Trimetazidine MR efficacy in patients with left ventricular dysfunction

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Abstract
Coronary artery disease is one of the causes of the left ventricular (LV) dysfunction. Trimetazidine, a cardioprotective agent, which has a major anti-ischemic efficacy in dilated ischemic cardiomyopathy. Patients who are already optimally treated with angiotensin converting enzyme-inhibitor (ACE-I), beta-blockers with addition of Trimetazidine also have been proven to significantly improves LV ejection fraction, NYHA class, quality of life; Moreover, in some extent has also noted to reduce angina attacks, all causes mortality, and heart failure hospitalization. Trimetazidine has also been confirmed for its efficacy in diabetics, elderly and post-CABG patients.

Key Words: Left Ventricular Dysfunction, Diabetics, Elderly, Post-CABG, Trimetazidine MR

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Trimetazidine MR significantly improves left ventricular function in patients with dilated ischemic cardiomyopathy.

Brottier et al (2), demonstrated that trimetazidine increased systolic ejection fraction (EF) in patients with severe ischemic cardiomyopathy. Lu-Chierchia et al (3), evaluated trimetazidine 20 mg, three times daily, being effective on ischemic left ventricle by echocardiogram and dobutamine stress test; the results showed that not only is was the myocardium protected from dobutamine-induced ischemic dysfunction, but also the left ventricular (LV) function was improved at rest without any influence on hemodynamic parameters. Belardinelli R and Purcaro A study (4), conducted in patients with an EF inferior at 30%, due to ischemic cardiomyopathy, showed that after two months of treatment with trimetazidine, in patients already optimally treated with ACEIs (angiotensin converting enzyme inhibitors) had an improvement of LVEF measured by wall motion score index (WMSI) from echocardiogram. Kuimov AD, et al (5), demonstrated the improvement with trimetazidine in patients already treated with nitrates, β-blockers, or ACEIs, who had heart failure from CAD.

Trimetazidine MR also demonstrated cardioprotective benefits in at-risk patients such as in diabetics, elderly and revascularized patients. Rosano et al’ s (6) results in diabetic ischemic cardiomyopathy patients, randomized to trimetazidine or placebo for 6 months, showed an increase in left ventricular EF. This cardioprotective benefit had also been demonstrated by Fragrasso (7), which also showed the short- and long-term beneficial effects of trimetazidine. Vitale et al study (8) also showed beneficial effects of trimetazidine MR in elderly patients with LV dysfunction and ischemic cardiomyopathy. After 6 months, the trial demonstrated an improvement in both LV function and quality of life. Romano M, et al study (9), investigated trimetazidine MR’s efficacy in 24 patients who had previous myocardial infarction, revascularization by coronary artery bypass graft (CABG), and moderate heart...
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They found that the time to 1-mm ST-segment depression, the total exercise depression as well as the left ventricular ejection fraction, increased significantly with trimetazidine MR compared to placebo. Fragrasso et al (10), showed evidence of the major cardioprotective benefits of trimetazidine in ischemic cardiomyopathy patients, already “optimally” treated with ACEIs (90%) and beta-blockers (nearly 80%). In these patients, the addition of trimetazidine MR to the standard regimens significantly improved LV ejection fraction, NYHA class and quality of life; moreover it significantly decreased BNP levels suggesting that it might have a positive impact on prognosis.

These results were confirmed by Di Napoli et al (11), which proved that by adding trimetazidine MR to the treatment of 50 patients with compensated ischemic cardiomyopathy, it significantly reduced plasma BNP level and cardiac troponin T (cTnT), another biological marker linked to post infarction ventricular remodeling and resulting in LV failure (false positive of cTnT from LV failure (12)) to the main factor affecting the progression of left ventricular dysfunction. In El-kady study (13), treatment with trimetazidine MR for 24 months of patients with ischemic cardiomyopathy also led to an improvement in myocardial perfusion and LV function (increase of LVEF from 35.6 ± 17.1 to 43.9 ± 21.2 %, compared to placebo 36.9 ± 13.9 to 37.1 ± 14.0 %) (p < 0.0001); the study also resulted in an increase in exercise test duration (p < 0.01) and also demonstrated better survival, as at the end of the study 92% of patients treated with trimetazidine were alive compared to 62% in the placebo group (p < 0.0001). Di Napoli et al (14,15), confirmed the beneficial cardioprotective effects of trimetazidine MR on top of conventional long term treatments in patients with severe dilated ischemic cardiomyopathy in an open-label, randomized trial of 61 patients who had a mean LVEF of approximately 30%. After four years the results showed that trimetazidine significantly improved LVEF starting from the 12th month of treatment (p < 0.001 versus control), whereas the LV function of patients who remained on conventional treatments continued to deteriorate over time. In addition, at the end of the four years trimetazidine added to the usual therapy, reduced all-cause mortality (-56%; p = 0.0047) and heart failure hospitalization (-47%; P = 0.002). More recently, Sisakian H et al (16) presented the efficacy of trimetazidine MR 35 mg twice daily, in combination with conventional treatments in 82 heart failure patients with ischemic cardiomyopathy for over three months’ follow-up. The results showed that trimetazidine MR significantly improved LV function and the functional capacities of patients with ischemic LV dysfunction. Belardinelli et al (17) confirmed the abovementioned study by adding trimetazidine to 116 coronary patients with altered left ventricular function (mean LVEF: 38%), who received conventional treatments. Trimetazidine significantly improved LVEF (+5.5% in absolute value, P<0.001 comparing to control). This improvement was even bigger when combined with an exercise training program (+7% in absolute value, P<0.05 compared to trimetazidine). Furthermore, functional capacity was significantly improved; V02 peak increased by 15% in the trimetazidine group and by 25% in the group where trimetazidine was combined with exercise training (P<0.001 vs controls). These two studies (16-17) proved the direct link existing between trimetazidine’s metabolic mode of action and its efficacy on LV function. Finally, Fragasso et al (18) in 2006 demonstrated that the improvement of cardiac function is was followed by an increased phosphocreatine/adenosine triphosphate (ATP) ratio. And more recently, by showing, in diabetic coronary patients that the improvement of cardiac function with trimetazidine MR did not modify myocardial perfusion, Belardinelli et al. brought new evidence to this metabolic intervention (19).

**Trimetazidine improves LV function in patients with dilated non-ischemic cardiomyopathy:**

Tuunanen H, et al (20) conducted a study in 19 patients with idiopathic dilated cardiomyopathy, and adding trimetazidine MR twice daily on top of conventional treatments for 3 months improved LVEF significantly compared with the baseline of 30.9 ± 8.5% to the follow up of 34.8 ± 12% (p = 0.027), whereas in the control group the LVEF worsened. The positive effect of trimetazidine might be from the synergistic effects of beta-blockade and trimetazidine on LVEF, increase in HDL cholesterol,
and metabolic shift hypothesis. Other studies (21-22) have been conducted on both ischemic and non-ischemic cardiomyopathy, and showed an improvement of LV dysfunction.

**Conclusion**

Trimetazidine MR significantly improves left ventricular systolic function in ischemic cardiomyopathy by increasing LVEF, survival, functional capacity. While improving the average NYHA classification and quality of life; it also significantly decreases hospitalization for LV failure and all causes mortality. It is well-demonstrated efficacy and safety in at-risk patients such as diabetic, elderly and revascularized ischemic cardiomyopathy patients. For the non-ischemic cardiomyopathy patients, additional studies are needed to further confirm the benefit of trimetazidine.

**References**


บทคัดย่อ
การเปลี่ยนแปลงของหัวใจห้องล่างซ้ายที่ทำงานแล้ว vaz ใยในโรคหลอดเลือดหัวใจ แนวทางการรักษา stable angina ของ ESC ฉบับล่าสุด ซึ่งเป็นวาระหัวใจห้องล่างซ้ายที่ทำงานไม่ดี ซึ่งเป็นปัจจัยในการพยากรณ์โรคที่สำคัญมาก สาเหตุประกอบด้วยการขาดสัณฐาน editar ของผู้ป่วย stable angina โดยมีการศึกษาในตัวอย่างต่างๆ ที่เป็นปัจจัยการขาดสัณฐาน editar ของกล้ามเนื้อหัวใจ เมื่อมีความเสื่อมของกล้ามเนื้อหัวใจที่หลากหลายจากโรคหลอดเลือดหัวใจ ซึ่งได้รับการรักษาเพียงพอรวมทั้งได้ยาซีอีไอ, ยาปิดกั้นเบต้า และผู้ป่วยยังมีโรคเบาหวาน, เสื้อสูง, เคยมีโรคหลอดเลือดหัวใจ อย่างไรก็ตามการว่าด้วยยาไตรเมทาซิดีนเอ็มอาร์มีประสิทธิภาพในด้านการต้านการขาดสัณฐาน editar ของกล้ามเนื้อหัวใจเมื่อมีการปรับปรุงการทำงาน ทำให้กล้ามเนื้อหัวใจทำงานได้มากขึ้น และรักษาพยาบาลให้ดีขึ้น ผลของการใช้ยาไตรเมทาซิดีนเอ็มอาร์มีการลดกล้ามเนื้อหัวใจการทำงาน ลดการตายจากสาเหตุต่างๆ และลดการนอนรักษาตัวจากภาวะหัวใจล้มเหลวในโรงพยาบาลด้วย

คำสำคัญ: ภาวะการทำงานผิดปกติของหัวใจห้องล่างซ้าย, ผู้ป่วยโรคเบาหวาน, ผู้ป่วยสูงอายุ, ผู้ป่วยหลังการทำหัตถการหลอดเลือดหัวใจ, ไตรเมทาซิดีนเอ็มอาร์