Sys Rev Pharm 2021; 12(4): 123-124
A multifaceted review journal in the field of pharmacy
E-ISSN 0976-2779 P-ISSN 0975-8453

Research Article

Finding the Effect of Minor Surgery Under Propofol Anaesthesia on Brain BDNF in Pakistan

Muhammad Zeeshan Pasha[1*], Naima Khan[2], Ifra Shafique[3]

[1]HO, Allied Hospital, Faisalabad, Pakistan
[2]WMO, Basic Health Unit, Mazharabad, Pakistan
[3]WMO, Basic Health Unit, Arifwala, Pakistan

Article History: *Submitted: 06.05.2021* *Accepted: 13.05.2021* *Published: 20.05.2021*

ABSTRACT

Introduction: Brain Derived Neurotrophic Factor (BDNF) is known to support neuronal survival, differentiation and several forms of synaptic plasticity, therefore BDNF plays an important role in synaptogenesis of the mammalian brain.

Objectives: The main objective of the study is to analyse the effect of minor surgery under propofol anaesthesia on brain BDNF and cognition.

Material and methods: This descriptive study was conducted in Allied Hospital Faisalabad during July 2019 to March 2020. Remembering that adult plasma BDNF concentrations are correlated with age, gender, and Body Mass Index (BMI), we planned to choose only male patients, from 40 to 60 years old, and with a BMI of 20 to 30.

Results: The data was collected from 40 patients. In group A, BDNF plasma concentrations were 196.1 ± 36.7 pg/ml at baseline and decreased to 120.9 ± 17.6 pg/ml 15 minutes after anesthesia induction. At the time point of skin closure, the BDNF plasma concentration increased to 167.3 ± 19.9 pg/ml and remained high (154.9 ± 28.6 pg/ml) 5 minutes after extubation. Twenty-four hours after the operation, the BDNF plasma concentrations fell below the baseline (126.8 ± 28.2 pg/ml). In group B, the baseline BDNF plasma concentration was 173.8 ± 40.0 pg/ml, which was comparable with that in group A.

Conclusion: It is concluded that general anesthesia could reverse the reduced BDNF plasma concentrations caused by anesthetics during and 24 hours after surgery.

Keywords: Brain Derived Neurotrophic Factor; Propofol anaesthesia; Plasma concentrations

***Correspondence:**

Muhammad Zeeshan Pasha, House Officer, Allied Hospital, Faisalabad, Pakistan, E-mail: Muhammadzeeshanpasha@gmail.com

INTRODUCTION

Brain Derived Neurotrophic Factor (BDNF) is known to support neuronal survival, differentiation and several forms of synaptic plasticity, therefore BDNF plays an important role in synaptogenesis of the mammalian brain. Synthesis, secretion and actions of BDNF are largely mediated by neuronal network activity and in turn, activity dependent secretion of BDNF caninduce both rapid and long-term changes in synaptic efficacy. In this field, both decrease and overexpression of BDNF in the forebrain might have a detrimental effect on learning and memory in rodents (Karege F, *et al.*, 2002).

As a member of the neurotrophin family of growth-promoting proteins, Brain-Derived Neurotrophic Factor (BDNF) plays an important role in neuronal survival, axon growth, and synaptic plasticity. In rodents, BDNF is highly correlated with learning, memory, and other advanced neuronal functions (Balkowiec A and Katz DM, 2002). Elevation of BDNF in the Central Nervous System (CNS) may significantly attenuate neuronal injuries caused by ischemia and also be beneficial for the treatment of degenerative diseases. Importantly, BDNF is detectable in blood, and a positive correlation has been found between serum and cortical BDNF concentrations (Goggi J, *et al.*, 2003). Thus, determinations of serum BDNF concentrations could help to investigate changes of BDNF concentrations in the CNS.

Anesthetics are known to inhibit neuronal activity in the CNS (Janke EL and Samra S, 2006) and cause sedation, amnesia, and post-operative cognitive dysfunction. Further studies have shown that such drugs could inhibit the release of BDNF from cortical neurons (Vutskits L, *et al.*, 2008). It has been proven clinically that perioperative use of anesthetics could lead to decreased plasma concentrations of BDNF in patients.

The highly selective α2-adrenoceptor agonist, Dexmedetomidine (DEX) has marked effects on hypnosis, anti-anxiety, and analgesia (Bhana N, *et al.*, 2000). Recent animal studies have revealed that DEX also has neuro-protective effects, due in part to the elevation of BDNF concentrations in the cortex and hippocampus. However, in humans, the impact of DEX on BDNF concentrations remains elusive.

OBJECTIVES

The main objective of the study is to analyse the effect of minor surgery under propofol anaesthesia on brain BDNF and cognition.

MATERIAL AND METHODS

This descriptive study was conducted in Allied Hospital Faisalabad during July 2019 to March 2020. Remembering that adult plasma BDNF concentrations are correlated with age, gender, and Body Mass Index (BMI), we planned to choose only male patients, from 40 to 60 years old, and with a BMI of 20 to 30.

Data collection

Patients with a history of alcohol abuse or use of antipsychotic drugs, as well as those with underlying organ disease or psychiatric illness, were not considered. Patients received 5 mg diazepam orally, 30 minutes before entering the operating room. In the waiting room, they were randomly allocated to one of the two groups by drawing lots; lidocaine cream was applied to the skin of each patient's arms in order to attenuate the pain of puncture. Two intravenous catheters were inserted, one in each of the patient's arms; one was used exclusively for the measurement of BDNF plasma concentrations and the other for anesthesia and volume management. After entering the operating room, 250 mL of Ringer's lactate was administered to

ensure rapid volume expansion. Routinely, we monitored (Dash 3000, GE Company, Milwaukee, WI, US) a five-lead ECG, non-invasive blood pressure, heart rate and peripheral capillary oxygen saturation. BIS Index was used to measure the depth of anesthesia.

Biochemical analysis

Five venous blood samples (5 mL each) were drawn from each patient: at T1 (baseline), T2 (15 minutes after intubation before the operation was started), T3 (after skin closure), T4 (10 minutes after extubation in the PACU), and T5 (24 hours after surgery). Blood samples were placed in Ethylene Diamine Tetraacetie Acid (EDTA) tubes and centrifuged for 15 minutes at 3,000 rpm. The plasma obtained was stored at -70°C until required for subsequent analysis of its contents. BDNF plasma concentrations were measured by Enzyme-Linked Immunosorbent Assays (ELISA).

Statistical analysis

The data was collected and analysed using SPSS version 20. All the values were expressed in mean and standard deviation.

RESULTS

The data was collected from 40 patients. In group A, BDNF plasma concentrations were 196.1 ± 36.7 pg/ml at baseline and decreased to 120.9 ± 17.6 pg/ml 15 minutes after anesthesia induction. At the time point of skin closure, the BDNF plasma concentration increased to 167.3 ± 19.9 pg/ml and remained high (154.9 ± 28.6 pg/ml) 5 minutes after extubation. Twenty-four hours after the operation, the BDNF plasma concentrations fell below the baseline (126.8 ± 28.2 pg/ml). In group B, the baseline BDNF plasma concentration was 173.8 ± 40.0 pg/ml, which was comparable with that in group A. Fifteen minutes after anesthesia induction, the BDNF concentration tended to decrease (167.3 ± 36.8 pg/ml). However, it was still higher than in group A. Twenty-four hours after the operation, BDNF plasma concentrations were maintained at 176.0 ± 26.9 pg/ml, which was higher than in group A. Both at skin closure and 10 minutes after the extubation, BDNF plasma concentrations increased to 165.3 ± 34.9 pg/ml and 164.8 ± 29.4 pg/ml, but there were no differences between the two groups *(Tables 1 and 2)*.

Table 1: BDNF plasma concentrations

	Group A (n=19)	Group B (n=18)
T1	196.1 ± 36.7 (141.4-268.6)	173.8 ± 40.0 (113.7-274.6)
T2	120.9 ± 17.6 (92.5-159.5)	167.3 ± 36.8a (109.4-264.9)
T3	167.3 ± 19.9 (113.6-192.5)	165.3 ± 34.9 (119.2-255.6)
T4	154.9 ± 28.6 (107.8-194.5)	164.8 ± 29.4 (114.2-254.4)
T5	126.8 ± 28.2 (90.4-190.4)	176.0 ± 26.9a (149.4-260.4)

Table 2: Duration of surgery, amount of bleeding and volume therapy, and the dose of induction anesthetics

	Group A	Group B
Duration of surgery (min)	109.3 ± 7.1	104.6 ± 10.6
Bleeding (mL)	102.1 ± 10.3	103.9 ± 9.2
Volume therapy (mL)	1442.1 ± 161.0	1436.1 ± 173.9
Propofol for induction (mg)	92.1 ± 15.1	36.9 ± 6.0a
Sulfentanil for induction (mg)	36.8 ± 5.06	20.4 ± 5.1a

DISCUSSION

BDNF in blood could readily be detected, and according to previous studies it is highly correlated with BDNF concentrations in the brain. It is mainly stored in platelets and may also be synthesized and secreted by visceral epithelia, vascular endothelia, and inflammation cells (Yan M, *et al.*, 2011). There is evidence to suggest that intravenous administration of BDNF labeled with 125I can result in entry into the CNS to promote neuron protection and regeneration, and after intracerebroventricular injection of exogenous BDNF an efflux of BDNF from brain to blood was also detected (Eser O, *et al.*, 2008). Clinically depressed patients were found to have lower levels of BDNF, both in the cortex and in plasma. In healthy individuals, Bernward Winter demonstrated that the improvement of short-term learning was highly correlated with an elevation in the serum concentration of BDNF. It appears that elevation of blood concentrations of BDNF could contribute to a better neural function. Therefore, one can suppose that if DEX could increase BDNF concentrations in plasma, it might produce neurological benefits (Yan M, *et al.*, 2011).

Anesthetics could inhibit the release of BDNF from cortical neurons. This reduction of plasma BDNF concentrations was proven to cause BDNF-dependent neuroapoptosis in the neonatal rat brain, which indicated that the BDNF signal was crucial to the CNS and could partly explain the mechanisms of neurotoxicity induced by anesthetics (Dahmani S, *et al.*, 2006; Lommatzsch M, *et al.*, 2005).

CONCLUSION

It is concluded that general anesthesia could reverse the reduced BDNF plasma concentrations caused by anesthetics during and 24 hours after surgery. Whether the elevation of plasma BDNF is beneficial to the patient remains to be unequivocally established.

REFERENCES

1. Karege F, Schwald M, Cisse M. Postnatal developmental profile of brain-derived neurotrophic factor in rat brain and platelets. Neurosci Lett. 2002; 3: 261-264.
2. Balkowiec A, Katz DM. Cellular mechanisms regulating activity-dependent release of native brain-derived neurotrophic factor from hippocampal neurons. J Neurosci. 2002; 23: 10399-10407.
3. Goggi J, Pullar IA, Carney SL, Bradford HF. The control of [125I] BDNF release from striatal rat brain slices. Brain Res. 2003; 967: 201-209.
4. Vutskits L, Lysakowski C, Czarnetzki C, Jenny B, Copin JC, Tramèr MR. Plasma Concentrations of brain-derived neurotrophic factor in patients undergoing minor surgery: a randomized controlled trial. Neurochem Res. 2008; 33: 1325-1331.
5. Janke EL, Samra S. Dexmedetomidine and neuroprotection. Seminars in Anesthesia, Perioperative Medicine and Pain. 2006; 25: 71-76.
6. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs. 2000; 59: 263-268.
7. Yan M, Dai H, Ding T, Dai A, Zhang F, Yu L, *et al.* Effects of dexmedetomidine on the release of glial cell line-derived neurotrophic factor from rat astrocyte cells. Neurochem Int. 2011; 58: 549-557.
8. Eser O, Fidan H, Sahin O, Cosar M, Yaman M, Mollaoglu H, *et al.* The influence of dexmedetomidine on ischemic rat hippocampus. Brain Res. 2008; 1218: 250-256.
9. Dahmani S, Rouelle D, Gressens P, Mantz J. Effect of dexmedetomidine on brain derived neurotrophic factor expression in rat hippocampal slices. Anesthesiology. 2006; 105: 681.
10. Lommatzsch M, Zingler D, Schuhbaeck K, Schloetcke K, Zingler C, Schuff-Werner P, *et al.* The impact of age, weight and gender on BDNF levels in human platelets and plasma. Neurobiol Aging. 2005; 26: 115-123.