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## Editorial

# Is magnesium sulfate friend or foe of off-pump coronary artery bypass surgery?



### ABSTRACT

#### Keywords:

Off-pump CABG  
Magnesium sulfate during off-pump CABG  
Magnesium sulfate and platelet dysfunction

Magnesium sulfate is often used empirically in cardiac surgical settings. Magnesium sulfate may cause platelet dysfunction leading to bleeding complication. This editorial commentary discusses the published study of intra-operative use of magnesium sulfate during off-pump coronary artery bypass grafting published in this issue of *Indian Heart Journal*.

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Old adage goes that no medicine is harmless. Every medicine has adverse effects but when benefits outweigh adverse effects, the therapeutic index of that medicine is more than 1 and it can be used clinically. The article published in this issue of *Indian Heart Journal* is an eye-opener for cardiac surgeons – particularly those who practice off-pump coronary artery bypass grafting (CABG) as the preferred mode of surgical revascularization.<sup>1</sup> Magnesium is not seen in the coagulation cascade. It is considered a harmless drug in the cardiac surgical setting. Magnesium is an intracellular ion similar to potassium. Patients on long-term diuretic therapy often develop magnesium deficiency which may lead to cardiac arrhythmias. As it is a systemic vasodilator, hypotension can happen if administered rapidly. Once deficiency is noted, recommended replacement is 6–8 g over several hours. There were reports that empirical magnesium sulfate therapy may improve survival after myocardial infarction<sup>2</sup> but it was not supported by large randomized controlled trial.<sup>3</sup>

There are evidences to believe that magnesium may protect cardiomyocytes from ischemia.<sup>4</sup> No wonder therefore, during conventional cardiac surgery, magnesium therapy was used with the hope of reducing ischemic injury associated with creating a still motionless heart. Such use of magnesium has been empiric in cardiac surgery. Preoperative oral magnesium orotate or IV magnesium sulfate has been used before traditional on-pump surgery with a hope of reducing myocardial damage by cardioplegia used during heart surgery using cardiopulmonary bypass (on-pump CABG). Magnesium sulfate is an important constituent of recently introduced Del Nido cardioplegia which offers superior myocardial protection for prolonged period.

After cardiac surgery, empirical magnesium sulfate has been studied extensively to reduce atrial fibrillation.<sup>5</sup> Prophylactic use

of magnesium sulfate after cardiac surgery is a grade A recommendation by European Association of Cardiothoracic Surgery<sup>6</sup> for prevention of atrial fibrillation. Canadian Cardiovascular Society Guideline suggests prophylactic use of magnesium in patients with contraindication to beta blocker and amiodarone for prevention of atrial fibrillation.<sup>7</sup> The advantage of magnesium sulfate is that it is a cheap drug with no known adverse effect other than systemic hypotension till date. In post-cardiac surgical setting with invasive arterial blood pressure monitoring, it is relatively easy to administer it as a slow infusion. In fact, magnesium sulfate postoperatively has been a part of routine postoperative therapy of the author for the last 14 years of independent cardiac surgical practice. It has been a practice to administer the drug when patient is hemodynamically stable.

The study published in this issue of *Indian Heart Journal*<sup>1</sup> brings out one important adverse effect of magnesium sulfate, i.e. impairing platelet function. This study involved 150 patients in the magnesium sulfate group compared with 450 patients in placebo group. There were no differences in the average number of grafts, operating time, or anticoagulation level between two groups. There was significant increase in intraoperative blood loss and postoperative bleeding in the magnesium sulfate group. Magnesium inhibits platelet aggregation at the cellular level.<sup>8</sup> This effect of magnesium sulfate (inhibition of platelet aggregation) may be responsible for increased bleeding noted in this study. This is the first study reporting bleeding complication after magnesium sulfate therapy. I could not help but notice that the reoperation rate in the control group was also high as compared to our experience. So there may be some component of surgical technique related factors, which have contributed to this result. Like any antithrombotic drug, this platelet inhibitory

effect of magnesium sulfate may result in improvement in graft patency rate after CABG. Off-pump CABG (OPCAB) techniques and protocol continue to evolve, particularly in India.<sup>9</sup> OPCAB differs from on-pump CABG as there is a hypercoagulable state after OPCAB as cardiopulmonary bypass induced coagulopathy is absent. Antiplatelet therapy after OPCAB is also debatable.<sup>9</sup> With the lack of established guideline about OPCAB, many surgeons use dual anti-platelet therapy after OPCAB. The author has personal preference for clopidogrel started within 4 h of surgery in twice daily regime and aspirin added afterwards.<sup>9</sup>

As a surgeon who practices OPCAB, I read this article and try to answer the key question 'how this article impacts my practice of off-pump CABG?' There are evidences to suggest that preoperative or intraoperative magnesium sulfate may lead to excessive bleeding and should be avoided as routine empirical therapy preoperatively. In presence of documented low level of serum magnesium (in patients with long-term diuretic therapy or malnutrition) or preoperative arrhythmia, patients may be given magnesium sulfate replacement before OPCAB. When preoperative magnesium sulfate therapy is given, platelet dysfunction must be taken into account during OPCAB. This is a very similar situation when a patient loaded with antiplatelet therapy (clopidogrel or prasugrel) is taken up for CABG. These patients will require meticulous hemostasis from the word go. We can expect more than expected blood loss during surgery. After reversing heparin in patients on antiplatelet therapy, the author would transfuse 4–6 units of platelet concentrate or one unit of single donor platelet. Similar platelet transfusion must be given in patients who received magnesium sulfate replacement before OPCAB. Surgical hemostasis during closure must be meticulous. So after reading this article, we will follow the same precaution about impaired platelet function during OPCAB in a patient who received preoperative magnesium sulfate.

However, I will continue with our routine protocol of using postoperative magnesium sulfate in the dose of 2 g (diluted in 100 g of saline) twice daily for 2–3 days given as slow infusion over 1 h. This may be extended more than 3 days if atrial fibrillation develops or in presence of left ventricular dysfunction and/or arrhythmia. This postoperative regime has been followed by the author for more than 14 years of independent practice. We have reported that a very low rate of reoperation for bleeding (0.17%) can be achieved in a series of more than 600 consecutive OPCAB<sup>10</sup> and postoperative magnesium sulfate was used in all these patients. We would only start magnesium sulfate infusion postoperatively after hemodynamic stability. This can be explained that a patient with significant bleeding will be hemodynamically unstable. So when we use magnesium sulfate in our patients, significant bleeding must have subsided and this can explain our results. I would advice caution of using magnesium sulfate in a patient with postoperative bleeding with or without coagulopathy and patients with preoperative antiplatelet therapy. Also, it is noteworthy that magnesium sulfate may improve graft patency after CABG. This can be easily explained that any drug that causes platelet dysfunction will promote graft patency after CABG. With this study proving antiplatelet action of magnesium sulfate in clinical settings, judicious use of magnesium sulfate after OPCAB will protect from arrhythmia and will also have positive impact of graft patency. Our experience has proved that magnesium sulfate can be used postoperatively without any increased risk of bleeding

complication in OPCAB patients.<sup>10</sup> Magnesium sulfate therapy needs to be further investigated for its antiplatelet action. It will be interesting to evaluate graft patency in the magnesium sulfate group versus placebo control. Future study should include platelet function study in patients receiving magnesium sulfate and possible synergistic action of magnesium sulfate with anti-platelet drugs.

## Conflicts of interest

The author has none to declare.

## REFERENCES

1. Sabzi F, Faraji R. The effect of magnesium sulphate on post off-pump coronary artery bypasses grafting bleeding. *Indian Heart J.* 2016;68:349–354.
2. Teo KK, Yusuf S, Collins R, et al. Effects of intravenous magnesium in suspected acute myocardial infarction: overview of randomised trials. *BMJ.* 1991;303:1499–1503.
3. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. *Lancet.* 1995;345:669–685.
4. Faghihi M, Sukhodub A, Jovanovic S, et al. Mg<sup>2+</sup> protects adult beating cardiomyocytes against ischaemia. *Int J Mol Med.* 2008;21:69–73.
5. Kohno H, Koyanagi T, Kasegawa H, et al. Three-day magnesium administration prevents atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg.* 2005;79:117–126.
6. Dunning J, Treasure T, Versteegh M, et al. Guidelines on the prevention and management of de novo atrial fibrillation after cardiac and thoracic surgery. *Eur J Cardiothorac Surg.* 2006;30:852–872.
7. Mitchell LB, CCS Atrial Fibrillation Guidelines Committee. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: prevention and treatment of atrial fibrillation following cardiac surgery. *Can J Cardiol.* 2011;27:91–97.
8. Hwang DL, Yen CF, Nadler JL. Effect of extracellular magnesium on platelet activation and intracellular calcium mobilization. *Am J Hypertens.* 1992;5:700–706.
9. Saha KK. Off-pump coronary artery bypass grafting in India. *Indian Heart J.* 2014;66:203–207.
10. Saha KK, Deval M, Kumar A, et al. Off-pump bilateral internal thoracic artery grafting. *Heart Lung Circ.* 2015. <http://dx.doi.org/10.1016/j.hlc.2015.02.021>.

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