Original Article

Lactate/pyruvate monitoring during carotid endarterectomy under general anaesthesia versus cervical plexus block: A randomised controlled study

Address for correspondence:
Dr. Gomaa Z Hussien,
Building 7, Al-Fariqu Ali Fahmy St., Mariottya, Giza, Egypt.
E-mail: gomaahussien2015@gmail.com

Gomaa Z Hussien, Ahmed M Elbadawy, Hossam A Elshamaa
Department of Anaesthesia, Faculty of Medicine, Cairo University, Giza, Egypt

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.IJA_545_16

Quick response code

ABSTRACT

Background and Aims: Carotid endarterectomy (CEA) reduces the risk of stroke in patients with significant carotid stenosis and may be performed under general anaesthesia (GA) or regional anaesthesia (RA). This study aimed to compare RA and GA with regard the jugular venous bulb blood lactate and pyruvate levels. **Methods:** This randomised-controlled trial was done between October-2013 and September-2015. Thirty-six patients were randomised into either GA or RA groups, with six excluded after randomisation. In the RA group, combined deep and superficial cervical plexus blocks were performed. In the GA group, anaesthesia was induced with propofol and fentanyl. In both groups, monitoring of neurological function was done. Sampling of the contralateral jugular bulb blood was done. The main outcome measures were lactate and pyruvate in the jugular venous blood. For comparing categorical data, Chi-square test was used, and for the numerical variables, *t*-test was used. **Results:** Demographics were comparable in the two Groups. Serum lactate and pyruvate levels were higher in the GA group than RA group. At 120 min under anaesthesia, lactate and pyruvate levels under RA vs. GA, respectively were 0.76±0.03 mEq/L vs. 1.14±0.06, p-0.001 mEq/L, and 0.08± 0.00 mEq/L vs. 0.10±0.01 mEq/L, p=0.006. Lactate/ pyruvate ratios were normal in both groups. The mean blood pressure was significantly lower in the GA group during anaesthesia. **Conclusion:** In patients undergoing Carotid endarterectomy, serum levels of both lactate and pyruvate were higher under general versus regional anaesthesia.

Key words: Carotid endarterectomy, cerebral ischaemia, lactate, pyruvate

INTRODUCTION

Carotid endarterectomy (CEA) is done to decrease the risk of stroke. However, it is associated with a 5%–7% risk of stroke.[1] Type of anaesthesia may impacts this risk. Regional anaesthesia (RA) allows the early detection of any neurological change, either during test clamping or during surgery itself and may guide appropriate use of selective shunting. In addition, the cardiac and pulmonary morbidity of general anaesthesia (GA) may be avoided. Yet, available data are not conclusive whether Regional anaesthesia (RA) is better than GA.[1] Detection of cerebral injury is a challenge under GA.[2] Changes in lactate/pyruvate (LP) levels and LP ratio occur during ischaemia, due to changes mitochondrial oxidative metabolism.[3-4] Their levels in the jugular blood may be used as surrogate markers for ischaemia[5-6]

This study compares RA and GA with regard to the impact on serum lactate, pyruvate and LP ratio. An anaesthetic technique which is not associated with increased serum lactate and pyruvate and that maintains a normal LP ratio may be a good choice, and may be associated with favourable outcome.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Hussien GZ, Elbadawy AM, Elshamaa HA. Lactate/pyruvate monitoring during carotid endarterectomy under general anaesthesia versus cervical plexus block: A randomised controlled study. Indian J Anaesth 2017;61:424-8.

© 2017 Indian Journal of Anaesthesia | Published by Wolters Kluwer - Medknow

METHODS

This study was conducted in one instiution during the period from October 2013 to September 2015. The study followed the principles of the Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects Act and was approved by the Medical Ethical Review Committee of the instiution.

The purpose of this study was clearly explained to all subjects before their enrolment to the study, and an informed consent form was signed by and obtained from all of those enrolled.

We recruited patients (males or females) with the American Society of Anesthesiologists' (ASA) physical Status II or III, who would undergo CEA. Routine pre-operative evaluation, including history taking, general examination and laboratory investigations, was performed for all patients, including liver and kidney function tests, blood suger level as well as coagulation profile and serum electrolytes. The patients with communication difficulties, patients unable to lie flat for a sufficient time for surgery, patients having any coagulation defects or receiving anticoagulants were excluded from the study. Preoperatve medications e.g., antihypertensives and antianginal drugs were continued till the day of surgery, other drugs e.g., dieurtics, anticoagulants and oral hypoglycaemics were discontiued at the day of surgery.

In the preparation room, an intravenous (IV) cannula was inserted under local anaesthesia (LA), IV midazolam 2 mg and IV ranitidine 50 mg were given to all patients. A cannula was inserted under LA in the radial artery on the contralateral side of surgery. Then, the patient was transferred to the operation room; monitors were applied (invasive blood pressure, pulse oximetry, electrocardiogram and core temperature).

We used the simple randomisation technique where sequence generation was created by a computerised random number generator (MS Excel model). Participants were intentionally allocated in equal numbers to each group in 1:1 ratio. The allocation sequence was concealed from the investigator enrolling and assessing participants in sequentially numbered, opaque-sealed envelopes.

The two groups were as follows, Group RA patients received superficial and deep cervical plexus block. Group GA patients received GA. In group RA, combined deep and superficial cervical plexus blocks were performed with the patients in the supine position with head turned to the contralateral side away from the side of surgery using a mixture of 20 mL 0.5% bupivacaine and 10 mL 2% lidocaine. Deep cervical plexus block was performed by injecting 3–5 mL mixture of 0.5% bupivacaine and 2% lidocaine at each of the transverse processes C_2, C_3 and C_4, while superficial cervical plexus block was performed with injection of 15 mL of local anaesthetics mixture (0.5% bupivacaine and 2% lidocaine) superiorly and inferiorly along the posterior border of the sternocleidomastoid muscle. Supplemental 2–3 mL 1% lidocaine was administered by the surgeon into the carotid sheath. Neurological monitoring was carried out by verbal communication with the patient and contralateral handgrip. Any deterioration in the either the level of consciousness (determined by asking the patient if he is feel alright and oriented to time and place and ability to perform simple tasks as counting backwards from 100) or handgrip was an indication for protective intraluminal shunt placement.

In group GA, anaesthesia was induced with intravenous propofol 2 mg/kg and fentanyl 2 μg/kg. Endotracheal intubation was facilitated with atracurium 0.5 mg/kg IV and mechanical ventilation was adjusted to keep the end-tidal carbon dioxide between 30 and 35 mmHg. Anaesthesia was maintained with 50% O_2, 50% air and isoflurane 1% to 1.5% with top up doses of atracurium 0.15 mg/kg IV every 20 min. Monitoring of neurological function during GA was based on carotid stump pressure and selective shunting used if stump pressure was below 50 mmHg. Restoration of the mean arterial pressure was done by administration of a bolus intravenous ephedrine 10mg. No patient required adrenaline infusion to keep the mean arterial pressure above 60 mmHg.

In both groups, a retrograde jugular venous catheter was inserted in the contralateral side using Seldinger technique. The catheter was advanced retrograde into the jugular bulb for sampling of jugular bulb venous blood. Proper position of the tip of the catheter was verified radiographically. The catheter was connected to a three-way stopcock, and a slow continuous infusion of 0.9% saline was started to prevent catheter blockage. In addition, the triple lumen central venous line was inserted into the right subclavian vein, except for those with the operation on the right side.

In all patients, age, gender, ASA status and duration of anaesthesia in minutes were recorded. Heart rate, mean blood pressure (MBP) were measured before the induction of anaesthesia (baseline) and every 15 min after that.

Primary outcome measures were jugular venous bulb blood lactate and pyruvate levels as well as the LP ratio before surgery (baseline) and every 30 min thereafter till the end of surgery.

Sample size calculation suggested that a minimum of 15 subjects per group is required to detect 10% difference in lactate or pyruvate levels between groups with a standard deviation (SD) of 0.0645 (taking Type I or α error of 5%, Type II or β error of 20%). The 10% difference was based on a pilot study on ten participants, five in each group. The sample size was calculated for each of lactate and pyruvate; the larger sample was chosen. To account for loss of data, 18 patients were included in each group ($n = 36$).

Data were statistically described in terms of mean ± SD or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's *t*-test for independent samples. For comparing categorical data such as gender and ASA, Chi-square test was performed. The Fisher's exact test was used instead when the expected frequency is <5. *T*-test was used to compare between groups for the numerical data at each point of the time. These variables were heart rate, MBP, pyruvate level, lactate level and LP ratio. $P < 0.05$ were considered statistically significant. All statistical calculations were done using computer program Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) release 19 for Microsoft Windows.

RESULTS

Thirty-nine subjects eligible for CEA operation who came to the centre were asked to participate in the study. Three subjects refused to participate before randomisation; thus, leaving a population of 36 eligible patients who were randomised in this trial. Six subjects, three from each group, were excluded after randomisation. The dispositions of these subjects are shown in [Figure 1].

The two groups were comparable with respect to age, gender and ASA status [Table 1]. The mean duration under anaesthesia was 105.73 (12.62) minutes in RA group, and 107.20 (12.71) minutes in the GA group, ($P = 0.754$). The heart rate was comparable between both groups in all recordings from baseline to end of anaesthesia [Figure 2]. There was significant ($P < 0.05$) decrease in MBP in the GA group than in the RA groups at the start of anaesthesia, 15 min, 45 min, 60 min and 75 min under anaesthesia. [Figure 3].

The serum lactate levels were higher in the GA group than RA group ($P < 0.05$), starting form 30 min under

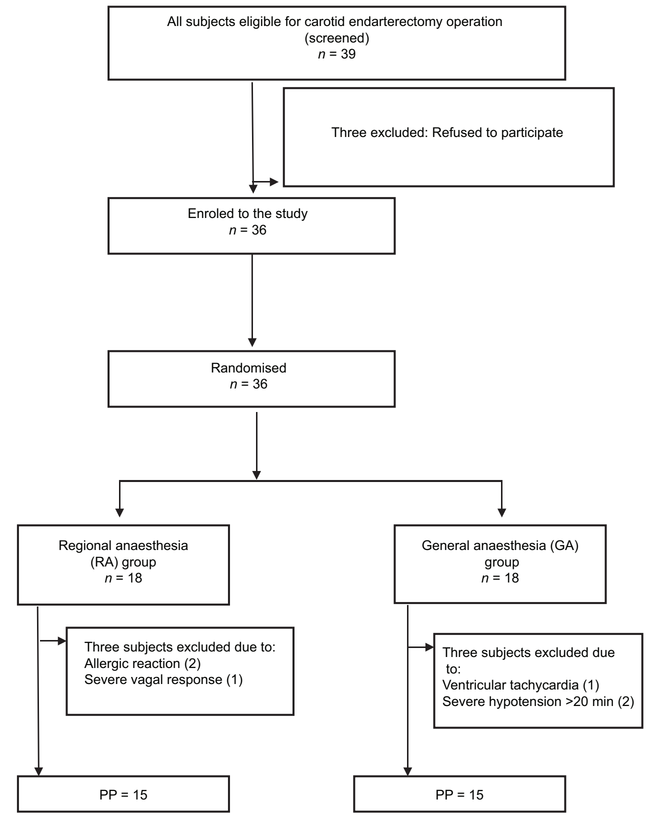

Figure 1: CONSORT diagram

Table 1: Patient's demographics and duration of anaesthesia

Variables	RA group *n*=15	GA group *n*=15	*P*
Gender			
Male	10	10	1.000
Female	5	5	
ASA			
Category I	4	5	1.000
Category II	11	10	
Age (years), mean (SD)	65.20 (4.06)	64.73 (4.06)	0.755
Weight (kg), mean (SD)	81.53 (7.57)	77.60 (8.36)	0.188
Duration of anaesthesia (min), mean (SD)	105.73 (12.62)	107.20 (12.71)	0.754

P<0.05 is significant. SD – Standard deviation; ASA – American Society of Anesthesiologists; RA – Regional anaesthesia; GA – General anaesthesia

anaesthesia [Table 2]. In addition, serum pyruvate levels were higher in the GA group than RA group ($P < 0.05$), starting from 30 min under anaesthesia [Table 2]. However, LP ratio was comparable between both groups, under anaesthesia [Table 2]. There was no significant difference between the two groups as regarding the incidence of any postoperative new neurological deficit, stroke, MI or death.

DISCUSSION

Our study showed that serum lactate and pyruvate levels were significantly higher in the GA group than RA group starting from 30 min under anaesthesia. However, LP ratio was comparable between both groups, under anaesthesia. In addition, the study showed that the MBP was lower in the GA group than in the RA group.

In ischaemia, there is a shift from aerobic to anaerobic metabolism with the consequence of changes in lactate and pyruvate level. The degree of this shift is dependent on the degree of ischaemia. The significant increase in both lactate and pyruvate level in GA more than in RA may be due to the decrease in MBP as well as the disruption of the cerebral blood flow (CBF) autoregulation and the vasoconstriction of cerebral blood vessels which may be greater during GA. As the cerebral perfusion is at great risk during the period of carotid cross-clamping, augmentation of arterial pressure to maintain cerebral perfusion is usually required, and augmentation of arterial pressure to 20% above baseline has been recently shown to reduce ischaemic hypoperfusion and decrease the anaerobic metabolism.

Moreover, increased lactate level in brain tissue with the consequent lactic acidosisis may be a manifestation of cerebral vasomotor paralysis, particularly the abolition of CBF autoregulation.[7,8]

However, in our study, despite the hypotension, there was no change in the L/P ratio, hence we cannot conclude that there was cerebral ischemia. The normal L/P pattern with elevated pyruvate and lactate levels here is matching that of accelerated hyperglycolyisis, not the anearobic metabolism due to ischaemia.

The debate about the relative benefits of GA or RA in patients undergoing CEA has not been resolved yet. There are many polarised opinions. From one side of the spectrum of opinions, one Cochrane Review (2004) concluded that RA has a potential benefit. The review included data from seven randomised studies and

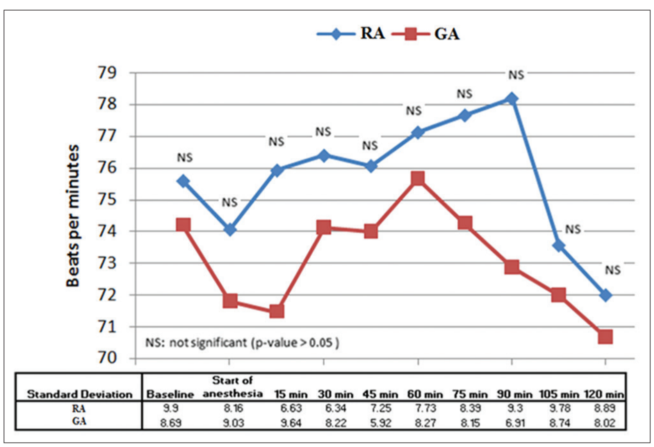

Figure 2: Heart rate under anaesthesia

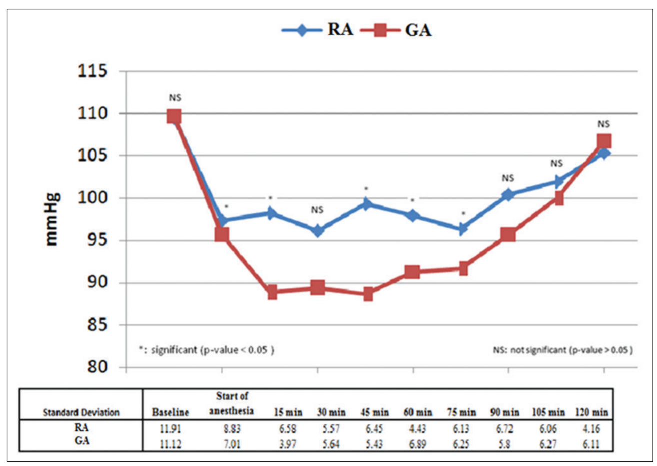

Figure 3: Mean blood pressure under anaesthesia

Table 2: Serum lactate, pyruvate and lactate/pyruvate ratio under anaesthesia

Timing	Lactate (mEq/L)			Pyruvate (mEq/L)			LP ratio		
	RA	GA	*P*	RA	GA	*P*	RA	GA	*P*
Baseline	0.36 (0.07)	0.34 (0.08)	0.601	0.04 (0.01)	0.04 (0.01)	0.796	8.43 (2.17)	8.04 (1.77)	0.602
0 min	0.44 (0.08)	0.39 (0.10)	0.131	0.05 (0.01)	0.05 (0.01)	0.918	9.32 (2.14)	8.15 (2.04)	0.138
30 min	0.55 (0.09)	0.62 (0.10)	0.037	0.06 (0.01)	0.07 (0.01)	0.020	9.68 (2.12)	9.58 (1.53)	0.883
60 min	0.65 (0.07)	0.79 (0.08)	<0.001	0.07 (0.01)	0.08 (0.01)	<0.001	10.14 (1.46)	10.11 (1.38)	0.958
90 min	0.77 (0.08)	0.97 (0.06)	<0.001	0.07 (0.01)	0.09 (0.01)	<0.001	10.54 (1.37)	10.60 (1.25)	0.901
120 min	0.76 (0.03)	1.14 (0.06)	0.001	0.08 (0.00)	0.10 (0.01)	0.006	9.16 (0.48)	11.36 (1.81)	0.327

RA – Regional anaesthesia; GA – General anaesthesia; LP – Lactate/pyruvate

26 non-randomised studies. The meta-analysis of the non-randomised studies showed that RA was associated with reductions in the odds of stroke and death 30 days after the operation. However, the evidence was insufficient.[1,9]

The GA-LAtrial, conducted between 2001 and 2007, included 3500 subjects from 95 centres, randomised to undergo CEA under GA or RA. There were no significant differences in the primary or secondary outcomes.[6] However, RA is associated with a significant reduction in postoperative wound haemorrhage.[10]

In 2008, the Cochrane group in their review updated the systematic review of literature comparing GA with RA for CEA, including the GA-LA trial, with a total ten randomised trials, of which eight investigated stroke or death within 30 days as an outcome (4083 subjects). The meta-analysis showed that the odds of 30-day stroke or death were similar. However, RA was associated with a significant reduction in post-operative haemorrhage.[9,11]

From the current evidence of literature, it is clear that major perioperative outcomes after CEA are similar between RA and GA. However, this does not mean that type of anaesthesia is not important.

Finally, the decision about the type of anaesthesia in CEA is multifactorial. The choice has to depend on factors such as other co-morbid conditions, patient preference, local facilities and expertise.

Although blood in the jugular bulb is derived from both cerebral hemispheres (approximately 70% ipsilateral and 30% contralateral), it is accepted that most patients have a dominant side of the venous drainage, usually the right.[12,13]

One limitation of our study is that it is a single centre study with small number of patients. Another limitation is that we cannot use the dominant jugular vein in all subjects because the operation was made on the same side in some subjects. Finally, the study was not designed to correlate the biochemical parameters with the patient-centred outcomes, such as postoperative stroke or maortality.

CONCLUSION

Carotid endarterectomy performed under regional anaesthesia was associated with lower lactate and pyruvate levels, but similar lactate to pyruvate ratio compared to surgery performed under general anaesthesia. We were unable to demonstrate evidence of cerebral hypoperfusion under general or regional anaesthesia.

Acknowledgment

We would like to acknowledge Dr. Emad R. H. Issak for his efforts in editing of this manuscript. In addition, we would like to thank all anaesthesia technicians in the operative rooms and all nurses in the post-anaesthesia care unit for their efforts and help achieve this work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Rerkasem K, Bond R, Rothwell PM. Local versus general anaesthesia for carotid endarterectomy. Cochrane Database Syst Rev 2004;(2):CD000126.
2. Espenell AE, McIntyre IW, Gulati H, Girling LG, Wilkinson MF, Silvaggio JA, *et al*. Lactate flux during carotid endarterectomy under general anesthesia: Correlation with various point-of-care monitors. Can J Anaesth 2010;57:903-12.
3. Jakobsen R, Halfeld Nielsen T, Granfeldt A, Toft P, Nordström CH. A technique for continuous bedside monitoring of global cerebral energy state. Intensive Care Med Exp 2016;4:3.
4. Dienel GA. Brain lactate metabolism: The discoveries and the controversies. J Cereb Blood Flow Metab 2012;32:1107-38.
5. Nielsen TH, Olsen NV, Toft P, Nordström CH. Cerebral energy metabolism during mitochondrial dysfunction induced by cyanide in piglets. Acta Anaesthesiol Scand 2013;57:793-801.
6. Nielsen TH, Schalén W, Ståhl N, Toft P, Reinstrup P, Nordström CH. Bedside diagnosis of mitochondrial dysfunction after malignant middle cerebral artery infarction. Neurocrit Care 2014;21:35-42.
7. Lassen NA. Control of cerebral circulation in health and disease. Circ Res 1974;34:749-60.
8. Lassen NA. The luxury-perfusion syndrome and its possible relation to acute metabolic acidosis localised within the brain. Lancet 1966;2:1113-5.
9. Ladak N, Thompson J. General or local anaesthesia for carotid endarterectomy? Contin Educ Anaesth Crit Care Pain 2012;12:92-6.
10. GALA Trial Collaborative Group, Lewis SC, Warlow CP, Bodenham AR, Colam B, Rothwell PM, *et al*. General anaesthesia versus local anaesthesia for carotid surgery (GALA): A multicentre, randomised controlled trial. Lancet 2008;372:2132-42.
11. Rerkasem K, Rothwell PM. Local versus general anaesthesia for carotid endarterectomy. Cochrane Database Syst Rev 2008;(4):CD000126.
12. Shenkin HA, Harmel MH, Kety SS. Dynamic anatomy of the cerebral circulation. Arch Neurol Psychiatry 1948;60:240-52.
13. Beards SC, Yule S, Kassner A, Jackson A. Anatomical variation of cerebral venous drainage: The theoretical effect on jugular bulb blood samples. Anaesthesia 1998;53:627-33.