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General anaesthesia and TrkA mRNA in peripheral blood mononuclear cells

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EDITOR:

Surgery and anaesthesia are known to compromise immune functions. Induction of general anaesthesia even before skin incision reportedly increases plasma concentration of proinflammatory cytokines (tumour necrosis factor (TNF)-α, interleukin (IL)-1β) and also induces TNF-α and IL-1β release from blood cells [1,2]. On the other hand, nerve growth factor (NGF) and its high-affinity receptor (tropomyosin-receptor kinase A, TrkA) are involved in the immune system and most inflammatory cells produce NGF and express TrkA [3–5]. NGF induces the production of TNF-α and IL-1β in macrophages under activation of TrkA [6,7]. Conversely, proinflammatory cytokines promote NGF synthesis in inflammatory tissues [4]. Therefore, NGF and proinflammatory cytokines would co-operate with each other to modulate immune responses after induction of general anaesthesia without surgical stress and trauma. In this study we tested our hypothesis that induction of general anaesthesia would change mRNA expressions of either NGF or TrkA in peripheral blood mononuclear cells (PBMC) before surgery, using real-time PCR (RT-PCR).

After obtaining approval from the institutional review board, we obtained written informed consent from eight ASA I or II patients aged 50–70 yr, who were scheduled for elective abdominal or thoracic surgery. None of the patients received premedication. General anaesthesia was induced with i.v. fentanyl 0.2 mg and propofol 2–2.5 mg kg^{-1} and tracheal intubation was facilitated by vecuronium bromide 0.15 mg kg^{-1}. Anaesthesia was maintained with propofol 5–7 mg kg^{-1} h^{-1} before skin incision. After arterial catheter was inserted into the radial artery, a blood sample (10 mL) was obtained before induction of anaesthesia. An additional blood sample was also obtained 20 min after induction of anaesthesia before skin incision. Human PBMC were isolated from blood by Pancoll (Funakoshi Co., Tokyo, Japan) gradient centrifugation. Briefly, heparinized whole blood was diluted to a volume of 20 mL with phosphate buffered saline 10 mL and underlayered with 15 mL of Pancoll. The 50 mL tube was centrifuged after which PBMC were collected at the interface layer and were transferred to a 15 mL tube. PBMC were collected from this tube and three volumes of phosphate buffered saline were added. The tube was gently inverted 20 times and then centrifuged. PBMC were drawn off by pipette and counted for recovery and viability using 0.4% Trypan blue (Sigma, St Louis, MO, USA) and then stored at −80°C. After total RNA was extracted from PBMC by using RNeasy Protect Mini Kit (QIAGEN, Hilden, Germany), cDNA was synthesized using ExScript RT reagent kit (TAKARA BIO Inc., Tokyo, Japan) according to manufacturer's instructions. We purchased primers of NGF, TrkA and β_2-microglobulin for Taqman Gene expression assays (Applied Biosystems, Tokyo, Japan). RT-PCR was performed using MiniOpticon (Bio-Rad, Hercules, CA, USA). The expression levels were normalized to β^2-microglobulin mRNA. Data were analysed by paired *t*-test. The statistical significance was established at the $P < 0.05$ level.

Although the threshold cycle (C_t) values for TrkA in RT-PCR analysis were 29–34, C_t values for NGF were over 37 or undetected, suggesting that NGF mRNA were not detectable in PBMC in this study. Relative expression level of TrkA mRNA in PBMC was significantly increased from 1.00 to 1.40 ± 0.36 (mean ± SD) after induction of anaesthesia, compared to that before induction ($P < 0.05$).

Induction of general anaesthesia increased TrkA mRNA expression in PBMC before skin incision. TrkA mRNA is expressed in human PBMC and TrkA protein is detected in natural-killer cells, monocytes and T-cells [5]. As TrkA has a role in both T- and B-cell physiology and influences

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cytokine production [3,5], up-regulation of TrkA mRNA in PBMC might play a role in the modulation of the immune system after induction of anaesthesia. Further study is needed to investigate the cause of change in TrkA expression in PBMC induced by general anaesthesia.

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Perioperative ulnar neuropathy following shoulder surgery under combined interscalene brachial plexus block and general anaesthesia

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Permanent neurological deficit, as a direct result of regional nerve blocks, is rare. Some physicians remain sceptical concerning the benefits of regional anaesthesia, and there is a tendency to instinctively attribute the development of a perioperative neuropathy to the performance of a contemporaneous regional nerve block. If other remedial causes are not considered, a delay in appropriate management may lead to a permanent, devastating injury. We describe a case of debilitating, permanent ulnar neuropathy that occurred following routine arthroscopic shoulder surgery performed under combined interscalene brachial plexus block and general anaesthesia. A diagnosis of ulnar neuropathy localized to the elbow secondary to postoperative immobilization of the limb in elbow flexion was eventually made following imaging and electrodiagnostic studies.

Interscalene brachial plexus block affords effective anaesthesia and analgesia for both arthroscopic and open shoulder surgery. Unease concerning the risk of neurological injury may result in this technique being underused. When a neurological complication develops after a regional technique has been performed, there is an instinct to attribute the injury to the anaesthetic technique and other causes may be overlooked. This can result in a delay in remedial management, apprehension on behalf of the anaesthetist and an unnecessary reform in anaesthetic practice.

This article uniquely highlights the importance of prompt investigation and accurate identification, where possible, of the aetiology, type and site of nerve injury, as timely surgical intervention for some lesions can effect a significant improvement in functional outcome and prognosis. Furthermore,

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