrane Library**
- **Web of Science**

Search terms were developed using Boolean operators and MeSH terms. A sample search string used in PubMed was:

("Pharmacogenetics" OR "Pharmacogenomics" OR "Genetic polymorphism") AND ("Adverse drug reaction" OR "Drug toxicity") AND ("Primary care" OR "Family medicine" OR "Dentistry" OR "Dental practice") AND ("Common medications" OR "Analgesics" OR "Antibiotics" OR "Anticoagulants" OR "Anesthetics")

The search covered publications from **January 2009 to May 2025**, restricted to human studies published in English.

2. Inclusion Criteria

- Peer-reviewed original research articles, systematic reviews, and meta-analyses.
- Studies assessing genetic variants associated with ADRs in commonly prescribed drugs in family or dental practice.
- Adult human subjects (≥18 years).
- Clear description of gene-drug-ADR associations.

3. Exclusion Criteria

- Studies on pediatric populations.
- Non-genetic biomarkers or general pharmacokinetics without ADR linkage.
- Experimental drugs not widely used in general or dental practice.
- Editorials, commentaries, case reports, or conference abstracts.

4. Study Selection Process

Two independent reviewers screened titles and abstracts for eligibility. Full-text articles were retrieved and assessed using the predefined criteria. Disagreements were resolved through discussion or by a third reviewer.

The study selection process is documented in a PRISMA flow diagram (see next section).

5. Data Extraction and Quality Assessment

A standardized data extraction sheet was used to collect the following information:

- Author(s), year, country
- Study design and population
- Medication(s) and ADR(s)
- Genetic variant(s) investigated
- Key outcomes and findings

The **Joanna Briggs Institute (JBI) critical appraisal tools** were used for quality assessment of included studies. Each study was scored and classified as high, moderate, or low quality.

Results

1. Overview of Included Studies

A total of **1,243 articles** were initially retrieved through systematic database searches. After the removal of duplicates and initial screening, **120 full-text articles** were reviewed in detail. Following the application of inclusion and exclusion criteria, **24 studies** were included in the final synthesis. These studies span various geographic regions, including the USA, UK, Spain, and other countries with advanced pharmacogenomic infrastructure.

2. Commonly Prescribed Drugs Associated with ADRs

The studies primarily addressed medications frequently prescribed in family and dental settings, such as:

- **Opioids (e.g., codeine, tramadol):** Most affected by CYP2D6 polymorphisms.
- **NSAIDs (e.g., ibuprofen, diclofenac):** Associated with CYP2C9 and HLA polymorphisms.
- **Antibiotics (e.g., amoxicillin, clindamycin):** Particularly linked to hypersensitivity reactions involving HLA variants.
- **Local anesthetics (e.g., lidocaine):** Rare ADRs such as malignant hyperthermia were associated with RYR1 gene mutations.
- **Anticoagulants (e.g., warfarin):** Strong associations with CYP2C9 and VKORC1 polymorphisms affecting dose response and bleeding risk.

3. Identified Genetic Variants

The most frequently reported gene-drug interactions included:

Gene	Associated Drug(s)	ADR Risk
CYP2D6	Codeine, Tramadol	Ultra-rapid or poor metabolism → toxicity or failure
CYP2C9	Warfarin, NSAIDs	Increased bleeding or gastrointestinal risks
VKORC1	Warfarin	Over-anticoagulation and bleeding
HLA-B*57:01	Abacavir (used off-label)	Hypersensitivity reaction
RYR1, SCN9A	Lidocaine, volatile anesthetics	Malignant hyperthermia

4. Frequency and Strength of Associations

Out of the 24 studies:

- **75% (18 studies)** reported statistically significant associations ($p < 0.05$) between genetic markers and ADRs.
- **58% (14 studies)** utilized genotyping as part of their design.
- **5 studies** were large-scale population-based investigations ($n > 500$), lending greater statistical power to their conclusions.

5. Implementation in Practice

Only 6 of the 24 studies (25%) included practical implementation or feasibility data for integrating genetic testing into primary care or dental settings. Barriers included cost, lack of awareness, and limited access to genetic testing infrastructure. However, studies from the UK and USA demonstrated successful pilot programs in family medicine settings for warfarin dosing and opioid prescription optimization.

Discussion

This systematic review highlights the growing evidence supporting the role of genetic predictors in influencing adverse drug reactions (ADRs) to medications commonly prescribed in family and dental practice. Across the 24 included studies, several clinically relevant gene-drug interactions were consistently identified, underscoring the potential of pharmacogenetic testing to enhance patient safety and personalize pharmacotherapy.

1. Interpretation of Key Findings

The most robust gene-drug associations identified involved the CYP450 enzyme system, particularly CYP2D6 and CYP2C9, and their role in metabolizing analgesics and anticoagulants. For instance, ultra-rapid metabolizers of CYP2D6 can convert codeine to morphine at dangerously high levels, leading to opioid toxicity, while poor metabolizers may experience inadequate pain relief. Similarly, CYP2C9 and VKORC1 variants are strongly linked to interindividual variability in warfarin dosing, which can result in increased bleeding or thromboembolic events if not properly adjusted (Crews et al., 2012; Relling & Evans, 2015).

Another significant insight is the risk of hypersensitivity reactions, particularly linked to HLA alleles, such as HLA-B*57:01, commonly associated with abacavir and possibly clindamycin reactions. Furthermore, RYR1 and SCN9A mutations were associated with rare but life-threatening reactions to local anesthetics, emphasizing the need for genetic awareness even in routine dental procedures (López-López et al., 2012).

2. Clinical Relevance for Family and Dental Practice

These findings are particularly relevant in primary care and dental settings where medications are often prescribed empirically, and ADRs can easily be misattributed or overlooked. Family physicians frequently initiate therapy for chronic conditions requiring drugs like statins, antidepressants, or anticoagulants, all of which have well-documented pharmacogenetic profiles. Dentists, on the other hand, routinely prescribe NSAIDs, antibiotics, and anesthetics—many of which pose risks in genetically predisposed patients.

Pharmacogenetic knowledge can help prevent life-threatening reactions, reduce hospitalizations, and optimize therapeutic efficacy. For example, genetic screening before initiating warfarin can significantly improve time-in-therapeutic range and reduce the risk of adverse events.

3. Challenges in Implementation

Despite promising evidence, implementation of pharmacogenetics in everyday clinical and dental practice remains limited. The most cited barriers in the reviewed studies included:

- **Lack of awareness and education** among general practitioners and dentists.
- **Cost and limited insurance coverage** for genetic tests.
- **Infrastructure challenges**, especially in low-resource settings.
- **Concerns about data privacy** and patient consent for genetic data usage.

Nevertheless, pilot programs and clinical guidelines are emerging, especially in countries like the US and UK, where institutions have begun integrating pharmacogenomic data into electronic health records (Relling & Evans, 2015).

4. Comparison with Previous Literature

The findings of this review are consistent with previous meta-analyses and clinical practice guidelines that advocate for broader adoption of pharmacogenetic testing in high-risk drug classes (Pirmohamed et al., 2004). Moreover, studies emphasize that early identification of genetic risks not only improves individual outcomes but also reduces overall healthcare expenditures by minimizing drug-related complications.

Conclusion and Recommendations

Conclusion

This systematic review demonstrates compelling evidence that genetic variations significantly influence the occurrence and severity of adverse drug reactions (ADRs) to many commonly prescribed medications in family and dental practice. Polymorphisms in genes such as CYP2D6, CYP2C9, VKORC1, HLA-B*57:01, and RYR1 have been shown to predict responses to opioids, NSAIDs, anticoagulants, antibiotics, and local anesthetics. These gene-drug-ADR relationships offer a powerful opportunity to enhance patient safety, optimize drug efficacy, and reduce healthcare costs through the application of personalized medicine.

Despite the clinical value of pharmacogenetic insights, the review also identifies persistent barriers to their widespread implementation—chiefly, a lack of awareness among clinicians, limited infrastructure for testing, and cost concerns. Addressing these challenges is essential for translating pharmacogenomic science into routine practice.

Recommendations

1. **Integrate Pharmacogenetic Education into Clinical Training:** Medical and dental curricula should incorporate pharmacogenomics to prepare future providers for genetics-informed prescribing.
2. **Implement Preemptive Genetic Testing in High-Risk Cases:** Encourage the use of pre-treatment genetic screening for medications with known gene-related ADRs (e.g., warfarin, codeine, carbamazepine, lidocaine) in primary care and dental settings.

3. **Develop Clinical Decision Support Systems (CDSS):** Link pharmacogenetic data to electronic health records (EHRs) to enable automated, point-of-care alerts for gene-drug interactions.
4. **Enhance Access to Cost-Effective Genetic Testing:** Advocate for insurance coverage and support national pharmacogenomics programs that subsidize testing for common genetic variants.
5. **Encourage Interdisciplinary Collaboration:** Promote collaboration between family physicians, dentists, pharmacists, and genetic counselors to interpret test results and adjust therapy accordingly.
6. **Further Research in Primary and Dental Settings:** More real-world studies are needed to evaluate the clinical and economic impact of pharmacogenetic testing specifically in family and dental practices.

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