



## Premedication Before Contrast-Enhanced Computed Tomography Scans : A Systematic Review

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### ABSTRACT

**Background:** The use of iodinated contrast media (ICM) in Computed tomography (CT) scan improves visualization but carries a risk of hypersensitivity and other adverse reactions. Premedication with corticosteroids and antihistamines is often recommended, though its effectiveness remains debated. **Objective:** This systematic review aimed to evaluate the efficacy of premedication in reducing adverse reactions to ICM in patients undergoing contrast-enhanced CT. **Methods:** Following PRISMA 2020 guidelines, a systematic search was conducted in PubMed, ProQuest, and ScienceDirect. Eligible studies included randomized controlled trials, cohort, and case-control studies involving premedication and reporting adverse outcomes after ICM administration. Risk of bias was assessed using the Cochrane RoB tool and Newcastle-Ottawa Scale. **Results:** Of 2675 records screened, five studies (one RCT and four cohorts; >8,000 exposures) were included. All reported a reduction in adverse reactions with premedication, though protective effects varied. Antihistamines consistently reduced recurrence of mild and late hypersensitivity reactions. Corticosteroids modestly lowered overall reaction rates but were less effective in high-risk patients compared with contrast substitution. One study showed diazepam reduced seizure incidence in glioma patients. **Conclusion:** In conclusion, Premedication reduces ICM-related adverse reactions, but its benefit depends on patient risk, prior reaction severity, and regimen used. Antihistamines are particularly effective for mild and late reactions, while contrast substitution may outperform corticosteroids in high-risk patients. **Keyword:** Adverse reactions, Computed tomography, Contrast media, Hypersensitivity, Premedication

### ABSTRAK

**Latar Belakang:** Penggunaan media kontras beryodium (ICM) dalam pemindaian tomografi terkomputasi (CT scan) meningkatkan visualisasi tetapi berisiko menyebabkan hipersensitivitas dan reaksi merugikan lainnya. Premedikasi dengan kortikosteroid dan antihistamin sering direkomendasikan, meskipun efektivitasnya masih diperdebatkan. Tujuan: Tinjauan sistematis ini bertujuan untuk mengevaluasi efikasi premedikasi dalam mengurangi reaksi merugikan terhadap ICM pada pasien yang menjalani CT scan dengan kontras. **Metode:** Mengikuti pedoman PRISMA 2020, pencarian sistematis dilakukan di PubMed, ProQuest, dan ScienceDirect. Studi yang memenuhi syarat meliputi uji coba terkontrol acak, studi kohort, dan studi kasus-kontrol yang melibatkan premedikasi dan pelaporan hasil yang merugikan setelah pemberian ICM. Risiko bias dinilai menggunakan alat Cochrane RoB dan Skala Newcastle-Ottawa. **Hasil:** Dari 2675 jurnal yang disaring, lima studi (satu RCT dan empat kohort; >8.000 paparan) diikutsertakan. Semua studi melaporkan penurunan reaksi merugikan dengan premedikasi, meskipun efek perlindungannya bervariasi. Antihistamin secara konsisten mengurangi kekambuhan reaksi hipersensitivitas ringan dan lanjut. Kortikosteroid sedikit menurunkan laju reaksi keseluruhan tetapi kurang efektif pada pasien berisiko tinggi dibandingkan dengan substitusi kontras. Satu studi menunjukkan diazepam mengurangi insiden kejang pada pasien glioma. **Kesimpulan:** Sebagai kesimpulan, premedikasi mengurangi reaksi merugikan terkait ICM, tetapi manfaatnya bergantung pada risiko pasien, tingkat keparahan reaksi sebelumnya, dan rejimen yang digunakan. Antihistamin khususnya efektif untuk reaksi ringan



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dan lanjut, sementara substitusi kontras dapat mengungguli kortikosteroid pada pasien berisiko tinggi.

**Kata Kunci:** Hipersensitivitas, Media kontras, Premedikasi, Reaksi yang tidak diinginkan, Tomografi terkomputasi

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## 1. Introduction

Computed tomography (CT) scans have become an essential diagnostic modality in modern medicine, enabling the generation of accurate cross-sectional representations of internal structures, soft tissues, and circulatory systems. In contrast to traditional radiography, CT obviates image superimposition and delivers enhanced spatial and contrast resolution, thereby enabling precise anatomical delineation and the timely identification of pathological alterations. CT's diagnostic reach has extended into numerous clinical disciplines, including oncology, cardiology, neurology, and emergency medicine, where rapid and exact imaging plays a vital role in effective patient management and sound therapeutic decisions.<sup>[1]</sup>

The diagnostic proficiency of computed tomography (CT) is considerably augmented via the utilization of iodinated contrast media (ICM), which enables the characterization of both vascular and parenchymal structures through the alteration of X-ray attenuation attributes. As such, the occurrence of contrast-enhanced computed tomography has markedly surged on a global scale, alongside the enhanced accessibility of sophisticated multidetector CT technologies.<sup>[2]</sup> Nevertheless, the broader implementation of ICM has inevitably led to an escalation in the incidence of contrast-associated adverse events. While the majority of these reactions are benign and self-resolving, a fraction of patients may encounter moderate to severe hypersensitivity reactions that could be clinically significant or even pose a threat to life.<sup>[3]</sup>

The adverse reaction related to iodine-containing media (ICM) can be grouped into three tiers, namely mild, moderate, and severe, which are assessed through the clinical indicators shown by the patient. Transitory occurrences of warmth, pruritus, or nausea are classified as mild reactions, as opposed to moderate reactions that may present more concerning symptoms such as urticaria or bronchospasm. Uncommon but noteworthy responses may present as hypotension, swelling in the throat area, or anaphylaxis, thus requiring rapid medical assistance. The key pathophysiological principles behind ICM reactions unify immunological and non-immunological dimensions. Immediate hypersensitivity manifestations may be influenced by immunoglobulin E (IgE), especially in acute situations, while responses deemed mild to moderate are typically non-allergic in essence.<sup>[4,5]</sup>

Premedication utilizing corticosteroids and antihistamines has been systematically integrated into clinical protocols to diminish the risk of recurrent adverse reactions or breakthrough reactions in individuals with a documented history of iodinated contrast media hypersensitivity.<sup>[6]</sup> Usual therapeutic strategies consist of administering corticosteroids multiple times, including drugs like prednisone or methylprednisolone, in tandem with antihistamines at designated intervals before encountering contrast agents. The key purpose behind premedication is to alleviate the inflammatory and allergic components of the hypersensitivity response, subsequently minimizing the risk and seriousness of negative events.<sup>[7]</sup> Even so, the actual medical usefulness of these preventive strategies remains a controversial point. Numerous studies have indicated a reduction in the recurrence of hypersensitivity incidents subsequent to premedication, whereas others have exhibited negligible or no appreciable advantage. Additionally, the finding of considerable responses generates increased uncertainty about the success of contemporary protocols. In light of the escalating global dependence on contrast-enhanced computed tomography (CT) examinations and the potential ramifications of premedication on patient safety, operational efficiency, and healthcare expenditure, an in-depth evaluation of its genuine effectiveness is imperative. Consequently, this systematic review aims to thoroughly evaluate the efficacy of premedication in averting adverse reactions to iodinated contrast media in patients undergoing contrast-enhanced CT.

## 2. Method

This systematic review was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>[8]</sup> The inclusion and exclusion criteria were formulated based on the Population, Intervention, Comparison, and Outcome (PICO) framework, as summarized in Table 1. These criteria were subsequently applied during the study selection and screening process. A comprehensive

systematic search was performed to identify randomized controlled trials (RCTs), clinical trials, cohort studies, and case–control studies. Eligible studies met the following criteria: patients who underwent contrast-enhanced computed tomography (CT); administration of premedication prior to contrast exposure; and documentation of adverse outcomes following contrast-enhanced CT. No restrictions were placed on the year of publication. Studies were excluded if they were written in languages other than English, lacked available full text, or involved non-human subjects.

Table 1. PICO framework.

Components of PICO	Description
Population	Contrast-enhanced CT scan patients
Intervention	Administration of premedication
Comparison	Patient without premedication
Outcome	Adverse reaction after contrast administration

### 2.1 Literature search and screening

A systematic search was conducted on August 15, 2025 in three electronic databases: PubMed, ProQuest, and ScienceDirect. The search strategy combined keywords and Medical Subject Headings (MeSH) related to “computed tomography,” “contrast media,” and “premedication”. We exported the studies retrieved from database searches into Rayyan online web application for duplicate removal and screening.<sup>[9]</sup> Studies were screened by their titles and abstracts, followed by full-text review of potentially eligible articles. Any disagreements between authors were resolved by discussion with all authors until consensus was reached.

### 2.2 Risk of Bias Assessment

The methodological quality and risk of bias of included studies were assessed using the Cochrane risk of bias (RoB) tool for randomized trials (RCT), and Newcastle-Ottawa Scale (NOS) for case control and cohort studies.<sup>[10,11]</sup> Any disagreement was resolved by discussion until consensus was reached.

### 2.3 Data Extraction

Data were extracted from eligible studies using a data extraction form. The following information was extracted: first authors’ names and publication year, study design, country of origin, sample size, type of contrast media, type of premedication, adverse outcomes and relevant findings.

## 3. Result

### 3.1 Study Selection

Our systematic literature search initially identified 2675 records. After duplicate removal, followed by screening of titles and abstracts, 2576 irrelevant articles were excluded, leaving 99 articles for full-text review. Full text of two studies cannot be retrieved, thus they were not included in full-text review. Ninety five studies were excluded after full text review, with the reason comprising of wrong publication type (reviews, case reports), wrong study design, no premedication used and no contrast used. Screening of studies were described in the PRISMA flow diagram (Figure 1). Ultimately, after full-text review, five studies (one RCT and four cohort studies) consisting of studies by Park *et al.*, Kang *et al.*, McDonald *et al.*, Pagani *et al.*, Lasser *et al.*<sup>[12-16]</sup> were selected for detailed analysis and synthesis. The selected studies was published from 1984 until 2021. Quality assessment using the RoB and NOS tool indicated that all five studies were of high methodological quality, with none rated as low quality.

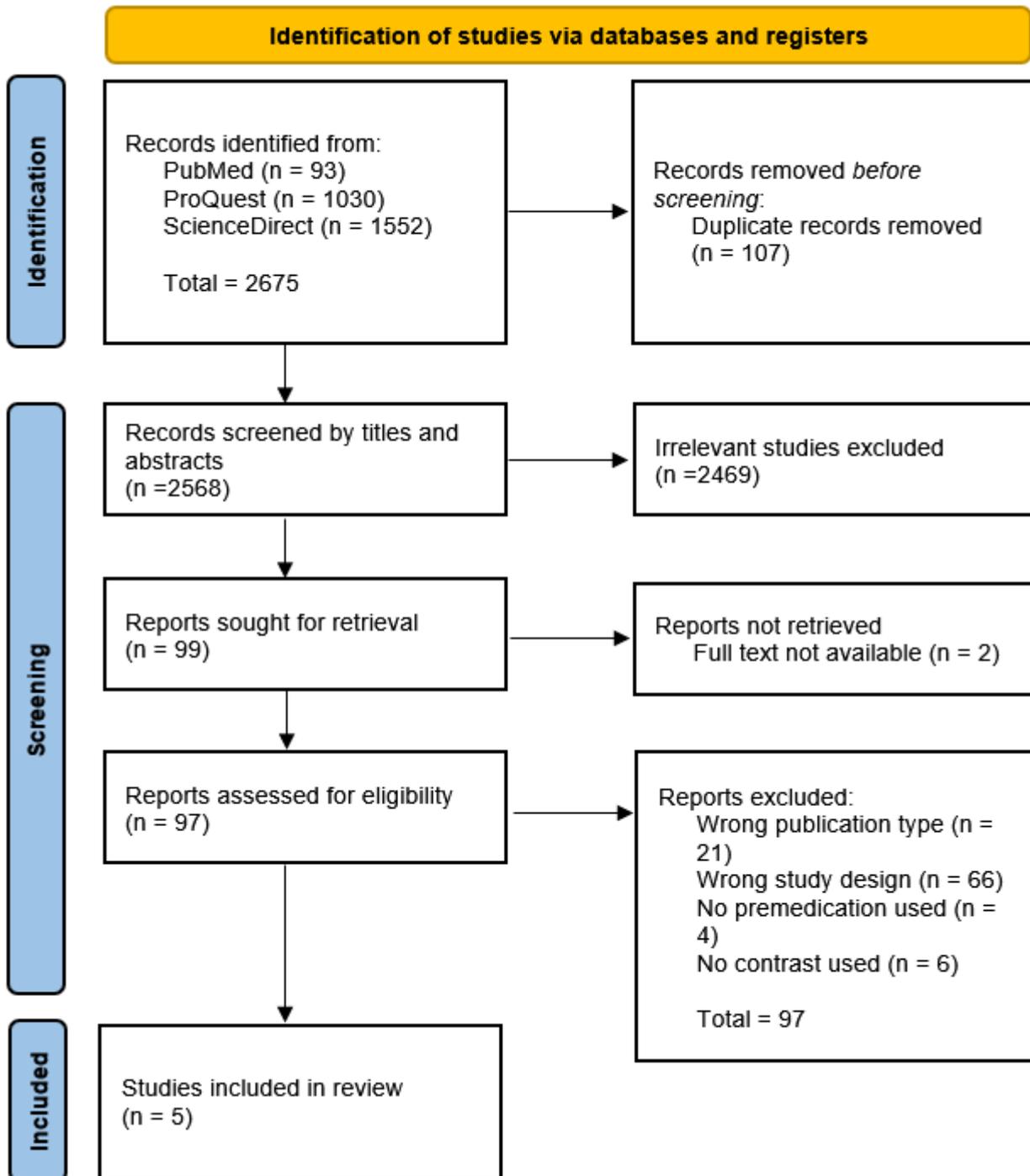


Figure 1. The PRISMA flow diagram of the literature search.

### 3.2 Study Characteristics

The included studies only came from two countries, which was the United States and South Korea, with over 8000 exposures to contrast-enhanced CT scans. Two studies involved high-risk patients who had a previous history of contrast-related adverse effects. Iodine-based contrast media were used in all of the studies, with four studies using low-osmolarity contrast media and one using high-osmolarity contrast media. Premedications used were steroids in 3 studies, antihistamines in 3 studies, and diazepam in one study. The characteristics of the included studies are presented in Table 2.

3.3 The Effect of Premedication on Adverse Effects

All five studies consistently demonstrated that administration of premedication was associated with a reduced incidence of adverse effects compared with no prophylaxis, though the degree of protection varied. The resulting adverse effects ranged from mild (e.g. hives, sneezing, etc.) to severe (e.g. anaphylaxis, seizure, etc.) The results are shown in Table 2

Table 2. Characteristics of the included studies

No	Authors, years of publication	Study design	Country	Sample size	Population	Contrast Agent	Type of premedication	Adverse effect rate
1	Park et al., 2018	Cohort retrospective	South Korea	1178 patient, 2388 contrast exposure	Patients who had previous history of mild HSR	Iobitridol, iohexol, iomeperol, iopamidol, iopromide, ioversol	4 mg of IV chlorpheniramine	Same contrast media, Without premedication: 85/273 (31.1%) With premedication: 107/441 (24.3%) (p=0.015) Different contrast media, Without premedication 105/872 (12%) 148/1947 (7.6%) (p=0.001)
2	Kang et al., 2021	Cohort prospective	South Korea	272 contrast exposure	Patients who underwent contrast-enhanced CT CT	Iobitridol, iohexol, iomeprol, iopamidol, iopromide, ioversol	Antihistamine (equivalent to 4 mg of chlorpheniramine) and/or steroids (equivalent to 40 mg of methylprednisolone)	Without premedication: 8/94 (8.5%) With premedication: 3/178 (1.7%) (p = 0.016)
3	McDonald et al 2021	Cohort retrospective	United States	1973 patients, 4360 contrast exposure	Adult and pediatric patients with previous allergic-like reaction to ICM, who underwent a contrast-enhanced	Iohexol, iopromide, iodixanol	Two oral doses of 32 mg of methylprednisolone at 12 and 2 hours before CT scan, with or without antihistamines	Same contrast media, Without premedication: 111/745 (15%)

					ced CT examination			With premedication: 80/423 (19%)
								Different contrast media, Without premedication: 10/322 (3%)
4	Pagani et al 1984	Cohort prospective	United States	169 patients	Patients with glioma who underwent contrast-enhanced CT	Meglumine diatrizoate	5 mg of IV diazepam	With premedication: 5/166 (3%) Without premedication: 14/86 (16%)
5	Lasser et al 1993	Randomized controlled trial	United States	1115 patients	Patients who underwent contrast-enhanced CT	Iohexol, ioversol	Two, 32 mg oral dose of methylprednisolone	With premedication: 2/83 (2%) Without premedication: 28/575 (5%) With premedication: 10/580 (2%) (p = 0.005)

CT: computed tomography; HSR: hypersensitivity reaction; ICM: iodinated contrast media; IV: intravenous

#### 4. Discussion

This systematic review consolidates current evidence on the use of premedication to reduce adverse reactions to iodinated contrast media. Across the included studies, a protective effect of premedication was observed, although the magnitude of benefit was heterogeneous and strongly dependent on the prophylactic regimen and the clinical setting.

Antihistamines demonstrated the most consistent benefit, particularly in patients with a history of mild or late reactions. Park *et al.* showed that the recurrence of immediate hypersensitivity reactions was markedly reduced when antihistamines were administered alongside contrast substitution.<sup>[12]</sup> While Kang *et al.* confirmed that antihistamines also reduced the incidence of late-onset reactions following low-osmolar contrast administration, although in their study, corticosteroid is also used and this may participate in the reduction of allergic reactions.<sup>[13]</sup> Antihistamines works by inhibiting H<sub>1</sub> receptor, thereby inhibiting allergic-inflammatory process. In contrast, corticosteroids work upstream the inflammatory pathway, by repressing the expression of pro-inflammatory genes and activating the expression of anti-inflammatory genes. This action of corticosteroid on genes may produce an effect in latter inhibition of inflammation.<sup>[13, 17]</sup> These findings support the central role of histamine-mediated pathways in both immediate and delayed reactions, corroborating earlier reports that histamine is the primary mediator of most contrast-induced urticarial and pruritic responses.<sup>[13]</sup> Other studies similarly concluded that antihistamines are useful for preventing mild, pruritic, or urticarial reactions in patients with previous contrast-related events.<sup>[18]</sup>

Corticosteroid premedication, by contrast, has produced mixed results. Lasser *et al.* demonstrated in a randomised controlled trial that an oral two-dose of 32 mg of methylprednisolone regimen significantly

lowered overall reaction rates, particularly for mild events.<sup>[14]</sup> However, later observational studies conducted in the era of low-osmolar agents, such as McDonald *et al.*, did not reproduce this protective effect, reporting similar rates of breakthrough reactions between patients who received corticosteroid premedication and those who did not.<sup>[15]</sup> This discrepancy may be explained by differences in contrast agent osmolality. High-osmolar contrast media, which were predominant when early trials were performed, carried substantially higher baseline risks of hypersensitivity and chemotoxic reactions.<sup>[19]</sup> As low-osmolar and nonionic agents have become standard, the relative contribution of corticosteroids has diminished, with some data suggesting that their benefit is marginal at best in modern practice.<sup>[13]</sup> Moreover, the requirement for prolonged premedication protocols creates logistical barriers in urgent imaging situations and introduces potential adverse effects from systemic corticosteroid use.<sup>[20]</sup>

Contrast substitution consistently emerges as a more effective preventive strategy in high-risk patients. Both Park *et al.* and McDonald *et al.* demonstrated that switching to a structurally distinct low-osmolar agent markedly reduced recurrence rates compared with re-exposure to the culprit medium, even with premedication.<sup>[12,15]</sup> These findings align with the broader literature showing that cross-reactivity among iodinated contrast agents is often structure-dependent, and that switching to a chemically dissimilar agent lowers the risk of recurrence.<sup>[21]</sup> Nevertheless, complete protection is not guaranteed, and certain substitutions have still been associated with breakthrough events, indicating the need for allergy evaluation and individualised contrast selection.

An additional dimension is highlighted by the work of Pagani *et al.*, who examined glioma patients at risk of contrast-induced seizures. Their study demonstrated that diazepam prophylaxis significantly reduced seizure incidence compared with controls.<sup>[16]</sup> Although mechanistically distinct from hypersensitivity reactions, this evidence underlines the principle that premedication should be tailored to the specific adverse effect profile relevant to each patient group. It also illustrates that preventive strategies may extend beyond immune-mediated mechanisms and must address the wider spectrum of potential contrast-related complications.

Overall, the available data suggest that premedication provides measurable benefit in selected contexts but should not be applied indiscriminately. Antihistamines are clearly effective for immediate and delayed mild hypersensitivity reactions. Corticosteroids may still be considered in some settings but appear to offer limited additional benefit when low-osmolar agents are used, and their role may be eclipsed by contrast substitution in high-risk populations. In specialised groups, such as patients with gliomas, targeted prophylaxis such as diazepam remains appropriate. Future research should prioritise multicentre randomised trials that directly compare these strategies, incorporate well-defined risk stratification, and adopt standardised outcome measures to improve comparability across studies.

In our study, there are limitations that should be acknowledged. First, the number of eligible studies was small, and the included studies varied in design, population, and premedication regimens, limiting direct comparability. Second, most studies were observational, with only one randomized controlled trial available, which may introduce bias and confounding. Third, all data were derived from only the United States and South Korea, potentially limiting global applicability. Finally, some studies had relatively small sample sizes for specific subgroups, reducing statistical power to detect differences in rare but severe reactions.

## 5. Conclusion

Premedications can reduce the risk of adverse reactions to iodinated contrast media in patients undergoing contrast-enhanced CT, although the degree of protection depends on the regimen and clinical context. Antihistamines demonstrated consistent benefit in patients with prior mild or late reactions, while corticosteroids were modestly effective in reducing overall incidence, particularly for mild reactions. Contrast substitution appeared more protective than steroid premedication alone in high-risk patients. In specific subgroups, such as glioma patients, diazepam showed efficacy in preventing contrast-induced seizures. Collectively, these findings suggest that no single protocol is universally effective, and premedication strategies should be individualized based on patient risk profile, severity of prior reaction, and feasibility of contrast substitution.

## Artificial Intelligence (AI) Use

The authors used Grammarly AI to perform an English grammar check during the manuscript writing process.

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