Original Article

CABG

When Drotaverine (No-spa) Injected in to the Perivascular Tissues of Internal Mammary Artery (IMA) Relives the Peri-operative Vascular Spasm and Increases the Blood Flow in IMA When Used as a Pedicle Graft in CABG

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ABSTRACT

Objective: To compare two groups of patients submitted to different modes of delivery of Drotaverine and its effect on internal mammary artery spasm during Coronary artery bypass grafting at The National Institute of Cardiovascular Diseases, Karachi.

Study Design: Experimental study.

Place and Duration of Study: This study was carried out at the National Institute of Cardiovascular Diseases Karachi from 1st Jan 2013 to 31st December 2013.

Materials and Methods: Data was analyzed from one hundred patients who underwent CABG at our institute. They were divided into two groups: Group 1 consisted of 50 patients in which Drotaverine (No-Spa) was sprayed topically over the IMA: Group 2 also consisted of 50 patients in which Drotaverine (No-Spa) was injected with blunt needle in the perivascular tissue of IMA.

Results: After Drotaverine application, the mean blood flow were significantly low in Group I was 117.2 ±4.87 ml/min as compared to Group II which was 136.2 ±7.11 ml/min ($p<0.01$).

Conclusion: Result of our study suggests ; Drotaverine injected perivascularly better relieves spasm of internal mammary artery and increases the blood flow .

Key Words: IMA (Internal mammary artery), CABG (Coronary artery bypass grafting), Drotaverine (No-spa)

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INTRODUCTION

Coronary artery bypass grafting is the standard mode of treatment for multivessel coronary artery disease. Introduction of internal mammary artery (IMA) as pedicle graft to bypass left anterior descending artery has been shown to improve 20 years[1]results and all current consensus that the IMA as a conduit of choice for coronary artery bypass grafting (CABG). IMA as pedicle or free graft has better patency than all other conduits used in CABG surgery[2]and that also result in better freedom from angina and patient's survival[2,3]. Vascular spasm is an often observed event during IMA manipulation while harvesting and anastomosis. Internal mammary artery spasm not only make the anastomosis technically difficult but also by decreasing the blood flow which have impact on morbidity/ mortality[4,5], therefore it can influence decision for IMA usage as a conduit. Therefore, the intraoperative pharmacologic dilatation of the internal mammary artery has become a routine procedure in coronary artery bypass surgeries[6, 7]. Papaverine is also used as spasmolytic agent during the IMA preparation[8] by many cardiac surgeons. Whereas our study is conducted on Drotaverine (also known as **No-Spa**) is an antispasmodic drug, structurally related to papaverine.

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MATERIALS AND METHODS

The study was conducted on 100 patients who underwent harvesting of the IMA by trained surgeons, planned for elective CABG between January 2013 to December 2013 at the National Institute of Cardiovascular Diseases Karachi. Exclusion criteria were emergency CABG, previous open heart operation and simultaneous cardiac procedures in which Left anterior descending artery was not a target vessel. Informed consent was taken from all patients. The range for subjects age were from 38 to 77 years (mean,

56.8 years), 62 males and 38 females. Patients were divided into 2 groups prior to surgical incision: Group 1 consisted of 50 patients in which Drotaverine (No-Spa) was sprayed topically over the IMA: Group 2 also consisted of 50 patients in which Drotaverine (No-Spa) was injected with blunt needle in the perivascular tissue of IMA. A total of 60 mg of Drotaverine hydrochloride in 30 ml of saline solution (pH 5.1) was administered in every patient. Both groups were similar in terms of preoperative risk factors except coronary artery disease characteristics. 90 Patients had multi-vessel disease , 7 patients had significant left main along with 3 vessels disease and 3 patients had single vessel disease(left anterior descending artery) . The left internal mammary artery was anastomosed to the left anterior descending artery (LAD) in 99 (99%) patients except in one case in which LIMA was anastomosed to the first large diagonal branch of the LAD because poor quality and short length of the target vessel.

Technique: Routine median sternotomy was performed. Left internal mammary artery was harvested with pedicle containing both satellite viens started proximally at the level of the subclavian vein up to the bifurcation of the vessel distally. Harvesting of LIMA was performed by trained surgeons with low power electrocautery and major branches were secured with metal clips. Heparin was then given systemically (400 units/kg); and subsequent to three minute wait, the LIMA was divided distally at its bifurcation and occluded with bulldog. In group I, diluted Drotaverine was applied topically over the internal mammary artery pedicle's whole length. In group II, the Drotaverine was injected into the perivascular tissue along the full length of the IMA with a blunt needle taking care not to injure the IMA. The mammary artery was left undivided wrapped in Drotaverine- soaked gauze to wait for anastomosis to the LAD. And it was anastomosed to LAD as the last of all distal anastomosis. Prior to anastomosis, the mammary artery was divided at its bifurcation . Blood flow was allowed free flow and collected into bowel for 1 minute under well controlled hemodynamic conditions, at 70 mm Hg. After the blood volume was documented, the collected blood was returned to the heart-lung machine through pump suckers.

RESULTS

Both groups were well controlled with respect to mean arterial pressure at the time of blood collection. The Internal mammary artery harvest time 26 ± 6.7min were similar. There were no IMA injuries found during harvesting. After drotaverine application, the mean blood flow were significantly low in Group I as shown in figure 1. Group 1 patients have mean flow (117.2± 4.87 ml/min) as compared to Group II (136.2±7.11 ml/min) ($p<0.01$) as shown in table 1. In one of the patients of Group 1, after the weaning of cardiopulmonary bypass, intra-aortic balloon pump was inserted due to low-output state and then it was removed on the 2nd postoperative day, when hemodynamic stabilization in the patient was observed. In Group I, ST elevation in anterior chest leads on electrocardiogram was observed in 3 patients . Two patients were re-opened due to postoperative bleeding. In one of these patients, bleeding was observed from the vascular bed of the LIMA and in second patient it was noticed from side branch of saphenous vein graft. The mean length of ICU stay was 3.2 days. The mean stay of hospitalization was 6.8 days post operatively. At the time of discharge all of the patients were ambulatory.

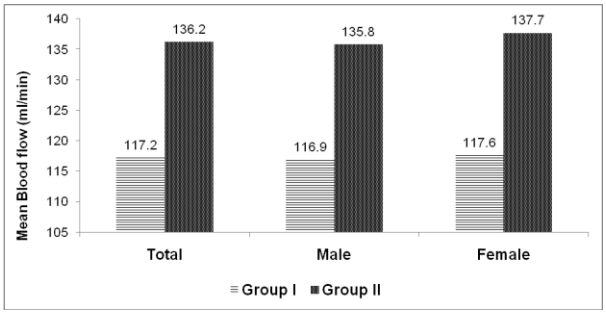
Table No.1: Comparing flow rates in two groups

Flow (ml/min)	Group I No. Mean ± S.D	Group II No. Mean ± S.D	P-value
Total	50 117.2 ± 4.87	50 136.2 ± 7.11	0.001
Male	31 116.9 ± 4.26	31 135.8 ± 6.79	0.001
Female	19 117.6 ± 5.72	19 137.7 ± 6.38	0.001

Statistically significant $p<0.05$

Group 1 consisted of fifty patients in which drotaverine (No-Spa) was sprayed and

Group 2 also consisted of fifty patients in which drotaverine (No-Spa) was injected



Group 1 consisted of fifty patients in which drotaverine (No-Spa) was sprayed and

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Figure No. 1: Showing mean flow in Two groups

DISCUSSION

Internal mammary artery has established long-term patency rates, resulting in improved survival in patients underwent CABG[1]. Today, the use of arterial grafts have become routine in CABG[9]. IMA is always prone to spasm during CABG making accurate placement of sutures difficult[8], therefore influencing quality of anastomosis resulting in morbidity and mortality. Different vasodilators are used to prevent LIMA spasm, but the best agent is not known[10]. Nevertheless Papaverine is the most studied agent clinically.

Papaverine hydrochloride is an alkaloid obtained from opium or prepared synthetically; it belongs to the benzyl iso quinoline group of alkaloids. A musculotropic agent, Papaverine reacts directly on vessel smooth muscle cells. It probably inhibits the catalysis of cAMP phosphodiesterase and the transmembranous transfer of calcium. It works independently of the resting innervation of vascular muscle. The effect of papaverine is particularly distinct when spasm (i.e., primary hypertonia of the smooth muscles) is present[13].While in our study we are using a different agent **Drotaverine**, structurally related to papaverine. It is a selective inhibitor of phosphodiesterase 4; Drotaverine is sold under the brand name of **No-Spa**[14]. Drotaverine is a spasmolytic agent by inhibiting PDE4 in smooth muscle cells. it inhibits phosphodiesterases hydrolyzing cAMP, thereby increasing cAMP concentration, decreasing calcium uptake of the cells and changing its distribution among the cells. It may also have minor allosteric calcium channel blocking properties. Different methods of delivery of these agents to the LIMA has been describe like topical spray, perivascular injection, intraluminal administration and hydrostatic dilation. The most effective method of administration is still under discussion[11, 12].

Cooper et al suggested sodium nitroprusside[15] most effective vasodilator compared to normal saline(placebo), papaverine, nifedipine, glyceryl trinitrate on IMA flow. Sasson and associates contradicted it suggesting that topical vasodilators have no significant effect [16] . Periarterial injection into the vascular pedicle is claimed by Hausmann et al as a better method of application [17]. Injecting Drotaverine with a blunt needle into the perivascular tissue of LIMA avoids injury to intima, while injecting the agent intraluminally may cause injury to intima and alters the blood flow in it. Also perivascular delivery allows for better exposure of Drotaverine to LIMA when harvested as pedicle graft over topical spray. This method of prolonged adventitial exposure of the drug increases duration of the agent's vasodilatory effects. Combine application of papaverin through both extraluminal and intraluminal exposure have better and prolonged effects on prevention of potassium induced contraction[18]. We have studied both methods of application, perivascular injection and topical spray of the Drotaverine on the IMA. Our findings suggest that significant flow increases (117.2 ml/min versus 136.2 ml/min) were observed in perivascular group. With methods used in our study, there were no complications observed. Dortaverine delivery to the perivascular tissues in LIMA harvesting treats spasm efficiently, increases blood flow, and is considered to be a safe and effective method to improve the quality of IMA.

CONCLUSION

The application of Drotaverine injection into the perivascular tissues of Internal mammary artery relieves the perioperative spasm with preserved safety and better results than topical application as it increases the blood flow in IMA when used as a pedicle graft in coronary artery bypass surgery.

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Cameron AAC, Green GE, Brogno DA, Thornton J. Internal thoracic artery grafts: 20-year clinical followup. J Am Coll Cardiol 1995;25: 188–92.
2. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. N Engl J Med 1986;314:1–6.
3. Olearchyk AS, Magovern GJ. Internal mammary artery grafting: clinical results, patency rates and long-term survival in 833 patients. J Thorac Cardiovasc Surg 1986;92:1082–7.
4. Sarabu MR, McClung JA, Fass A, Reed GE. Early postoperative spasm in left internal mammary artery bypass grafts. Ann ThoracSurg 1987; 44:199–200.
5. Mills NL, Bringaze WL. Preparation of the internal mammary artery graft. Which is the best method? J Thorac Cardiovasc Surg 1989;98:73–9.
6. vonSegesser LK, Lehmann K, Turina M. Deleterious effects of shock in internal mammary artery anastomoses. Ann Thorac Surg 1989;47: 575-9.
7. Segesser L, Simonet F, Meier B, Finci L, Faidutti B. Inadequate flow after internal mammary-coronary artery anastomoses. Thorac Cardiovasc Surg 1987;35:352-4.
8. Singh RN, Sosa JA. Internal mammary artery: a “live”conduit for coronary bypass. J Thorac Cardiovasc Surg 1984;87: 936–8.
9. Acinapura AJ, Rose DM, Jacobowitz IJ, Kramer MD, Robertazzi RR, Feldman J, et al. Internal mammary artery bypass grafting: influence on recurrent angina and survival in 2,100 patients. Ann Thorac Surg 1989;48:186-91.
10. He GW, Rosenfeldt FL, Buxton BF, Angus JA. Reactivity of human isolated internal mammary artery to constrictor and dilator agents. Implications for treatment of internal mammary artery spasm. Circulation 1989;80:I141–50.
11. Dregelid E, Heldal K, Andersen KS, Stangeland L, Svendsen E. Dilation of the internal mammary artery by external papaverineapplication to the pedicle-an improved method. Eur J Cardiothorac Surg 1993;7:158-63.

12. Hillier C, Watt PA, Spyt TJ, Thurston H. Contraction and relaxationof human internal mammary artery after intraluminal administration of papaverine. Ann Thorac Surg 1992;53:1033-7.
13. Forth W, Henschler D, Rummel W. Allgemeine und speziellePharmakologie und Toxikologie. BibliographischesInstitut, Mannheim S 1987;114.
14. http://www.drugbank.ca/drugs/DB06751
15. Cooper GJ, Wilkinson AL, Angelini GD. Overcoming perioperative spasm of the internal mammary artery.Which is the best vasodilator? J Thorac Cardiovasc Surg 1992; 104: 465–8.
16. Sasson L, Cohen AJ, Hauptman E, Schachner. Effect of topical vasodilators on internal mammary arteries. Ann Thorac Surg 1995; 59: 494–6.
17. Hausmann H, Photiadis J, Hetzer R. Blood flow in the internal mammary artery after the administration of papaverine during coronary artery bypass grafting. Tex Heart Inst J 1996;23: 279–83.
18. Chester AH, Panda R, Borland JAA, et al. Effect of mode of application of papaverine on the contractile response of the internal mammary artery. Br J Surg 1994;81:527–531.