

Original article

The use of electronic notifications to improve guideline adherence in amiodarone adverse reaction monitoring

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Abstract

Background: Amiodarone is an anti-arrhythmic drug that can cause side effects on the thyroid, liver, lungs, vision, and nervous system. Guidelines for monitoring and surveillance of these side effects have been in place since 2000, but adherence to them remains low in many countries, including Thailand. An electronic alert system has been implemented at Vajira Hospital, Navamindradhiraj University, Thailand, to remind physicians of the monitoring guidelines since August 2023.

Objectives: This study aimed to compare adherence with the amiodarone guideline before and after implementing an electronic notification system and to evaluate the incidence of amiodarone-related adverse reactions.

Methods: This cohort study used electronic medical records of patients who visited the outpatient department at Vajira Hospital, Thailand, and received amiodarone for at least 1 month between February 2022 and February 2025. Adherence to the amiodarone guideline and incidence of adverse reactions were compared before and after implementing the electronic alert system in August 2023. The primary outcome was to compare adherence before and after the implementation of an electronic notification system. The secondary outcome was to assess the incidence of amiodarone-related side effects.

Results: We screened 201 patients who received amiodarone during that period, but only 110 patients received amiodarone continuously throughout the period of the electronic notification system (August 2023). The overall adherence to the amiodarone guideline increased from 11.8% to 46.4% (adjusted relative risk 3.92, 95% confidence interval [2.13–7.21]) following the implementation of the electronic alert system. Adherence to chest x-ray, liver function tests, and thyroid function tests also improved substantially after the intervention. The most common adverse reaction suspected from amiodarone usage was abnormal thyroid-stimulating hormone (TSH) levels. The incidence of abnormal TSH levels increased from 18.2% before the notification system to 23.6% after, although the difference was not significant.

Conclusion: The electronic alert system improved adherence to the guideline for monitoring amiodarone side effects in overall aspects. This intervention has the potential to enhance patient safety by facilitating the early detection of amiodarone-related adverse effects. We encourage the implementation of an electronic alert system in hospitals, particularly in the cardiology clinic, to monitor for potential amiodarone-related side effects.

Keywords: Adverse event, amiodarone, guideline adherence.

Amiodarone is an anti-arrhythmic drug that is commonly used in cardiology clinics.⁽¹⁾ However, amiodarone has potential side effects that should be considered, especially with long-term use. Several studies have demonstrated that the long-term use of

amiodarone can lead to abnormal thyroid function tests, resulting in hyperthyroidism or hypothyroidism.^(2, 3) Moreover, it can cause abnormal liver function tests in approximately 15.0%–50.0% of cases⁽⁴⁾ and may affect the respiratory system, resulting in symptoms such as cough, dyspnea, or abnormalities detected in lung tissue via computer tomography scan (CT scan) or pulmonary function tests.⁽⁵⁾

Due to these potential complications, the North American Society of Pacing and Electrophysiology published practical guidelines for clinicians treating patients with amiodarone in 2000,⁽⁶⁾ which were

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subsequently updated in 2007 and 2016.^(7,8) The latest update recommended performing liver function tests, thyroid function tests, and chest X-rays (CXR) before initiating amiodarone therapy, followed by periodic monitoring thereafter. In addition, the guidelines suggest performing optical and neurological examinations when indicated for patients.

Despite the publication of these guidelines, relatively low adherence rates have been reported. A study conducted in Israel indicated an adherence rate of 10.0–60.0%,⁽⁹⁾ while a similar study in the UK reported rates between 7.0% and 22.0%.⁽¹⁰⁾ However, there is currently no available data on adherence rates to amiodarone guidelines in Thailand.

At Vajira Hospital in Thailand, an electronic medical record system is utilized to record patient data, laboratory results, and treatment information, including prescriptions. Leveraging this system to implement electronic alerts that remind physicians to adhere to the amiodarone side-effect monitoring guidelines could improve treatment outcomes for patients and facilitate side-effect monitoring. Previous studies have demonstrated the benefits of using electronic alert systems in clinical settings, such as in heart failure clinics.⁽¹¹⁾ This study aimed to compare adherence to the amiodarone side-effect guidelines before and after the implementation of an electronic notification system.

Materials and methods

This study was conducted in accordance with the Declaration of Helsinki and its subsequent updates and was reviewed and approved by the local Ethics Committee of the Institutional Review Board of the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University (IRB no. 054/66). Informed consent was waived because only retrospective data were used.

The electronic alert system was implemented on August 10, 2023, which triggered an alarm on the computer when physicians prescribe oral amiodarone via the electronic medical record system. The alarm is the pop-up box with the following sentences: 1) Do liver function tests at baseline and every 6 months; 2) Do thyroid function tests at baseline and every 6 months; and 3) Do a chest x-ray at baseline and every 1 year.

Study design

This study is a retrospective cohort study conducted at the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Thailand.

Study population

We included all patients aged 18 and older who received oral amiodarone for at least a month between February 2022 and February 2025. Patients with pre-existing liver disease, thyroid disease, chronic neuropathy, and chronic lung disease were excluded from the study.

Data sources

The reporting of this study conforms to the STROBE statement.⁽¹²⁾ Electronic medical records were reviewed for baseline characteristics, underlying diseases, and indications for amiodarone use. The percentage of adherence to the monitoring guidelines for amiodarone use was evaluated, as was the incidence of adverse effects of chronic amiodarone use.

Outcomes

The primary outcome of this study was to compare adherence to the amiodarone guideline before and after the implementation of an electronic alert system. Secondary outcomes include adherence to individual guideline components (CXR, liver function tests, and thyroid function tests) and the incidence of amiodarone-related adverse reactions, including abnormal thyroid function tests, abnormal liver function tests, abnormal CXRs, and other complications.

The electronic alert system was implemented on August 10, 2023, which triggers an alarm when physicians prescribe oral amiodarone via the electronic medical record system. The alarm prompts monitoring of liver function tests, thyroid function tests, and CXRs according to the guidelines.

Adherence to the amiodarone guideline is defined as follows:

1. Liver function test at baseline and every 6 months or at least 2 times
2. Thyroid function test at baseline and every 6 months or at least 2 times
3. CXR at baseline and every 1 year or at least 1 time

Patients must undergo evaluation for all three components to be considered adherent to the guideline. The flow chart of the study is shown in **Figure 1**.

The definitions of amiodarone-related adverse reactions include

1. Abnormal alanine aminotransferase (ALT) is defined as $ALT \geq 3 \times$ upper limit of normal.
2. Abnormal TSH is defined as a TSH level below or above the laboratory reference range.
3. Abnormal CXR is defined as abnormal opacity in the lungs.

Sample size calculation

We included every patient aged 18 and older who received oral amiodarone for at least 1 month from February 2022 to February 2025.

Statistical analysis

Statistical analyses were performed using Stata version 13.0 (Stata Corporation, College Station, TX, United States). Categorical data are presented as frequencies (n) and percentages (%). Continuous variables are presented as the mean $\pm$ standard deviation or the median with interquartile range (IQR), depending on their distribution. Multilevel Poisson regression was conducted to investigate adherence to the amiodarone guidelines and adverse reactions suspected from amiodarone use after implementation of the electrical alert system, compared with the period before the alert system. $P < 0.05$ was considered statistically significant.

Results

This study enrolled patients who received oral amiodarone continuously and visited the outpatient department from February 2022 to February 2025. A total of 201 patients were screened, with 110 patients enrolled. The mean age was 73.0, and the majority of patients were prescribed amiodarone for atrial fibrillation and atrial flutter (70.0%). The average follow-up period was 18 months, and patient demographics are shown in **Table 1**.

The overall adherence to the guideline was 11.8% before the electronic alert system was implemented, increasing significantly to 46.4% after the system was implemented. The adjusted relative risk (RR) was 3.92 (95% confidence interval (CI) 2.13–7.21), $P < 0.001$. For individual components, adherence rates for CXR were 35.5% vs. 58.2% [adjusted RR 1.64 (95% CI: 1.10–2.44)], $P = 0.015$; for liver function tests were

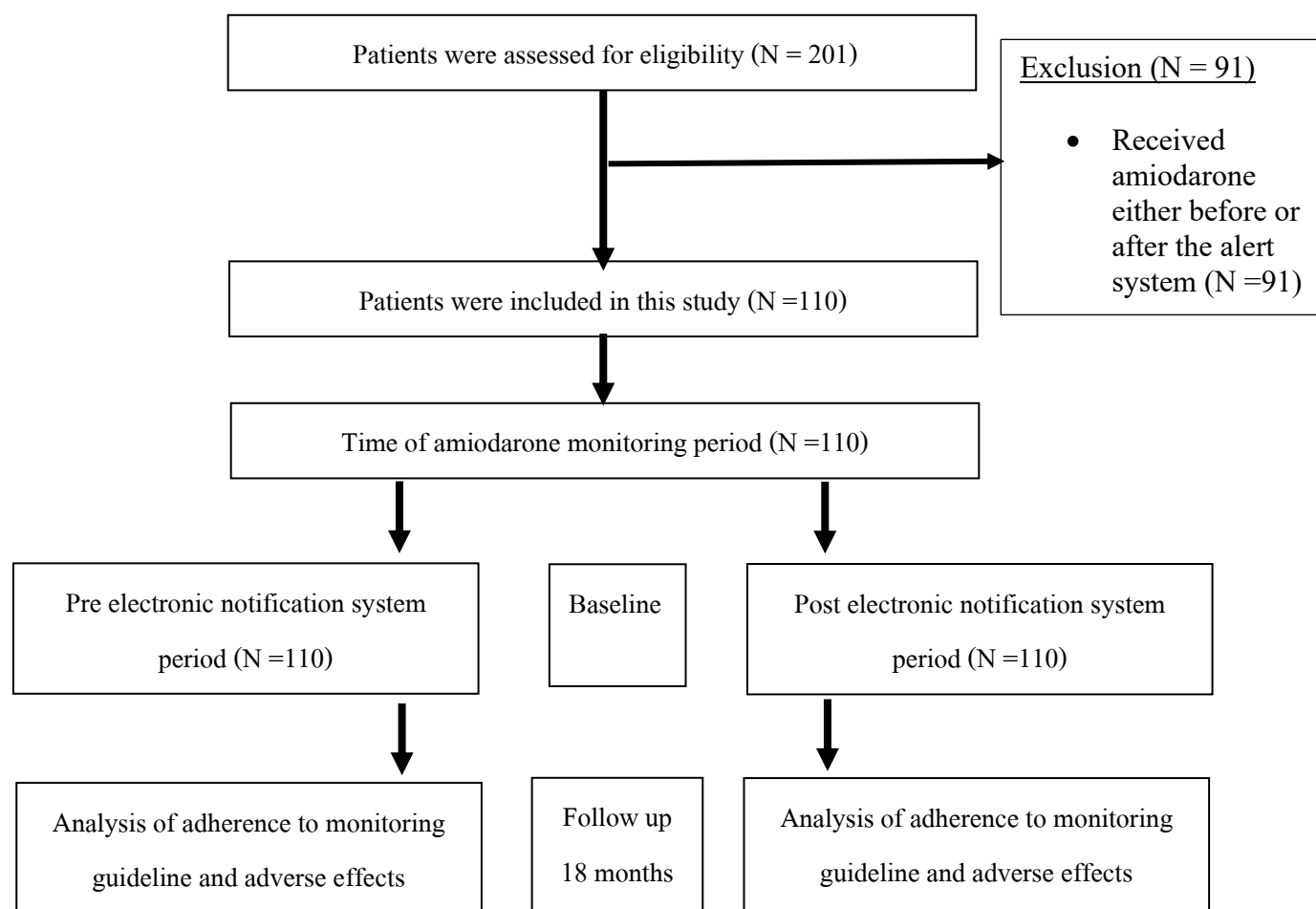


Figure 1. CONSORT diagram.

Table 1 Baseline characteristics of study populations.

Characteristics	Total n = 110 (%)
Age (years)	73.0 (62.0–79.0)
Sex: Male	57 (51.8)
Body mass index (kg/m ²)	24.4 (21.9–27.4)
Underlying diseases	
Hypertension	89 (80.9)
Diabetes	36 (32.7)
Dyslipidemia	96 (87.3)
Chronic kidney disease	33 (30.0)
Coronary artery disease	33 (30.0)
Heart failure	32 (29.0)
Indication	
Atrial fibrillation and atrial flutter	77 (70.0)
Ventricular tachycardia	19 (17.3)
Others (SVT, PAC, PVC)	14 (12.7)
Dose of amiodarone (mg/day)	200.0 (100.0–200.0)

PAC, premature atrial complex; PVC, premature ventricular complex; SVT, supraventricular tachycardia.

Table 2. Adherence to amiodarone guideline before and after implementation of the electronic alert system.

Adherence	Before alert (n = 110)	After alert (n = 110)	Adjusted RR (95% CI)	P-value*
Overall adherence to guideline	13 (11.8)	51 (46.4)	3.92 (2.13–7.21)	<0.001
Adherence to CXR monitoring	39 (35.5)	64 (58.2)	1.64 (1.10–2.44)	0.015
Adherence to LFT monitoring	23 (20.9)	69 (62.7)	3.00 (1.87–4.81)	<0.001
Adherence to TFT monitoring	20 (18.2)	82 (74.6)	4.10 (2.51–6.68)	<0.001

*P-value from univariable multilevel Poisson regression. Statistically significant at $P < 0.05$. CI, confidence interval; CXR, chest X-ray; LFT, liver function test; TFT, thyroid function test; RR, relative risk.

20.9% vs. 62.7% [adjusted RR 3.00 (95% CI: 1.87–4.81)], $P < 0.001$; and for thyroid function tests were 18.2% vs. 74.6% [adjusted RR 4.10 (95% CI: 2.51–6.68)], $P < 0.001$. Adherence increased significantly in every aspect, as shown in **Table 2**.

Adverse reactions suspected from amiodarone use in this study included abnormal thyroid function tests and abnormal liver function tests. Abnormal TSH levels were detected in 18.2% of patients in the pre-notification system period, whereas 23.6% were detected after notification system implementation. However, the increase in abnormal TSH detection did not reach statistical significance. There was one patient who was diagnosed with myxedema coma and two patients diagnosed with hypothyroidism, which were detected after the alert system was implemented. Only one patient from this study cohort had abnormal ALT levels attributable to amiodarone use, as shown in **Table 3**. No abnormal CXR findings were reported for patients from amiodarone use.

Discussion

The results revealed a significant increase in overall adherence to the amiodarone guideline, from 11.8% to 46.4%, after the implementation of the electronic alert system, compared with before its implementation. In addition, each component of the guideline (CXR, liver function tests, and thyroid function tests) also exhibited significant improvement. Compared with previous studies in Israel and the UK,^(9, 10) this study had LFT adherence to guidelines (before intervention) similar to that in the UK (21.0% in our study vs. 28.0% in the UK and 96.0% in Israel). For thyroid function test adherence, all three studies reported low baseline adherence rates (18.2% in our study vs. 21.0% in the UK and 56.0% in Israel). For CXR adherence, our study showed a baseline adherence of 35.0%, whereas Israel's study showed adherence of only 10.0%. Adherence varied among laboratories in each study; however, the overall adherence rate remained low.

Table 3. Adverse reaction suspected from amiodarone usage before and after implementation of the electronic alert system.

Adverse events	Before alert (n = 110)	After alert (n = 110)	Adjusted RR (95% CI)	P-value*
Abnormal CXR	0	0	–	–
Abnormal ALT	0	1 (0.9)	–	–
Abnormal TSH	20 (18.2)	26 (23.6)	1.30 (0.73–2.33)	0.378
Unstable bradycardia	0	0	–	–
Death	0	0	–	–

*Adjusted for age, sex, dose and duration of amiodarone use. ALT, alanine transaminase; CI, confidence interval; CXR, chest X-ray; RR, relative risk; TSH, thyroid stimulation hormone.

After implementation of the electronic alert system, the overall adherence rate improved significantly to 46.4%, surpassing that of the UK study, thus indicating the benefit of the electronic alert system. Although overall adherence improved markedly, the adherence rate of 46.4% remains suboptimal. We believe this may be due to clinician inertia, as doctors often perceive adverse effects as unlikely and therefore do not prioritize follow-up despite the alert system.

This study also reported adverse events from amiodarone use, revealing that some patients experienced abnormal thyroid function tests after using amiodarone (18.2% before and 23.6% after the electronic alert system implementation). Compared with a previous study, which reported 35.0% of patients developed abnormal thyroid function tests,⁽²⁾ our study had a lower incidence, possibly due to the low rate of thyroid function tests performed before the electronic alert system (18.2%). Only one patient in this study had abnormal ALT levels suspected to be attributable to amiodarone use, an incidence that is lower than that reported in previous studies, in which abnormal liver function tests were observed in approximately 15.0–50.0% of cases.⁽⁴⁾ This may be explained by the definitions used in our study, which differ from those used in previous studies, particularly for abnormal ALT levels. The low rates of liver function tests performed may also explain the low incidence. In addition, many patients in our study who were taking amiodarone received more than one medication that could cause abnormal liver function test levels; therefore, the abnormal liver function test results cannot be definitively attributed to amiodarone use. Furthermore, no abnormal CXR findings were reported in these patients. A meta-analysis reported incidences of 1.5% and 1.9% for pulmonary and visual adverse effects, respectively.⁽³⁾ The underpowering of the study may explain this result due to the low incidence of these adverse events, and some symptoms, such as cough, may have been underestimated and not recorded in the electronic medical record data.

This study has some limitations. First, not all guideline adherence parameters were included in the study, such as ophthalmological evaluation at baseline for patients with visual impairment or symptoms, pulmonary function tests with diffusing capacity of the lungs for carbon monoxide (DLCO), and high-resolution CT scans if pulmonary toxicity was suspected due to resource and data limitations. Therefore, there is room for further improvement in studies. Second, the duration of electronic alert implementation was relatively short; therefore, the results may be exaggerated due to the lack of an alert-fatigue effect. Alert fatigue occurs when an overwhelming number of alerts desensitizes individuals tasked with responding, which leads to missed or ignored alerts or delayed responses. If the duration of alert implementation is prolonged, the results of this study may change because of alert fatigue.^(13,14) Long-term monitoring of adherence rates may be required to assess this effect.

Conclusion

The electronic alert system improved overall adherence to the guideline for monitoring amiodarone side effects. This intervention has the potential to enhance patient safety by facilitating the early detection of amiodarone-related adverse effects. Thus, we encourage the implementation of an electronic alert system in hospitals, particularly in cardiology clinics, to monitor for potential amiodarone-related side effects.

Author contributions

NS, TL, and TA contributed substantially to the study's concept and design, data acquisition, literature review, and data interpretation. NS and TL contributed substantially to data acquisition. TL and TA contributed to drafting the manuscript. NS and TA edited the manuscript critically for important intellectual content. All authors approved the final version submitted for publication and take responsibility for statements made in the published article.

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Conflict of interest statement

The authors declare no conflicts of interest.

Data sharing statement

All data generated or analyzed during the present study are included in this published article. Further details are available for non-commercial purposes from the corresponding author on reasonable request.

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