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Real-World Study on Adverse Reactions to Technetium (Tc99m) Medronate Based on VigiAccess Database Mining

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Abstract: *Objective:* This study aims to explore adverse events related to Technetium (Tc99m) Medronate using the VigiAccess database, uncover potential risk signals, and provide comprehensive reference for rational clinical drug use to ensure patient safety. *Methods:* The study retrieved adverse event reports related to Technetium (Tc99m) Medronate from the VigiAccess database, preprocessed the data, and employed the Reporting Odds Ratio (ROR) method to detect signals and analyze the characteristics and intensity of adverse events. *Results:* A total of 543 adverse event reports related to Technetium (Tc99m) Medronate were retrieved. The data showed that reports from female patients accounted for 48.62%, higher than the 26.15% from male patients, and the 18–64 age group had a higher proportion of reports at 52.89%. In terms of adverse event distribution, skin and subcutaneous tissue disorders accounted for 24.12%, general disorders and administration site conditions accounted for 21.68%, and nervous system disorders accounted for 14.83%. These three types of disorders were the most common adverse reactions during the use of Technetium (Tc99m) Medronate. Further ROR analysis revealed strong associations between Technetium (Tc99m) Medronate and adverse events such as product efficacy issues, vasodilation, and decreased therapeutic response. The ROR value for product efficacy issues was as high as 379.29 (95% CI: 180.18, 798.47), vasodilation was 60.75 (95% CI: 45.91, 80.51), and decreased therapeutic response was 36.35 (95% CI: 20.48, 64.81). *Conclusion:* This study analyzed adverse events related to Technetium (Tc99m) Medronate using the VigiAccess database, finding that female patients and the age group of 18 to 64 had a higher proportion. The related adverse events were mainly concentrated in skin and subcutaneous tissue disorders, general disorders and administration site conditions, and nervous system disorders. Adverse events such as product efficacy issues, vasodilation, and decreased therapeutic response were strongly associated with Technetium (Tc99m) Medronate, indicating the need for special attention to these adverse reactions in clinical use, strengthening drug monitoring and management to ensure patient safety, and providing important reference for clinicians in the rational use of Technetium (Tc99m) Medronate.

Keywords: Technetium (Tc99m) Medronate; VigiAccess; Adverse reactions; Signal mining; Reporting odds ratio

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1. Introduction

Pharmacovigilance is the scientific activity of monitoring adverse drug reactions (ADRs) and related issues during the market use of drugs, which is crucial for ensuring patient safety. VigiAccess is a public database launched by the World Health Organization (WHO) to provide global information on adverse drug reactions. Its data sources are anonymous reports from member countries of the WHO International Drug Monitoring Program (PIDM), covering over 39 million reports. The data from VigiAccess can provide researchers with a global perspective on drug safety information; however, it should be noted that these data only indicate a suspected association between the drug and adverse reactions and do not confirm causality.

Technetium (Tc99m) Medronate is a radiopharmaceutical used to treat diseases such as rheumatoid arthritis and osteoporosis. Its mechanisms of action include inhibiting inflammatory responses, immune modulation, inhibiting bone destruction, and promoting bone repair [1]. Clinical studies have shown that Technetium (Tc99m) Medronate has significant efficacy in treating rheumatoid arthritis with relatively few adverse reactions. However, the safety monitoring of the drug is an ongoing process, especially after widespread application, when some adverse reactions not observed in clinical trials may emerge [2]. Therefore, utilizing the VigiAccess database to conduct real-world research on adverse events related to Technetium (Tc99m) Medronate can provide a more comprehensive reference basis for rational clinical drug use and further ensure patient safety.

2. Data processing and statistical methods

2.1. Data source

Data was retrieved from the VigiAccess database (https://vigiaccess.org/), data retrieval date was on May 29, 2025.

2.2. Data extraction and processing

Using Python 3.10 with the requests package, all drug BASENAMES in the WHO DRUG dictionary were retrieved, and JSON data returned from the front-end page was obtained. The JSON data was visualized using the Pandas package and exported to Excel to complete the download of all publicly available drug data. Subsequent statistical analysis was performed using SAS 9.4 software.

2.3. Signal detection methods and calculation

Proportional imbalance method was used for signal detection of adverse drug events. ROR method was employed for detecting adverse event signals.

2.4. Target drug

The target drug in this study was Technetium (Tc99m) Medronate.

3. Results

3.1. Basic characteristics of adverse event reports

Table 1 presents the analysis results of adverse events related to Technetium (Tc99m) Medronate, mainly showing the basic characteristics of adverse events, including gender, age, region, and report year. In terms of gender distribution, female patients reported the most adverse events, accounting for 48.62% (264 cases), while male patients accounted for 26.15% (142 cases). This indicates that female patients have a higher probability of

reporting adverse reactions when using Technetium (Tc99m) Medronate. Regarding age distribution, the 18–44 age group reported the most adverse events, accounting for 17.13% (93 cases), followed by the 45–64 age group at 23.76% (129 cases), and the 65–74 age group at 10.87% (59 cases). Patients aged 75 and above accounted for 6.63% (36 cases), those aged 12–17 accounted for 3.68% (20 cases), and patients aged 2–11 and 28 days to 23 months reported fewer cases, accounting for 1.1% (6 cases) and 0.55% (3 cases), respectively. From the regional distribution perspective, reports from the Americas were the most, accounting for 90.06% (489 cases) of the total reports, indicating that Technetium (Tc99m) Medronate is more widely used in this region or that the adverse reaction monitoring system in this region is more comprehensive. Reports from Asia, Europe, and Oceania accounted for 1.47% (8 cases), 4.97% (27 cases), and 3.5% (19 cases), respectively. Regarding the report year, adverse events were reported from 1981 to 2024, with fewer early reports. The number of reports increased after 2000, reaching a small peak in 2005 (50 cases, 9.21%).

Table 1. Characteristics of adverse event reports

Characteristics	***n* (%)**
Sex	
Female	264 (48.62)
Male	142 (26.15)
Unknown	137 (25.23)
Age	
28 days to 23 months	3 (0.55)
2–11 years	6 (1.1)
12–17 years	20 (3.68)
18–44 years	93 (17.13)
45–64 years	129 (23.76)
65–74 years	59 (10.87)
75 years and above	36 (6.63)
Unknown	197 (36.28)
Continent	
Americas	489 (90.06)
Asia	8 (1.47)
Europe	27 (4.97)
Oceania	19 (3.5)
Report year	
1981	1 (0.18)
1982	5 (0.92)
1983	7 (1.29)
1984	3 (0.55)
1985	5 (0.92)
1986	50 (9.21)

Table 1 (Continued)

Characteristics	*n* (%)
1987	1 (0.18)
1988	20 (3.68)
1989	17 (3.13)
1990	27 (4.97)
1991	19 (3.5)
1992	26 (4.79)
1993	15 (2.76)
1994	33 (6.08)
1995	14 (2.58)
1996	9 (1.66)
1997	7 (1.29)
1998	3 (0.55)
1999	9 (1.66)
2000	24 (4.42)
2001	12 (2.21)
2002	3 (0.55)
2003	12 (2.21)
2004	7 (1.29)
2005	8 (1.47)
2006	7 (1.29)
2007	1 (0.18)
2008	18 (3.31)
2009	7 (1.29)
2010	14 (2.58)
2011	29 (5.34)
2012	5 (0.92)
2013	5 (0.92)
2014	2 (0.37)
2015	9 (1.66)
2016	12 (2.21)
2017	33 (6.08)
2018	14 (2.58)
2019	16 (2.95)
2020	5 (0.92)
2021	5 (0.92)

Table 1 (Continued)

Characteristics	*n* (%)
2022	9 (1.66)
2023	4 (0.74)
2024	11 (2.03)

3.2. Proportion of adverse events by system organ class

As shown in **Figure 1**, adverse events associated with Technetium (Tc99m) Medronate are primarily concentrated in skin and subcutaneous tissue disorders, general disorders and administration site conditions, and nervous system disorders. Specifically, skin and subcutaneous tissue disorders are the most common, accounting for 24.12% (296 cases) of the total adverse events. General disorders and administration site conditions follow closely, comprising 21.68% (266 cases). This indicates that skin reactions and systemic reactions are relatively common during the use of Technetium (Tc99m) Medronate, requiring special attention. Adverse events related to nervous system disorders account for 14.83% (182 cases), suggesting that the use of Technetium (Tc99m) Medronate may have some impact on the nervous system. Additionally, gastrointestinal disorders account for 13.04% (160 cases), indicating that the drug also has a significant impact on the gastrointestinal tract. Adverse events involving other system organs are relatively fewer. Vascular disorders account for 4.81% (59 cases), respiratory, thoracic, and mediastinal disorders account for 3.59% (44 cases), musculoskeletal and connective tissue disorders account for 3.26% (40 cases), and immune system disorders account for 2.20% (27 cases). Cases of injury, poisoning, and procedural complications account for 2.12% (26 cases), indicating that apart from the main adverse reaction sites, the impact of Technetium (Tc99m) Medronate on other systems cannot be ignored. Systems with relatively fewer reported cases include psychiatric disorders (1.47%, 18 cases), cardiac disorders (1.30%, 16 cases), infections and infestations (1.14%, 14 cases), and renal and urinary disorders (1.06%, 13 cases). Other rarer reactions include ear and labyrinth disorders, metabolic and nutritional disorders, etc., all with proportions below 1%.

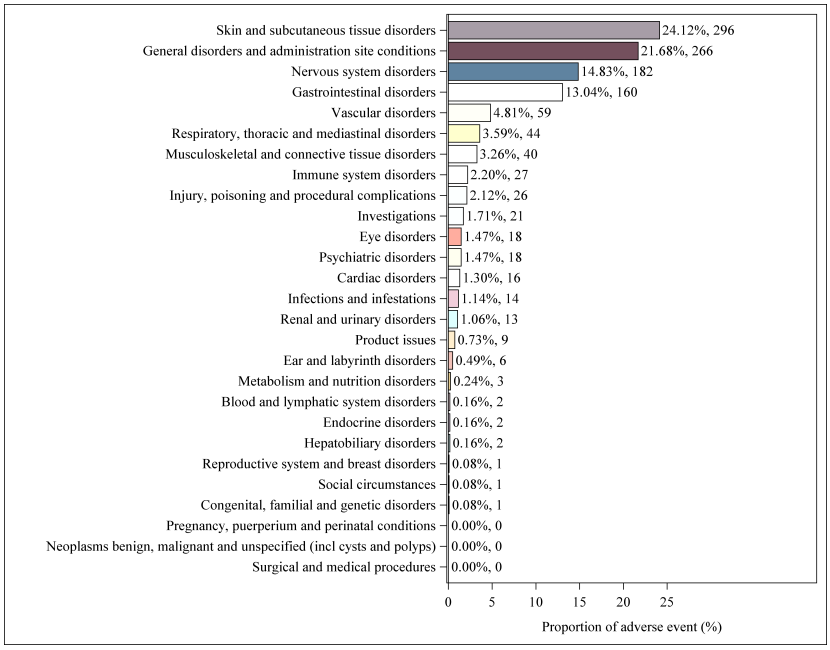

Figure 1. Proportion of adverse events by SOCs

3.3. The proportion of adverse events categorized by preferred terms

Figure 2 shows that Technetium (Tc99m) Medronate-related adverse events are mainly concentrated in the following categories. Skin and subcutaneous tissue disorders are the most common category of adverse events, with pruritus accounting for 6.44% (79 cases), rash accounting for 6.11% (75 cases), and urticaria accounting for 6.03% (74 cases). This indicates that skin reactions are one of the most common side effects when using Technetium (Tc99m) Medronate. Secondly, adverse events related to the nervous system and systemic reactions are also significant. These include nausea accounting for 4.16% (51 cases), headache accounting for 3.10% (38 cases), dizziness accounting for 3.75% (46 cases), and fatigue accounting for 1.14% (14 cases). Additionally, feedback on decreased efficacy is also quite common, such as therapeutic response decreased accounting for 3.83% (47 cases) and drug ineffective accounting for 3.75% (46 cases), which suggests that attention needs to be paid to the efficacy of Technetium (Tc99m) Medronate and patients' responses to the drug. Adverse events of the respiratory and cardiovascular systems should not be ignored, such as dyspnea accounting for 1.87% (23 cases), syncope accounting for 1.47% (18 cases), and hypotension accounting for 1.30% (16 cases). These reactions indicate that it is necessary to monitor the respiratory and cardiovascular health of patients when using Technetium (Tc99m) Medronate. Other relatively common adverse events include vomiting (accounting for 2.85%, 35 cases), vasodilatation (accounting for 1.96%, 24 cases), fatigue (accounting for 1.14%, 14 cases), and pain (accounting for 1.14%, 14 cases). This shows that Technetium (Tc99m) Medronate may cause reactions in multiple body systems, requiring comprehensive monitoring and management. A few reports include face edema, chest pain, and palpitations, each accounting for less than 1%, but they also need to be noted.

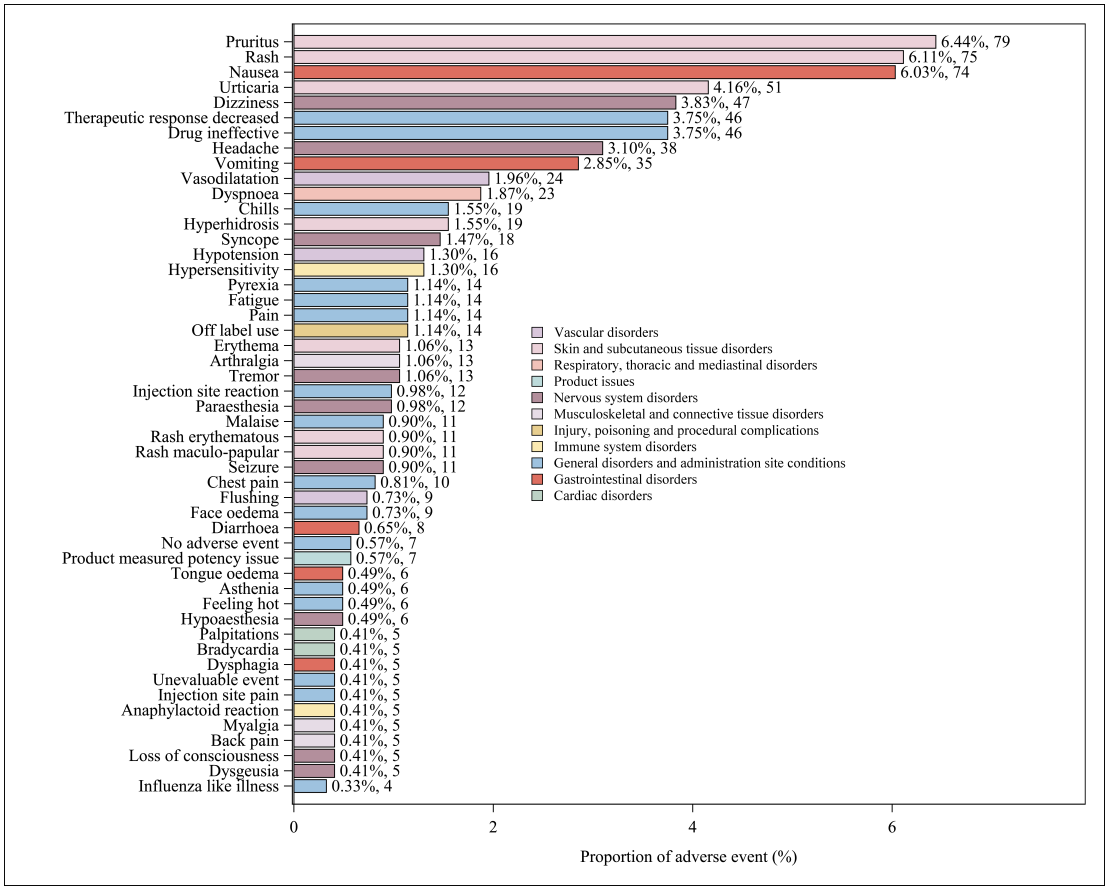

Figure 2. Proportion of adverse events by PTs

3.4. Forest plot of positive signal strength

A higher ROR value indicates a stronger association between a specific drug and a particular adverse event. A higher ROR value suggests that this adverse event is more common among patients using the drug, indicating a potential causal relationship. **Figure 3** illustrates the signal strength for various adverse reactions. The issue of product potency has the highest ROR value at 379.29 (95% CI: 180.18, 798.47), indicating a significant association between Technetium (Tc99m) Medronate and product potency issues. Vasodilatation (60.75, 95% CI: 45.91, 80.51) and decreased therapeutic response (36.35, 95% CI: 20.48, 64.81) also present significant positive signals, suggesting a high risk of association with Technetium (Tc99m) Medronate in these areas. Other notable positive signals include laryngospasm (26.35, 95% CI: 9.81, 48.84), tongue edema (24.57, 95% CI: 11.04, 54.80), and pharyngitis (9.65, 95% CI: 2.25, 25.75), indicating that Technetium (Tc99m) Medronate may cause significant respiratory and oral-related issues. Circulatory collapse (6.72, 95% CI: 1.27, 20.97), throat tightness (6.43, 95% CI: 4.17, 11.16), syncope (6.19, 95% CI: 3.88, 9.85), and dermatitis (6.03, 95% CI: 2.86, 12.08) also demonstrate high ROR values, suggesting these symptoms are more pronounced when using Technetium (Tc99m) Medronate. For more common but lower ROR adverse reactions, including face edema (5.03, 95% CI: 2.61, 9.69), urticaria (4.74, 95% CI: 3.58, 6.27), bronchospasm (4.55, 95% CI: 1.64, 11.11), and hypotension (3.66, 95% CI: 2.23, 5.98), these adverse reactions, although lower in signal strength, still warrant attention. Other areas of concern include various nervous system, skin, and subcutaneous tissue-related symptoms, such as injection site reaction (4.45, 95% CI: 2.52, 7.86), pruritus (4.28, 95% CI: 3.41, 5.38), and drug ineffective (2.71, 95% CI: 2.03, 3.64), which also display notable positive signals. Overall, these data indicate that Technetium (Tc99m) Medronate may cause a range of systemic adverse reactions, particularly in areas such as product potency, vasodilatation, decreased therapeutic response, and respiratory and oral-related issues, which have higher ROR values, suggesting these are high-risk areas to monitor closely when using Technetium (Tc99m) Medronate. Close monitoring and early intervention for these adverse reactions are essential to ensure patient safety.

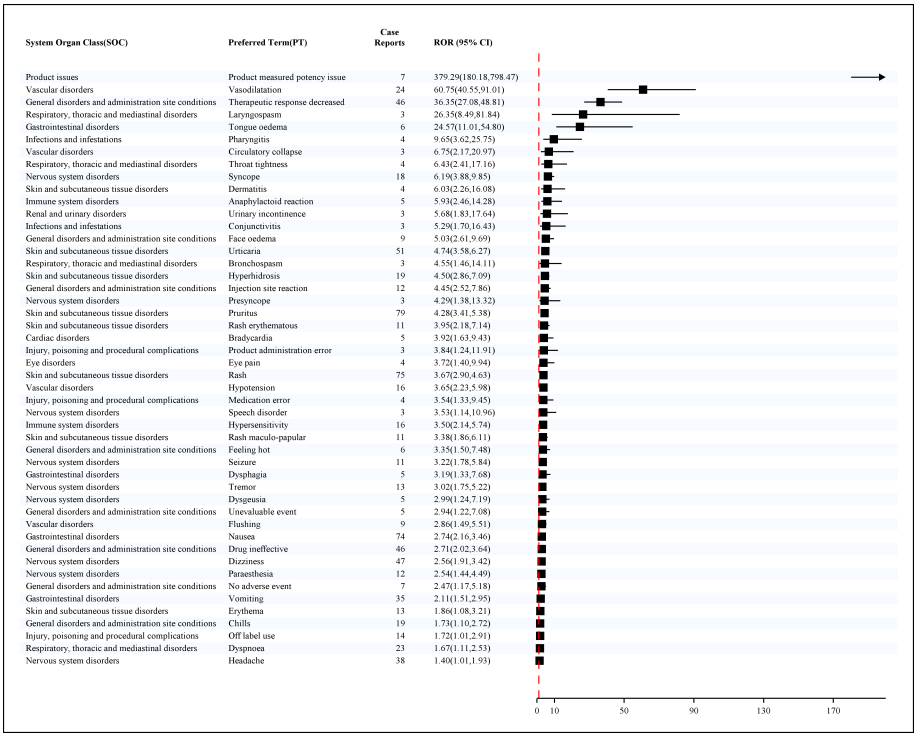

Figure 3. Forest plot of positive signal strength by ROR

3.5. Summary

This study, based on the VigiAccess database, analyzed adverse events related to Technetium (Tc99m) Medronate and found that the number of reports from female patients was higher, with a significant proportion in the age group of 18 to 64 years. The related adverse events were mainly concentrated in skin and subcutaneous tissue diseases, general disorders and administration site reactions, and nervous system diseases. Adverse events such as product efficacy issues, vasodilation, and reduced therapeutic response were strongly associated with Technetium (Tc99m) Medronate.

4. Discussion

This analysis of Technetium (Tc99m) Medronate-related adverse events based on the VigiAccess database provides valuable perspectives and data support for a deeper understanding of the safety profile of this drug in real-world use. From the basic characteristics of adverse event reports, the number of reports from female patients is significantly higher than that of males, accounting for nearly half. This gender difference may be related to multiple factors. On the one hand, in the populations suffering from diseases such as rheumatoid arthritis and osteoporosis, which Technetium (Tc99m) Medronate is commonly used to treat, the proportion of female patients is relatively higher [3]; thus, the number of female patients using Technetium (Tc99m) Medronate is naturally higher, leading to an increase in corresponding adverse reaction reports [4]. On the other hand, females may be more sensitive to drug reactions due to physiological characteristics such as hormonal changes, which may interact with the drug's metabolism and action process in the body, making adverse reaction symptoms more likely to appear and be reported [5]. Additionally, social and cultural factors may also play a role, as women are generally more attentive to their health and more inclined to seek medical attention and report discomfort during drug use, while men may have higher tolerance to body symptoms or delay medical reporting due to traditional beliefs. Regarding age distribution characteristics, the number of reports is higher in the age group of 18 to 64 years, especially in the 45 to 64 years age group, which aligns with the age profile of the primary indications for Technetium (Tc99m) Medronate, such as rheumatoid arthritis and osteoporosis, which are more common in middle-aged and elderly populations [6]. Therefore, this age group uses Technetium (Tc99m) Medronate more frequently, resulting in an increase in adverse reaction reports. The proportion of reports from the Americas is as high as 90.06%, far exceeding other regions [7]. This phenomenon may suggest that Technetium (Tc99m) Medronate is more widely used in the Americas, possibly related to the local medical market's recognition of the drug, the distribution of medical resources, and the characteristics of the disease spectrum. It may also reflect that the adverse drug reaction monitoring system in this region is relatively more complete and mature, encouraging healthcare professionals and patients to actively report adverse events, making the relevant data more fully collected and presented. From the trend of report years, early reports were fewer, gradually increasing after 2000, with a small peak in 2006. This may be related to the widespread clinical application of Technetium (Tc99m) Medronate over time, increasing awareness among doctors and patients, and the gradual enhancement of adverse drug reaction monitoring awareness, leading to more adverse reactions being discovered and reported.

In the classification of adverse events by system organ class, skin and subcutaneous tissue diseases, general disorders and administration site reactions, and nervous system diseases have higher proportions [8]. Common skin reactions such as itching, rash, and urticaria may be related to Technetium (Tc99m) Medronate as a radionuclide drug, whose unique pharmacological mechanism may affect the physiological state of the skin to some extent,

stimulating immune responses or causing allergic reactions [9]. The prominence of general disorders and administration site reactions suggests that the drug may interfere with the body's overall metabolism and immune functions after entering the body, and local administration sites may develop inflammation due to drug irritation. The high proportion of nervous system adverse events is also noteworthy, as the complexity and importance of nervous system functions mean that such adverse reactions could significantly impact patients' quality of life and health [10]. Technetium (Tc99m) Medronate may cause symptoms like headache and dizziness by affecting neurotransmitter levels, nerve cell metabolism, or directly acting on nerve tissues, and the specific mechanisms require further in-depth research.

From the ROR positive signal analysis results, the product efficacy issue has an extremely high ROR value, which may indicate that in actual use, Technetium (Tc99m) Medronate has certain efficacy instability or does not meet expectations [5,7]. The influencing factors may be multifaceted, such as quality control fluctuations in drug production, substandard storage, and transportation conditions affecting drug efficacy, and individual differences in patients affecting drug absorption and utilization. High signal strengths for vasodilation and reduced therapeutic response suggest that we need to re-examine whether there are areas for improvement in Technetium (Tc99m) Medronate's drug development, clinical application guidance, and patient education to optimize its clinical efficacy and safety [8]. Significant positive signals for respiratory and oral issues like throat spasm and tongue edema also warn that corresponding symptoms and signs should be closely monitored when using Technetium (Tc99m) Medronate, with preventive and responsive measures taken in advance to avoid severe adverse events.

However, this study also has some limitations. Firstly, the data in the VigiAccess database are from voluntary reports from various countries, which may lead to reporting bias, such as more severe adverse events being more likely to be reported while minor events might be overlooked, resulting in data not entirely accurately reflecting the actual situation. Secondly, the level of detail in the database is limited, and some reports may lack complete patient basic information, medication history, and comorbidities, which to some extent affects the accurate judgment and in-depth analysis of the causal relationship between adverse events and Technetium (Tc99m) Medronate. Furthermore, this study only conducted statistical analysis based on existing data without further clinical validation trials, so the potential signals and mechanisms discovered still require more experimental research and clinical observations to confirm.

5. Conclusion

In summary, this study revealed the characteristics, distribution patterns, and potential risk signals of adverse reactions to Technetium (Tc99m) Medronate in real-world use by thoroughly mining the Technetium (Tc99m) Medronate-related adverse event information in the VigiAccess database. It provides important references for clinicians to use Technetium (Tc99m) Medronate rationally, enhance medication monitoring, and for pharmaceutical companies to improve product quality. It also points the way for further safety research on Technetium (Tc99m) Medronate in the future, helping to continuously improve its pharmacovigilance system, ensuring patient medication safety, and promoting its better role in clinical treatment.

Disclosure statement

The authors declare no conflict of interest

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