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Effect of Low-Dose Colchicine on Inflammatory Markers Post-Myocardial Infarction: A Randomized Controlled Trial

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ABS TRAC T

Background: Myocardial infarction (MI) triggers a profound systemic and localised inflammatory response that contributes to adverse left ventricular remodelling and increased risk of recurrent cardiovascular events. Colchicine, a well-established anti-inflammatory agent with a pleiotropic mechanistic profile, has emerged as a promising adjunctive therapy in the post-MI setting. This randomized controlled trial evaluated the effect of low-dose colchicine on serial inflammatory biomarkers and cardiac functional parameters in patients with acute MI in an Egyptian tertiary care population. ***Methods:*** A prospective, double-blind, placebo-controlled, randomized trial was conducted at Badr University Faculty, Egypt. One hundred and twenty patients with acute MI (STEMI or NSTEMI) were randomized 1:1 to receive colchicine 0.5 mg twice daily for 30 days (n=60) or matching placebo (n=60), commencing within 24 hours of hospital admission, in addition to standard guideline-directed medical therapy. The primary outcome was the change in high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and tumour necrosis factor-alpha (TNF-α) at 72 hours and 30 days from baseline. Secondary outcomes included left ventricular ejection fraction, pericardial effusion, post-MI pericarditis, and major adverse cardiovascular events (MACE) at 30 days. Safety and tolerability were systematically assessed. ***Results:*** Both groups were well matched at baseline. At 72 hours, hs-CRP was significantly lower in the colchicine group compared with placebo (9.1 ± 3.8 vs 15.6 ± 5.4 mg/L; p<0.001). Reductions in IL-6 (21.4 ± 8.3 vs 36.9 ± 12.6 pg/mL; p<0.001), IL-1β (4.2 ± 1.8 vs 7.6 ± 2.9 pg/mL; p<0.001), and TNF-α (14.3 ± 5.4 vs 21.8 ± 7.7 pg/mL; p<0.001) were similarly significant. At 30 days, colchicine maintained markedly lower levels of all inflammatory markers compared with placebo (all p<0.001). LVEF at 30 days was significantly higher in the colchicine group (52.7 ± 6.4% vs 49.4 ± 7.1%; p=0.038). Post-MI pericarditis was significantly less frequent with colchicine (3.3% vs 13.3%; p=0.041). Gastrointestinal adverse events were numerically more frequent in the colchicine group (23.3% vs 10.0%; p=0.058), though not statistically significant. ***Conclusion:*** Low-dose colchicine administered within 24 hours of acute MI significantly attenuated the post-infarction inflammatory cascade across multiple biomarker axes at both 72 hours and 30 days, with a concomitant improvement in left ventricular systolic function and a significant reduction in post-MI pericarditis. These findings support the adjunctive use of colchicine in the early post-MI period and contribute further evidence to the growing body of research establishing the central role of inflammation in post-MI pathophysiology.

Keywords: *Colchicine, Myocardial Infarction, Inflammation, hs-CRP, Interleukin-6, IL-1β, TNF-α, Randomized Controlled Trial, Post-MI, Egypt.*

INTRODUCTION

Acute myocardial infarction (AMI), resulting from the rupture or erosion of an atherosclerotic coronary plaque with superimposed thrombotic occlusion and consequent myocardial ischaemia and necrosis, constitutes one of the leading causes of morbidity and mortality worldwide. Despite transformative advances in reperfusion therapy — including primary percutaneous coronary intervention (PCI) and pharmacological thrombolysis — and in

secondary prevention pharmacotherapy, a substantial residual burden of post-MI adverse events persists, driven in part by processes extending beyond the initial ischaemic insult [1]. It is now well established that the inflammatory response triggered by MI, rather than representing a purely reparative phenomenon, exerts maladaptive effects on the infarcted and peri-infarct myocardium that promote pathological left ventricular remodelling, infarct expansion, and vulnerability to recurrent ischaemic events.

The inflammatory cascade activated in the immediate post-MI period involves a coordinated activation of the innate immune system, with rapid recruitment of neutrophils and monocytes to the ischaemic zone, elaboration of pro-inflammatory cytokines including interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α), and upregulation of acute-phase reactants — most notably high-sensitivity C-reactive protein (hs-CRP) — in the systemic circulation [2]. The NLRP3 (NOD-like receptor protein 3) inflammasome, a cytosolic multiprotein complex activated by danger-associated molecular patterns released from necrotic cardiomyocytes, serves as the proximate driver of IL-1β and IL-18 maturation, establishing a self-amplifying inflammatory loop that propagates well beyond the initial ischaemic event [3]. Elevated circulating levels of hs-CRP, IL-6, and IL-1β in the post-MI setting are consistently associated with increased infarct size, adverse LV remodelling, higher incidence of heart failure, and elevated long-term cardiovascular mortality — providing the mechanistic rationale for targeting the post-MI inflammatory response as a therapeutic strategy.

Colchicine, an alkaloid derived from Colchicum autumnale with centuries of clinical use in gout and pericardial disease, exerts its anti-inflammatory effects through multiple mechanistic pathways particularly relevant to the post-MI milieu. Its primary mechanism involves disruption of microtubule polymerisation via tubulin binding, impairing neutrophil chemotaxis, adhesion, and superoxide generation [4]. Beyond this, colchicine potently inhibits NLRP3 inflammasome assembly and activation, thereby suppressing IL-1β and IL-18 release, and attenuates NF-kB signalling, endothelial adhesion molecule expression, and inflammasome-independent inflammatory amplification pathways. The low-dose regimen of 0.5 mg twice daily — now validated across cardiovascular trials — achieves these anti-inflammatory effects with an acceptable gastrointestinal tolerability profile that significantly improves upon the higher doses historically employed in rheumatological practice.

Clinical evidence for colchicine's cardiovascular benefit has accumulated substantially over the past decade. The COPE (Colchicine for acute PEricarditis) and ICAP (Investigation on Colchicine for Acute Pericarditis) trials established its efficacy in reducing recurrence of acute and recurrent pericarditis [5]. More recently, the landmark COLCOT (Colchicine Cardiovascular Outcomes Trial) randomized 4,745 patients with recent MI to colchicine 0.5 mg daily or placebo and demonstrated a 23% relative risk reduction in the composite of cardiovascular death, resuscitated cardiac arrest, MI, stroke, and urgent coronary revascularisation (HR 0.77; 95% CI 0.61–0.96; p=0.02) over a median follow-up of 22.6 months [6]. The LoDoCo2 (Low-Dose Colchicine 2) trial subsequently demonstrated a 31% relative risk reduction in MACE among patients with stable coronary artery disease over a median of 28.6 months, further consolidating colchicine's position as an evidence-based anti-inflammatory adjunct to standard secondary prevention pharmacotherapy [7].

Despite this evolving evidence base, the precise temporal kinetics of colchicine's anti-inflammatory effects — specifically its impact on the rapid early post-MI inflammatory surge as quantified by serial multiplex cytokine profiling — remain incompletely characterised. Existing pharmacodynamic data are predominantly derived from European and North American trial populations, and data from Middle Eastern and North African (MENA) populations, including Egypt, where cardiovascular risk factor profiles, dietary patterns, genetic backgrounds, and concomitant medication exposures may differ from Western cohorts, remain limited [8]. Furthermore, whether the colchicine-mediated attenuation of the early inflammatory response translates into measurable improvements in left ventricular function and a reduction in post-MI inflammatory complications — including post-MI pericarditis, a clinically significant and frequently underdiagnosed complication — within the 30-day post-infarction window requires further prospective evaluation.

Egypt, as the most populous nation in the Arab world and a country experiencing a significant and growing burden of cardiovascular disease — with ischaemic heart disease constituting the leading cause of mortality nationally — represents an important and underrepresented setting for cardiovascular clinical research [9]. The present randomized controlled trial was therefore designed to evaluate the effect of low-dose colchicine, initiated within 24 hours of acute MI, on serial inflammatory biomarkers including hs-CRP, IL-6, IL-1β, and TNF-α at 72 hours and 30 days, cardiac functional parameters, and early clinical outcomes, in Egyptian patients receiving standard post-MI care. The results are intended to contribute locally relevant pharmacodynamic and outcomes data to the growing international evidence base supporting colchicine's use in the post-MI setting [10].

AIMS AND OBJECTIVES

The primary aim of this randomized controlled trial was to evaluate the effect of adjunctive low-dose colchicine (0.5 mg twice daily for 30 days), administered within 24 hours of acute myocardial infarction, on serial circulating inflammatory biomarkers — specifically high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and tumour necrosis factor-alpha (TNF-α) — at 72 hours and 30 days from randomization, in comparison with matching placebo, in Egyptian patients receiving guideline-directed standard post-MI therapy.

The secondary objectives were to compare erythrocyte sedimentation rate (ESR) and white blood cell count between the two groups at 72 hours and 30 days; to evaluate the between-group difference in left ventricular ejection fraction, left ventricular end-diastolic and end-systolic diameters, diastolic function parameters, and pericardial effusion at 30 days by transthoracic echocardiography; to determine the incidence of post-MI pericarditis and new-onset atrial fibrillation; to assess major adverse cardiovascular events (MACE) — defined as the composite of all-cause mortality, recurrent MI, unplanned coronary revascularisation, and hospitalisation for heart failure — at 30 days; and to systematically document the safety profile, gastrointestinal tolerability, and drug discontinuation rates associated with low-dose colchicine in this population.

MATERIALS AND METHODS

Study Design and Setting

This investigation was conducted as a prospective, randomized, double-blind, placebo-controlled trial at the Department of Cardiology, Badr University,Cairo, Egypt, from Aug 2022 to July 2023. The study was conducted in accordance with the principles of the Declaration of Helsinki and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines. Ethical approval was obtained from the Institutional Review Board. The trial was registered with ClinicalTrials.gov prior to participant enrolment. All participants provided written informed consent prior to randomization.

Sample Size

Sample size was calculated based on the primary endpoint of reduction in hs-CRP at 72 hours. Referencing prior pharmacodynamic data, a mean hs-CRP of 18 mg/L was expected at 72 hours in the placebo group, with a clinically meaningful difference of 6 mg/L in the colchicine group (SD 8 mg/L), corresponding to an effect size of 0.75. Using a two-sided alpha of 0.05 and a power of 80%, a minimum of 46 patients per group was required. Inflating for a 25% attrition and non-evaluability rate, 60 patients per group (total n=120) were enrolled.

Randomization and Blinding

Eligible patients were randomized in a 1:1 ratio using a computer-generated block randomization sequence (block size 4), stratified by MI type (STEMI vs NSTEMI) and diabetes mellitus status. The allocation sequence was concealed in sequentially numbered, sealed, opaque envelopes prepared by an independent statistician not involved in patient care or outcome assessment. Colchicine tablets (0.5 mg) and matching placebo tablets were prepared by the hospital pharmacy and were identical in appearance, size, and packaging. Both participants and all clinical personnel directly involved in patient assessment and outcome adjudication were blinded to treatment allocation throughout the study period. Unblinding was permitted only in the event of a suspected serious adverse event directly attributable to the study drug and requiring immediate clinical management.

Inclusion Criteria

Adult patients aged 18 to 70 years admitted with a confirmed diagnosis of acute myocardial infarction — either STEMI (based on symptoms of ischaemia with new ST-elevation or new left bundle branch block and elevated cardiac troponin) or NSTEMI (elevated cardiac troponin with ischaemic ECG changes in the absence of ST-elevation) — who were commenced on standard guideline-directed medical therapy and who were able to provide informed consent within 24 hours of symptom onset were eligible for enrolment.

Exclusion Criteria

Patients were excluded if they had known hypersensitivity to colchicine or prior adverse reaction, current use of colchicine for any indication, severe renal impairment (eGFR <30 mL/min/1.73 m^2), severe hepatic impairment (Child-Pugh Class B or C), known haematological dyscrasias, active infectious disease or sepsis at presentation, concurrent use of potent P-glycoprotein or CYP3A4 inhibitors (such as clarithromycin, ketoconazole, or cyclosporin), prior cardiac surgery within 90 days, inflammatory bowel disease, pregnancy or lactation, cardiogenic shock, or anticipated inability to maintain 30-day follow-up. Patients already receiving corticosteroids or other systemic anti-inflammatory agents were also excluded.

Treatment Protocol

Patients in the colchicine group received colchicine 0.5 mg twice daily orally, commenced within 24 hours of confirmed MI diagnosis and continued for 30 days. To minimise gastrointestinal adverse events, patients were instructed to take colchicine with food. Patients in the placebo group received an identical-appearing placebo tablet twice daily for 30 days. Both groups received standard post-MI pharmacotherapy in accordance with contemporary ACC/AHA and ESC guidelines, including dual antiplatelet therapy, high-intensity statin, beta-blocker, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and mineralocorticoid receptor antagonist where indicated.

Reperfusion therapy (primary PCI or pharmacological thrombolysis) was performed where clinically appropriate.

Blood Sampling and Laboratory Analysis

Venous blood samples were collected at three time points: at baseline (prior to study drug administration), at 72 hours post-randomization, and at 30 days. Serum hs-CRP was measured by turbidimetric immunoassay (Abbott Architect ci4100). Plasma IL-6, IL-1β, and TNF-α concentrations were quantified using enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, USA) by laboratory personnel blinded to treatment allocation. Erythrocyte sedimentation rate (ESR) was measured by the Westergren method. Complete blood count, serum creatinine, liver enzymes, and creatine kinase were measured using standard autoanalyser methods. Peak troponin I was measured at the time of presentation using a high-sensitivity assay.

Echocardiographic Assessment

Transthoracic echocardiography was performed at baseline and at 30 days by a single cardiologist blinded to treatment allocation using a Phillips CX50 portable echocardiography system with a 2–4 MHz phased-array transducer. Left ventricular ejection fraction was measured by the biplane Simpson method in the apical four-chamber and two-chamber views. LV end-diastolic and end-systolic diameters were measured from the parasternal long-axis view. Diastolic function was evaluated by the E/e' ratio using pulsed-wave tissue Doppler imaging at the medial mitral annulus. Regional wall motion abnormalities (RWMA) were assessed in the standard 17-segment model. The presence and size of pericardial effusion were documented. All echocardiographic measurements were averaged over three cardiac cycles in sinus rhythm or five cycles in the presence of atrial fibrillation.

Outcome Definitions

The primary outcome was the change from baseline in serum hs-CRP, IL-6, IL-1β, and TNF-α at 72 hours and 30 days, compared between treatment groups. MACE was defined as the composite of all-cause mortality, recurrent MI (confirmed by ECG changes and troponin re-elevation), unplanned coronary revascularisation, and hospitalisation for acute decompensated heart failure at 30 days. Post-MI pericarditis was diagnosed based on the presence of pleuritic chest pain with pericardial rub, new or worsening pericardial effusion on echocardiography, and/or ST-segment changes consistent with pericarditis on ECG, occurring within 30 days of the index MI. All clinical events were adjudicated by an independent clinical events committee blinded to treatment allocation.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 27.0. Continuous variables were assessed for normality by the Shapiro-Wilk test and expressed as mean ± SD or median (IQR) as appropriate. Categorical variables were presented as frequencies and percentages. Between-group comparisons of continuous variables at each time point were performed using the independent samples t-test or Mann-Whitney U test. Within-group changes from baseline to each time point were assessed by paired t-test or Wilcoxon signed-rank test. Analysis of covariance (ANCOVA) was used to compare 30-day endpoint values between groups with baseline values as the covariate. Categorical variables were compared by Chi-square or Fisher's exact test. The primary efficacy analysis was conducted on an intention-to-treat (ITT) basis, with sensitivity analysis using per-protocol population. Odds ratios with 95% confidence intervals were calculated for binary outcomes. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Participant Flow and Baseline Characteristics

A total of 148 patients were screened for eligibility, of whom 120 were randomized — 60 to the colchicine group and 60 to the placebo group. The most common reasons for exclusion were severe renal impairment (n=11), active infection (n=7), and use of excluded concomitant medications (n=6). Four patients (2 in each group) were lost to follow-up prior to the 30-day endpoint and were included in the ITT analysis using the last observation carried forward. No interim stopping criteria were triggered during the trial. Baseline demographic, clinical, and laboratory characteristics were well matched between the two groups and are summarised in Table 1. The mean age was 57.2 ± 9.4 years in the colchicine group and 58.1 ± 9.8 years in the placebo group (p=0.591). STEMI constituted 63.3% and 60.0% of index presentations respectively (p=0.704). Baseline LVEF was comparable (48.3 ± 7.1% vs 47.8 ± 7.4%; p=0.709), and reperfusion therapy was administered in over 90% of patients in both groups.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Colchicine Group (n=60)	Placebo Group (n=60)	p-value
Age (years), Mean ± SD	57.2 ± 9.4	58.1 ± 9.8	0.591
Male sex, n (%)	44 (73.3%)	42 (70.0%)	0.681
BMI (kg/m²), Mean ± SD	27.8 ± 3.6	28.1 ± 3.9	0.649
Diabetes mellitus, n (%)	24 (40.0%)	26 (43.3%)	0.706
Hypertension, n (%)	36 (60.0%)	34 (56.7%)	0.703
Dyslipidaemia, n (%)	31 (51.7%)	29 (48.3%)	0.707

Current smoker, n (%)	22 (36.7%)	24 (40.0%)	0.700
Prior MI, n (%)	8 (13.3%)	9 (15.0%)	0.790
STEMI, n (%)	38 (63.3%)	36 (60.0%)	0.704
NSTEMI, n (%)	22 (36.7%)	24 (40.0%)	0.704
LVEF at baseline (%), Mean ± SD	48.3 ± 7.1	47.8 ± 7.4	0.709
Reperfusion therapy (PCI/thrombolysis), n (%)	56 (93.3%)	55 (91.7%)	0.720

Primary Outcome: Inflammatory Biomarkers at 72 Hours and 30 Days

The evolution of inflammatory biomarkers at baseline, 72 hours, and 30 days is presented in Tables 2 and 3. At 72 hours, hs-CRP was significantly lower in the colchicine group compared with placebo (9.1 ± 3.8 vs 15.6 ± 5.4 mg/L; p<0.001), representing a 41.4% greater reduction from baseline in the colchicine group relative to 12.8% in the placebo group. IL-6 levels at 72 hours were significantly attenuated in the colchicine arm (21.4 ± 8.3 vs 36.9 ± 12.6 pg/mL; p<0.001), as were IL-1β concentrations (4.2 ± 1.8 vs 7.6 ± 2.9 pg/mL; p<0.001) and TNF-α (14.3 ± 5.4 vs 21.8 ± 7.7 pg/mL; p<0.001). ESR and WBC count were likewise significantly lower in the colchicine group at 72 hours (p<0.001 and p=0.003 respectively). Baseline values of all inflammatory markers were comparable between the two groups (all p>0.05).

Table 2: Inflammatory Biomarkers at Baseline and 72 Hours

Biomarker	Colchicine Baseline	Colchicine 72 hours	Placebo Baseline	Placebo 72 hours	p-value (72 h)
hs-CRP (mg/L), Mean ± SD	18.4 ± 6.2	9.1 ± 3.8*	17.9 ± 6.5	15.6 ± 5.4	<0.001
IL-6 (pg/mL), Mean ± SD	42.3 ± 14.7	21.4 ± 8.3*	41.8 ± 15.1	36.9 ± 12.6	<0.001
IL-1β (pg/mL), Mean ± SD	8.7 ± 3.1	4.2 ± 1.8*	8.4 ± 3.3	7.6 ± 2.9	<0.001
TNF-α (pg/mL), Mean ± SD	24.6 ± 8.8	14.3 ± 5.4*	24.1 ± 9.2	21.8 ± 7.7	<0.001
ESR (mm/hr), Mean ± SD	48.2 ± 14.3	29.4 ± 10.1*	47.6 ± 15.1	42.3 ± 13.6	<0.001
WBC count (x10⁹/L), Mean ± SD	11.8 ± 2.9	8.2 ± 2.1*	11.6 ± 3.1	10.4 ± 2.7	0.003
* p<0.05 vs baseline within group; p-value column = between-group comparison at 72 h					

At 30 days, colchicine maintained a substantially greater suppression of all inflammatory indices compared with placebo (Table 3). Mean hs-CRP was 3.2 ± 1.6 mg/L in the colchicine group versus 8.4 ± 3.2 mg/L in the placebo group (mean difference −5.2, 95% CI −6.1 to −4.3; p<0.001). IL-6 remained significantly lower (11.3 ± 4.8 vs 24.7 ± 9.3 pg/mL; mean difference −13.4, 95% CI −15.9 to −10.9; p<0.001). IL-1β and TNF-α differences were similarly highly significant (p<0.001 for both), confirming sustained inflammasome suppression throughout the 30-day treatment period. ESR and WBC count were also significantly lower in the colchicine group at 30 days (p<0.001 for both).

Table 3: Inflammatory Biomarkers at 30 Days

Biomarker	Colchicine 30 days	Placebo 30 days	Mean Difference (95% CI)	p-value
hs-CRP (mg/L)	3.2 ± 1.6	8.4 ± 3.2	−5.2 (−6.1 to −4.3)	<0.001*
IL-6 (pg/mL)	11.3 ± 4.8	24.7 ± 9.3	−13.4 (−15.9 to −10.9)	<0.001*
IL-1β (pg/mL)	2.1 ± 0.9	5.3 ± 2.1	−3.2 (−3.8 to −2.6)	<0.001*
TNF-α (pg/mL)	8.6 ± 3.4	16.2 ± 6.1	−7.6 (−9.3 to −5.9)	<0.001*
ESR (mm/hr)	18.3 ± 7.2	31.4 ± 10.8	−13.1 (−16.2 to −10.0)	<0.001*
WBC count (x10⁹/L)	7.1 ± 1.8	8.9 ± 2.4	−1.8 (−2.5 to −1.1)	<0.001*

Cardiac Functional Parameters

Echocardiographic parameters at baseline and 30 days are presented in Table 4. After adjustment for baseline values using ANCOVA, LVEF at 30 days was significantly higher in the colchicine group (52.7 ± 6.4% vs 49.4 ± 7.1%; p=0.038). LV end-diastolic diameter was significantly lower in the colchicine group at 30 days (50.1 ± 6.2 vs 52.3 ± 6.9 mm; p=0.044), as was LV end-systolic diameter (35.4 ± 5.1 vs 37.6 ± 5.6 mm; p=0.029), suggesting attenuation of adverse post-MI ventricular remodelling. The E/e' ratio, an echocardiographic index of LV filling pressure and diastolic function, was significantly lower in the colchicine group at 30 days (9.8 ± 2.3 vs 11.2 ± 2.7; p=0.031). Pericardial effusion at 30 days was present in significantly fewer colchicine-treated patients (3.3% vs 11.7%; p=0.042). Regional wall motion abnormalities did not differ significantly between groups at 30 days (p=0.419). Baseline peak troponin I was comparable between the two groups (28.4 ± 11.6 vs 27.9 ± 12.1 ng/mL; p=0.798).

Table 4: Echocardiographic and Cardiac Parameters at Baseline and 30 Days

Parameter	Colchicine Baseline	Colchicine 30 days	Placebo Baseline	Placebo 30 days	p†
LVEF (%)	48.3 ± 7.1	52.7 ± 6.4	47.8 ± 7.4	49.4 ± 7.1	0.038*
LV end-diastolic diameter (mm)	52.4 ± 6.8	50.1 ± 6.2	52.8 ± 7.1	52.3 ± 6.9	0.044*
LV end-systolic diameter (mm)	37.6 ± 5.4	35.4 ± 5.1	37.9 ± 5.7	37.6 ± 5.6	0.029*
E/e' ratio (diastolic function)	11.4 ± 2.8	9.8 ± 2.3	11.6 ± 2.9	11.2 ± 2.7	0.031*
RWMA present, n (%)	38 (63.3%)	29 (48.3%)	36 (60.0%)	34 (56.7%)	0.419
Pericardial effusion, n (%)	6 (10.0%)	2 (3.3%)	5 (8.3%)	7 (11.7%)	0.042*
Peak troponin I (ng/mL)	28.4 ± 11.6	—	27.9 ± 12.1	—	0.798
† p-value = between-group comparison at 30 days (ANCOVA, baseline-adjusted)					

MACE and Secondary Clinical Outcomes

Clinical outcomes at 30 days are summarised in Table 5. The composite MACE endpoint occurred in 5 patients (8.3%) in the colchicine group versus 12 patients (20.0%) in the placebo group (OR 0.37; 95% CI 0.12–1.12; p=0.077). Although this difference did not reach statistical significance in this sample, the observed effect size and directionality were consistent with those reported in larger colchicine cardiovascular trials. Post-MI pericarditis was significantly less frequent in the colchicine group (3.3% vs 13.3%; OR 0.22; 95% CI 0.04–1.08; p=0.041), representing a clinically meaningful and statistically significant protective effect. All-cause mortality at 30 days occurred in 1 (1.7%) versus 2 (3.3%) patients respectively (p=0.562). Recurrent MI was observed in 2 (3.3%) versus 5 (8.3%) patients (p=0.254). New-onset atrial fibrillation was numerically lower in the colchicine group (5.0% vs 10.0%; p=0.308) but did not attain statistical significance.

Table 5: MACE and Secondary Clinical Outcomes at 30 Days

Outcome	Colchicine (n=60)	Placebo (n=60)	OR (95% CI)	p-value
MACE composite, n (%)	5 (8.3%)	12 (20.0%)	0.37 (0.12–1.12)	0.077
All-cause mortality, n (%)	1 (1.7%)	2 (3.3%)	0.49 (0.04–5.62)	0.562
Recurrent MI, n (%)	2 (3.3%)	5 (8.3%)	0.38 (0.07–2.05)	0.254
Unplanned revascularisation, n (%)	1 (1.7%)	3 (5.0%)	0.32 (0.03–3.19)	0.307
Heart failure hospitalisation, n (%)	2 (3.3%)	5 (8.3%)	0.38 (0.07–2.05)	0.254
Post-MI pericarditis, n (%)	2 (3.3%)	8 (13.3%)	0.22 (0.04–1.08)	0.041*
New-onset atrial fibrillation, n (%)	3 (5.0%)	6 (10.0%)	0.47 (0.11–2.02)	0.308

Safety and Tolerability

Safety data are presented in Table 6. Any adverse event was reported by 18 patients (30.0%) in the colchicine group versus 9 (15.0%) in the placebo group (OR 2.4; 95% CI 1.0–5.8; p=0.048). Gastrointestinal adverse events, predominantly diarrhoea (16.7% vs 6.7%) and nausea/vomiting (13.3% vs 5.0%), were numerically more frequent with colchicine, though neither difference achieved statistical significance individually after correction. Drug discontinuation due to adverse events occurred in 5 patients (8.3%) in the colchicine group versus 1 patient (1.7%) in the placebo group (p=0.096). One patient in the colchicine group experienced a creatine kinase elevation exceeding three times the upper limit of normal, considered possibly related to the study drug; this patient did not develop symptomatic myopathy and recovered fully after drug discontinuation. No cases of bone marrow suppression or peripheral neuropathy were recorded. No clinically significant changes in renal or hepatic biochemical parameters were identified in either group.

Table 6: Adverse Events and Tolerability

Adverse Event	Colchicine (n=60)	Placebo (n=60)	OR (95% CI)	p-value
Any adverse event, n (%)	18 (30.0%)	9 (15.0%)	2.4 (1.0–5.8)	0.048*
Gastrointestinal — any, n (%)	14 (23.3%)	6 (10.0%)	2.7 (0.97–7.6)	0.058
Diarrhoea, n (%)	10 (16.7%)	4 (6.7%)	2.8 (0.84–9.3)	0.094
Nausea/vomiting, n (%)	8 (13.3%)	3 (5.0%)	2.9 (0.74–11.3)	0.124
Abdominal cramps, n (%)	5 (8.3%)	2 (3.3%)	2.6 (0.48–14.3)	0.268
Serious adverse event (SAE), n (%)	1 (1.7%)	0 (0.0%)	—	0.315
Drug discontinuation due to AE, n (%)	5 (8.3%)	1 (1.7%)	5.3 (0.60–47.2)	0.096
Myotoxicity (CK elevation >3x ULN), n (%)	1 (1.7%)	0 (0.0%)	—	0.315
Neutropaenia (ANC <1.5 x 10^9/L), n (%)	0 (0.0%)	0 (0.0%)	N/A	N/A

DISCUSSION

The present randomized controlled trial demonstrated that adjunctive low-dose colchicine, initiated within 24 hours of acute MI and continued for 30 days, produced a rapid and sustained attenuation of the post-infarction inflammatory response across multiple biomarker axes — including hs-CRP, IL-6, IL-1β, and TNF-α — at both 72 hours and 30 days, with a concomitant improvement in left ventricular systolic and diastolic function and a significant reduction in post-MI pericarditis, in an Egyptian patient population receiving contemporary standard post-MI care. These findings extend the growing body of evidence supporting the role of targeted anti-inflammatory therapy in the post-MI setting to a MENA-region population and provide insight into the pharmacodynamic kinetics of colchicine's multi-cytokine effects in the acute post-MI phase.

The magnitude and rapidity of hs-CRP suppression achieved with colchicine in the present study — a 41.4% greater reduction at 72 hours compared with 12.8% in the placebo group — is consistent with colchicine's established mechanism of NLRP3 inflammasome inhibition and consequent downstream IL-1β and IL-6 suppression, with resulting reduction in hepatic CRP synthesis [3]. The COLCOT trial biomarker substudy similarly reported significant reductions in hs-CRP and IL-6 in colchicine-treated post-MI patients, with reductions in inflammatory markers mediating a significant proportion of the observed MACE benefit [6]. The specific contribution of IL-1β attenuation in the present study is mechanistically important: the CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study) trial, which targeted IL-1β specifically using canakinumab, established that IL-1β inhibition alone produces a significant reduction in recurrent cardiovascular events independent of LDL cholesterol modification, confirming the causal role of this cytokine axis in post-MI risk [11].

The significant improvement in LVEF (52.7 ± 6.4% vs 49.4 ± 7.1%; p=0.038) and the attenuation of LV dilatation indices at 30 days in the colchicine group suggest that early suppression of the post-MI inflammatory surge translates into measurable structural cardioprotection within the 30-day follow-up window. This is mechanistically plausible, as experimental and human data consistently demonstrate that the magnitude of the post-MI inflammatory response is a determinant of infarct zone expansion, adverse remodelling, and late cardiomyocyte loss.[2] A small Egyptian RCT by Abd-El Aziz *et al.*, reported similar echocardiographic findings with colchicine post-STEMI, including significant attenuation of LV remodelling at 6 months, providing preliminary regional corroboration for the structural cardioprotective signal observed in the present study [12].

The significant reduction in post-MI pericarditis (3.3% vs 13.3%; p=0.041) observed in the colchicine group is a clinically meaningful finding consistent with the drug's established efficacy in pericardial inflammatory disease. Post-MI pericarditis — encompassing both early post-MI pericarditis (occurring within the first few days) and Dressler syndrome (delayed autoimmune pericarditis weeks to months after MI) — is a recognised complication that exacerbates patient discomfort, prolongs hospitalisation, and may contribute to haemodynamic instability through pericardial effusion and tamponade in severe cases.[5] Current ESC Guidelines on pericardial disease already recommend colchicine for acute and recurrent pericarditis; the present data support its potential role in preventing this specific post-MI complication. While individual component MACE events were directionally lower in the colchicine group, the trial was not powered to detect statistically significant differences in individual clinical endpoints at 30 days — a limitation consistent with the short follow-up period and sample size, and consistent with the COLCOT trial's requirement for 4,745 patients and a median 22.6-month follow-up to achieve MACE significance [7].

The gastrointestinal adverse event profile of colchicine in the present trial — predominantly diarrhoea (16.7%) and nausea/vomiting (13.3%) — is consistent with the known tolerability limitations of colchicine and is comparable with prior trial data, including the COLCOT trial, which reported diarrhoea in 9.7% of colchicine-treated patients versus 8.9% in the placebo group [6]. The higher gastrointestinal event rates in the present trial may reflect the twice-daily dosing regimen employed (vs once daily in COLCOT), the administration in an acute post-MI inpatient setting where concurrent medications and physiological stress may augment gastrointestinal susceptibility, and potentially dietary and microbiome differences in the Egyptian population. Drug discontinuation in 8.3% of the colchicine group, while numerically higher than placebo, did not reach statistical significance and did not exceed rates reported in contemporary colchicine cardiovascular trials. No life-threatening haematological or myotoxic complications were encountered, supporting the safety of the low-dose regimen in this acute clinical setting [13].

Certain limitations of the present study deserve acknowledgement. The relatively modest sample size (n=120) and short 30-day follow-up period limit the ability to draw conclusions about longer-term clinical efficacy and the durability of echocardiographic improvements. The open-label design at the level of pharmacy preparation, despite patient and assessor blinding, introduces a theoretical risk of performance bias. Cytokine measurements were not standardised against an external reference laboratory, and the

absence of a dedicated cardiac MRI subgroup analysis precludes definitive infarct size quantification. The single-centre design and hospital-based enrolment may limit generalisability to the broader Egyptian or MENA population. Nevertheless, the robust inflammatory biomarker findings across four cytokine axes, the consistency of the echocardiographic and clinical protective signals, and the transparent safety reporting collectively strengthen the internal validity of the study.

CONCLUSION

The present randomized controlled trial demonstrated that adjunctive low-dose colchicine (0.5 mg twice daily for 30 days), initiated within 24 hours of acute myocardial infarction, produced a statistically significant and clinically meaningful suppression of the post-MI inflammatory response across hs-CRP, IL-6, IL-1β, and TNF-α axes at both 72 hours and 30 days in an Egyptian patient cohort. Colchicine was associated with a significant improvement in left ventricular ejection fraction, attenuation of adverse LV remodelling, reduction in pericardial effusion, and a significant reduction in post-MI pericarditis at 30 days. The MACE composite was directionally lower with colchicine, though the trial was not powered for definitive clinical event analysis at this time horizon. The drug was generally well tolerated, with gastrointestinal adverse events representing the principal safety concern. These findings provide locally relevant pharmacodynamic and early clinical outcomes data from Egypt, reinforcing the growing international evidence base supporting the incorporation of colchicine into post-MI secondary prevention protocols and providing a mechanistic foundation for larger multi-centre trials in the MENA region.

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