BJA

Effects of stellate ganglion block on cerebral haemodynamics as assessed by transcranial Doppler ultrasonography

M. M. Gupta[1], P. K. Bithal[1]*, H. H. Dash[1], A. Chaturvedi[1] and R. P. Mahajan[2]

[1]*Department of Neuroanaesthesiology, All India Institute of Medical Sciences (A.I.I.M.S.), New Delhi, India.*
[2]*University Department of Anaesthesia and Intensive Care, Queen's Medical Centre, Nottingham, UK*
*Corresponding author. E-mail: pkbithal@hotmail.com

Background. Stellate ganglion block (SGB) causes vasodilatation in the skin of the head and neck because of regional sympathetic block. Its effects on cerebral haemodynamics, in health or in disease, are not clear. We evaluated the effects of SGB on ipsilateral middle cerebral artery flow velocity (MCAFV), estimated cerebral perfusion pressure (eCPP), zero flow pressure (ZFP), carbon dioxide reactivity (CO_2R) and cerebral autoregulation using transcranial Doppler ultrasonography (TCD).

Methods. Twenty male patients, with pre-existing brachial plexus injury, and undergoing SGB for the treatment of complex regional pain syndrome of the upper limb, were studied. For SGB, 10 ml of plain lidocaine 2% was used and the onset of block was confirmed by presence of ipsilateral Horner's syndrome. The MCAFV, eCPP, ZFP, CO_2R, and cerebral autoregulation were assessed before and after SGB using established TCD methods. The changes in these variables were analysed using Wilcoxon's signed rank test.

Results. The block caused a significant decrease in MCAFV from median (inter-quartile range) value of 61 (53, 67) to 55 (46, 60) cm s^{-1}, a significant increase in eCPP from 59 (51, 67) to 70 (60, 78) mm Hg, and a significant decrease in ZFP from 32 (26, 39) to 25 (16, 30) mm Hg. There were no significant changes in CO_2R or cerebral autoregulation.

Conclusion. The increase in eCPP, decrease in ZFP, and no changes in CO_2R or cerebral autoregulation suggest that the SGB decreases cerebral vascular tone without affecting the capacity of the vessels to autoregulate. These effects may be of therapeutic advantage in relieving cerebral vasospasm in certain clinical settings.

Br J Anaesth 2005; **95**: 669–73

Keywords: anaesthetic techniques, regional, stellate ganglion; autoregulation, cerebral; blood, flow, cerebral; blood, transient hyperaemic response test; brain, cerebral perfusion pressure; carbon dioxide, reactivity; measurement techniques, transcranial Doppler; zero flow pressure

Accepted for publication: July 11, 2005

Stellate ganglion block (SGB) has an established use in treating patients with disorders mediated by the sympathetic nervous system in which pain and/or circulatory insufficiency are predominant symptoms. These disorders include post-herpetic neuralgia[1] and complex regional pain syndromes, such as reflex sympathetic dystrophy.[2] In addition, SGB has also been used, albeit somewhat controversially, in management of traumatic brain oedema,[3] schizophrenia,[4] and complicated cervical migraine.[5] Recently, however, the use of cervical sympathetic block has been described in reversing delayed ischaemic neurologic deficit following aneurysmal subarachnoid haemorrhage.[6]

The cerebral blood vessels, in particular the pial vessels, have a dense non-adrenergic sympathetic nerve supply that originates mainly in the cervical ganglia and accompanies the carotid artery to project into the ipsilateral hemisphere.[7 8] There is controversy over the physiological significance of sympathetic innervation of the cerebral vasculature and the effect of SGB on it.[6–12] The intracerebral vessels constrict in response to cervical sympathetic stimulation and dilate when these fibres are interrupted.[7 8] The release and re-uptake of neurotransmitters, such as bradykinin, which is released during injury, can be prevented by sympathectomy.[8] A recent report has suggested that cervical sympathetic block may be beneficial in patients with subarachnoid haemorrhage[6] and that SGB may have therapeutic value in relieving cerebral vasospasm in certain neurological conditions.

Transcranial Doppler ultrasonography (TCD) has been used to assess a number of cerebral haemodynamic

variables.[13] These include estimated cerebral perfusion pressure (eCPP), zero flow pressure (ZFP), carbon dioxide reactivity (CO_2R), and cerebral autoregulation. The eCPP can be calculated from simultaneously measured values of middle cerebral artery (MCA) flow velocity (FV), and arterial pressure.[14][15] In concept, eCPP is the difference between the mean arterial pressure (MAP) (upstream pressure) and ZFP (downstream pressure), hence eCPP= MAP–ZFP. Recent studies have shown that, in patients without raised intracranial pressure, the cerebral vascular tone is the main determinant of the downstream pressure.[16][17] Therefore, changes in ZFP can be taken to reflect changes in vascular tone.

The physiological effects of SGB on cerebral haemodynamics, which include eCPP, ZFP indicating cerebral vascular tone, CO_2R, and cerebral autoregulation, are not well described in the literature. This is an important point of reference, and also indicates whether or not SGB has any unwanted effects on the cerebral blood vessels. In particular, any loss of cerebral autoregulation or CO_2R would indicate inability of cerebral vessels to respond to changes in systemic arterial pressure or carbon dioxide, respectively. Also, disturbances in cerebral vascular reactivity or cerebral autoregulation can be associated with poor neurological outcome.[13]

We aimed to study the effects of SGB on cerebral haemodynamic variables including MCAFV, eCPP, ZFP, CO_2R, and cerebral autoregulation using TCD in patients with no evidence of intracranial pathology.

Materials and methods

We studied 20 consecutive male patients, aged 18–55 yr and ASA I, who presented with a pre-existing brachial plexus injury, and were to undergo SGB as part of treatment for chronic pain resulting from sympathetic dystrophy. The hospital ethics committee approved the study and written informed consent was obtained from all subjects. The patients were excluded if they had previously undergone intracranial surgery, or suffered from pre-existing cardiovascular, carotid artery, neurological, respiratory, or metabolic disorder. They were also excluded if SGB was contraindicated as a result of the presence of coagulation disorders or history of drug allergy.

The study was performed in a quiet room with the subject in the supine position. Peripheral i.v. access was secured on the contralateral upper limb. Monitoring consisted of ECG, non-invasive arterial pressure, end-tidal carbon dioxide (PE'_{CO_2}), and oxygen saturation (Sp_{O_2}) (Datex Engstrom AS/3 multiparameter monitor, Datex Engstrom Helsinki, Finland). The PE_{CO_2} was monitored continuously using a mouthpiece in conjunction with a nose clip. The ipsilateral MCA was located through the temporal acoustic window using a 2 MHz transcranial Doppler ultrasound probe (FOUR-VIEW™ RIMED LTD, Israel), at a depth of 50–55 mm. The identity of the MCA was confirmed by

using standard criteria.[13] The transcranial Doppler ultrasound probe was fixed at a constant angle using a headband and a stable continuous tracing of waveform of MCAFV was established. While breathing room air, the values of baseline systolic, diastolic, and mean MCAFV and arterial pressure, along with heart rate, PE'_{CO_2} and Sp_{O_2} were recorded.

The following haemodynamic variables were assessed or calculated.

The eCPP was calculated by using the method described by Belfort and colleagues[14] and recently validated by Athanassiou and colleagues[15]

$$eCPP = MFV \times (MBP–DBP)/(MFV–DFV).$$

Where, MBP and DBP are mean and diastolic arterial pressures, and MFV and DFV are mean and diastolic MCA blood flow velocities.

The ZFP was calculated using the following formula:[14]

$$ZFP = MAP–eCPP.$$

CO_2R was measured while breathing room air. The patients were asked to increase the rate and depth of their breathing sufficient to decrease end-tidal carbon dioxide by 1–1.5 kPa from the baseline. Once steady state was achieved, arterial pressure, PE'_{CO_2} and MCAFV were recorded. CO_2R was defined as the percentage change in mean MCAFV per kPa change in PE'_{CO_2}.[13]

Cerebral autoregulation was assessed by the transient hyperaemic response test (THRT) using transient hyperaemic response ratio (THRR) as the index of autoregulation. The test was carried out by compressing the common carotid artery ipsilateral to the insonated MCA for 10 s, followed by sudden release of compression.[18] Criteria for the acceptance of a THRT were:

- A sudden and maximal decrease in flow velocity at the onset of compression.
- Stable heart rate for the period of compression.
- Steady Doppler signal for the duration of compression.
- Absence of flow transients following release of compression.

THRR was calculated as described by Mahajan and colleagues[18]

$$THRR = F3/F1.$$

Where F1 is the mean MCAFV calculated immediately before compression and F3 is the mean MCAFV immediately after the release of the compression.

For calculating the TCD variables the time averaged mean of outer envelope of the flow velocity profile was used.

All the measurements including heart rate, MAP, PE'_{CO_2}, Sp_{O_2} and MCAFV were continuously displayed throughout the study. The tests for cerebral autoregulation and CO_2R were performed before (baseline) and after SGB.

The SGB was performed using anterior paratracheal approach with 25-gauge needle under full aseptic conditions

and lignocaine hydrochloride 2% (10 ml) was given. After 10–15 min, onset of SGB was established by the presence of an ipsilateral Horner's syndrome along with pain relief. After establishing SGB, simultaneous recordings of MCAFV and arterial pressure were taken to calculate eCPP and ZFP; also measurements were made to assess CO_2R and cerebral autoregulation. If any complication arose during or after performing SGB, or in the event of unsuccessful block, the study was abandoned.

On the basis of previous studies,[19 20] we calculated that 20 patients would be required to detect a 20% change in the value of ZFP with 90% power ($\beta=0.9$) at a significance level of $\alpha<0.05$ assuming 30% coefficient of variation for the values. The data were analysed for normality in distribution using Anderson–Darling test. Since some data were not distributed normally all the changes in different variables before and after SGB were analysed using Wilcoxn's signed rank test; $P<0.05$ was considered to be significant.

Results

The 20 adult male patients who completed the study had a median (interquartile range) age of 28 (22, 39) yr and weight of 60 (56, 70) kg. Fourteen patients underwent right-sided and six left-sided SGB. The SGB was successful in all the patients. The presence of successful block was established between 10 and 20 min, and all the measurements during established block were taken between 15 and 30 min after the injection of local anaesthetic.

The haemodynamic measurements and $P\mathrm{E'_{CO_2}}$ before and after the block were stable, and no significant changes were noted (Table 1). The block caused a significant decrease ($P<0.05$) in MCAFV from a median (inter-quartile range) of 61 (53, 67) to 55 (46, 60) cm s^{-1}. Despite no change in MAP (Table 1), the eCPP increased significantly from 59 (51, 67) to 70 (60, 78) mm Hg ($P<0.01$); this was because of significant corresponding decrease in the downstream vascular tone as indicated by a decrease in ZFP from 32 (26, 39) to 25 (16, 30) mm Hg ($P<0.05$). The values of CO_2R [26 (18, 27)] and THRR [1.26 (1.14, 1.42)] did not change significantly after SGB [22 (17, 24) and 1.27 (1.13, 1.16) respectively] (Table 2).

Discussion

In this study, we have shown that, in patients with no central neurological disorder, SGB produced significant decreases in ZFP, a surrogate measure of cerebral vascular tone.[13–15] Our results suggest that, despite this decrease in the tone, the capacity of cerebral vessels to autoregulate, or to react to the changes in carbon dioxide, remained unchanged. We believe that these findings are in support of the recently suggested use of cervical sympathetic block to relieve cerebral vascular spasm in patients with subarachnoid haemorrhage,[6] and provide a starting point for further studies in patients with

Table 1 The median (interquartile range) values of HR, MAP, $P\mathrm{E'_{CO_2}}$, and MCAFV before and after SGB. $^*P<0.05$

	Before SGB	After SGB
HR (beats min^{-1})	72 (66, 76)	75 (60, 83)
MAP (mm Hg)	90 (85, 93)	92 (86, 100)
$P\mathrm{E'_{CO_2}}$ (kPa)	5.3 (5.1, 5.3)	5.3 (5.1, 5.3)
MCAFV (cm s^{-1})	61 (53, 67)	55 (46, 60)*

Table 2 The eCPP, ZFP, CO_2R, and THRR before and after SGB. The values are given as median (interquartile range)

	Before SGB	After SGB	P-value
eCPP (mm Hg)	59 (51, 67)	70 (60, 78)	0.002
CO_2R	26 (18, 27)	22 (17, 24)	NS
THRR	1.26 (1.14, 1.42)	1.27 (1.13, 1.16)	NS
ZFP	32 (26, 39)	25 (16, 30)	0.04

neurological disorders so that informed decisions can be made about the judicious use of SGB in clinical settings.

The decrease in cerebral vascular tone in this study can be explained on the basis of block of cervical sympathetic nerve activity. Anatomically, the stellate ganglion contains the cell bodies of the inferior cervical ganglion and the first thoracic sympathetic ganglion; therefore, the sympathetic post-ganglionic fibres that supply the upper arm, neck, and head. The sympathetic pre-ganglionic fibres that make synaptic connection with post-ganglionic neurons in the upper and middle cervical ganglia pass through the stellate ganglion.[7] The cerebral vasculature receives a non-adrenergic sympathetic nerve supply mainly through the fibres that originate in the cervical ganglion, accompany the carotid artery, and project into the ipsilateral cerebral hemisphere.[7–9] The vasodilatation of the cerebral vasculature induced by cervical sympathectomy has been shown to increase regional cerebral blood flow in healthy volunteers[9–11 21 22] and patients with subarachnoid haemorrhage.[6]

There are few reports on the changes in cerebral blood flow velocity following SGB, and the results are controversial. Ono and colleagues[11] reported that MCAFV did not change, but Ohinata and colleagues[12] found an increase in carotid and vertebral blood flow velocity after SGB. Treggiari and colleagues[6] reported that after cervical sympathetic block there was increased cerebral circulating time determined by angiography, indicating a decrease in cerebral blood flow velocity. The flow velocity through a blood vessel is directly proportional to the total blood flow and inversely proportional to the diameter of the vessel.[13] We have shown a small but significant decrease in MCAFV after SGB in our study. The changes in MCAFV can be taken to reflect the changes in cerebral blood flow only if it can be assumed that SGB had no effect on the diameter of MCA. This is one of the limitations of TCD methodology and this study.[13] It has been proposed that larger blood vessels (>50 μm in diameter) are under neural control whereas smaller ones are controlled chemically.[7 8 23] Therefore, it is

possible that in our study SGB may have changed MCA diameter and, under these circumstances, the cerebral blood flow would be normal or increased. However, the other variables that we studied, that is eCPP, ZFP, THRR, and CO_2R are unlikely to be affected by changes in vascular diameter as the calculation of these variables are based on the ratios (and not absolute values) of MCA flow velocities.

Estimation of ZFP as a surrogate measure of cerebral vascular tone has gained importance recently.[13] It has been shown that, in patients without raised intracranial pressure, cerebral vascular tone is the main determinant of ZFP or the effective downstream pressure of cerebral perfusion, so that eCPP=MAP–ZFP.[16] Thus, manipulation of ZFP may be an effective tool in modifying cerebral perfusion pressure without changing the MAP. A number of methods have been described to estimate eCPP and ZFP.[14 16 17 24] In the present study, we used a non-invasive method of estimating cerebral perfusion pressure and ZFP as described by Belfort and colleagues.[14] The method is a modification of previously validated method of Aaslid and colleagues.[24] It calculates the eCPP using simultaneously measured values of mean and diastolic MCFV and arterial pressure. A recent study has shown that this method is sensitive in assessing the changes in cerebral vascular tone induced by carbon dioxide.[17] The method has been validated experimentally for estimating the changes in ZFP,[15] and has been used recently to assess cerebral vascular tone in a clinical setting[25] or in the presence of vasoactive substances.[19 20] Our results suggest that SGB significantly decreases cerebral vascular tone and thus increases eCPP. These effects have not been reported before and may explain why previous studies have shown increased regional blood flow following SGB in healthy subjects,[9–11 21 22] and cervical sympathetic block benefited patients with subarachnoid haemorrhage and symptoms of cerebral insufficiency.[6]

In patients with neurological disorders, disturbances in cerebral vascular reactivity or cerebral autoregulation are associated with poor outcome.[13] Thus, it is important that any intervention that is intended for use in patients with neurological disorders should not impair cerebral vascular reactivity or cerebral autoregulation. We have shown that neither CO_2R nor THRR are significantly affected by SGB. We believe that this is an important result in the use of SGB in clinical setting. However, further studies will be required in patients with neurological disorders. From the physiological point of view, the role of sympathetic innervation in determining CO_2R or cerebral autoregulation is not clear. Using TCD during changes in carbon dioxide and a head up tilt/ganglion block to augment/diminish sympathetic tone, Jordan and colleagues[26] suggested that sympathetic tone may attenuate the carbon dioxide-induced increase in cerebral blood flow. On the other hand, sympathomimetics, such as ephedrine, dobutamine, and dopexamine, do not alter CO_2R in the healthy volunteers.[19] Our results suggest that sympathetic innervation of cerebral blood vessels has little role in determining the capacity of the vessels to react to the changes in carbon dioxide or to autoregulate.

The present study is limited in that it was performed only on the side of the SGB. This was because of a lack of equipment that could give simultaneous bilateral measurements of MCAFV. Therefore, the haemodynamic state on the contralateral side is not known. The study design allows patients to act as their own controls, but this is limited by the lack of data after the termination of effects of SGB. The return to the baseline of values of MCAFV, eCPP, and ZFP after the termination of effects of SGB would have strengthened our findings. However, we were limited by the logistics as we could not have confined these patients under investigation for an unpredictable time period. Another option would have been to take the measurements again in the following few days, which was not possible as the majority of our patients had travelled long distances. However, the changes in MCAFV, eCPP and ZFP were consistent in our patients and the changes in MCAFV waveform appeared only after appearance of signs of Horner's syndrome.

In conclusion, we have shown that SGB decreases cerebral vascular tone without affecting the capacity of cerebral blood vessels to react to the changes in carbon dioxide or to autoregulate. These results suggest that SGB may have a therapeutic role in patients where cerebral insufficiency can be attributed to cerebral vasospasm. Further studies of the role of SGB in preventing or treating cerebral vasospasm in subarachnoid haemorrhage are required.

References

1 Chaturvedi A, Dash HH. Sympathetic blockade for the relief of chronic pain. *J Indian Med Assoc* 2001; **99**: 698–703

2 Owen-Falkenberg A, Olsen KS. Continuous stellate ganglion blockade for reflex sympathetic dystrophy. *Anesth Analg* 1992; **75**: 1041–2

3 Floyd JB. Traumatic cerebral edema relieved by stellate ganglion anesthesia. *South Med J* 1987; **80**: 1328

4 Takano M, Takano Y, Sato I. Unexpected beneficial effect of stellate ganglion block in a schizophrenic patient. *Can J Anaesth* 2002; **49**: 758–9

5 Ullrich J. Stellate ganglion block under EEG control in the treatment of complicated cervical migraine. *J Neurol* 1975; **209**: 301–6

6 Treggiari MM, Romand JA, Martin JB, Reverdin A, Rufenacht DA, de Tribolet N. Cervical sympathetic block to reverse delayed ischemic neurological deficits after aneurysmal subarachnoid hemorrhage. *Stroke* 2003; **34**: 961–7

7 Tuor UI. Local distribution of the effects of sympathetic stimulation on cerebral blood flow in the rat. *Brain Res* 1990; **529**: 224–31

8 Edvinsson L. Neurogenic mechanisms in the cerebrovascular bed: autonomic nerves, amine receptors and their effects on cerebral blood flow. *Acta Physiol Scand Suppl* 1975; **427**: 1–35

9 Umeyama T, Kugimiya T, Ogawa T, Kandori Y, Ishizuka A, Hanaoka K. Changes in cerebral blood flow estimated after stellate ganglion block by single photon emission computed tomography. *J Auton Nerv Syst* 1995; **50**: 339–46

10 Nitahara K, Dan K. Blood flow velocity changes in carotid and vertebral arteries with stellate ganglion block: measurement by

magnetic resonance imaging using a direct bolus tracking method. *Reg Anesth Pain Med* 1998; **23**: 600–4

11 Ono K, Kaneko T, Iwatsuki N, *et al.* The effects of stellate ganglion block and oxygenation on head blood flow. *Pain Clin* 1989; **10**: 211–6

12 Ohinata Y, Makimoto K, Kawakami M, Haginomori S, Araki M, Takahashi H. Blood flow in common carotid and vertebral arteries in patients with sudden deafness. *Ann Otol Rhinol Laryngol* 1997; **106**: 27–32

13 Moppett IK, Mahajan RP. Transcranial Doppler ultrasonography in anaesthesia and intensive care. *Br J Anaesth* 2004; **93**: 710–24

14 Belfort MA, Saade GR, Yared M, *et al.* Change in estimated cerebral perfusion pressure after treatment with nimodipine or magnesium sulphate in patients with preeclampsia. *Am J Obstet Gynecol* 1999; **181**: 402–7

15 Athanassiou L, Hancock SM, Mahajan RP. Doppler estimation of zero flow pressure during changes in downstream pressure in a bench model of a circulation using pulsatile flow. *Anaesthesia* 2005; **60**: 133–8

16 Weyland A, Buhre W, Grund S, *et al.* Cerebrovascular tone rather than intracranial pressure determines the effective downstream pressure of the cerebral circulation in the absence of intracranial hypertension. *J Neurosurg Anesth* 2000; **12**: 210–6

17 Hancock SM, Mahajan RP, Athanassiou l. Non-invasive estimated cerebral perfusion pressure and zero flow pressure in healthy volunteers: the effects of changes in end-tidal carbon dioxide. *Anesth Analg* 2003; **96**: 847–51

18 Mahajan RP, Civill G, Simpson EJ. Reliability of the transient hyperemic response test in detecting changes in cerebral autoregulation induced by the graded variations in end-tidal carbon dioxide. *Anesth Analg* 1998; **87**: 843–9

19 Moppett IK, Wild MJ, Sherman RW, Latter JA, Miller K, Mahajan RP. Effects of ephedrine, dobutamine and dopexamine on cerebral haemodynamics: transcranial Doppler studies in healthy volunteers. *Br J Anaesth* 2004; **92**: 39–44

20 Hancock SA, Eastwood JR, Mahajan RP. Effects of inhaled nitrous oxide 50% on estimated cerebral perfusion pressure and zero flow pressure in healthy volunteers. *Anaesthesia* 2005; **60**: 129–32

21 Iwama H. A study of cerebral circulation following cervical sympathetic block. *Masui* 1992; **41**: 1250–9

22 Okubo Y, Ogata H. Brain blood volume measured with near infrared spectroscopy increased after stellate ganglion block. *Masui* 1995; 3; **44**: 423–7

23 Gotoh F, Fukuuchi Y, Amano T, *et al.* Comparison between pial and intraparenchymal vascular responses to cervical sympathetic stimulation in cats. Part I. Under normal resting conditions. *J Cere Blood Flow Metab* 1986; **6**: 342–7

24 Aaslid R, Lunder T, Lindegaard K-F, Nornes H. Estimated cerebral perfusion pressure from arterial blood pressure and transcranial Doppler recordings. In: Miller JD, Teasdale GM, Rowan JO, *et al.* eds. *Intracranial Pressure VI*. Berlin: Springer Verlag, 1986; 226–9

25 Sherman RW, Bowie RA, Henfrey MM, Mahajan RP, Bogod D. Cerebral haemodynamics in pregnancy and pre-eclampsia as assessed by transcranial Doppler ultrasonography. *Br J Anaesth* 2002; **89**: 687–92

26 Jordan J, Shannon JR, Diedrich A, *et al.* Interaction of carbon dioxide and sympathetic nervous system activity in the regulation of cerebral perfusion in humans. *Hypertension* 2000; **36**: 383–8