Effect of different concentrations of morphine and tramadol on the differentiation of human helper T cells in vitro

Editor—We investigated the effect of different concentrations of morphine and tramadol on the differentiation of human adult helper T cells in vitro. Twenty outpatients without any immune diseases were selected and their peripheral blood was collected. Whole blood or peripheral blood mononuclear cells (PBMCs) were pretreated with different concentrations of morphine or tramadol for 48 h, while the control group received neither. The ratio of CD4+IFN-γ+IL-2+CD4+IL-4+IL-10+ was analysed by three-color flow cytometry. The intracellular cytokines, after stimulation with PMA and ionomycin (Ion), were detected by trace whole blood technology. The CD4+CCR5+ and CD4+CCR3+ cells in PBMCs were counted in order to observe the imbalance of Th1/Th2. After treatment with morphine or tramadol, the number of Th2 increased significantly and the ratio of Th1/Th2 decreased dramatically in both groups. At the same time the number of CD4+IFN-γ+IL-2+ cells decreased and CD4+IL-4+IL-10+ cells increased sharply as compared with the control group. Both morphine and tramadol can direct Th0 cells toward Th2, especially morphine. The Th2 redirection, as well as the changes in cytokines, showed a dose dependent fashion in both drugs.

Although tissue wound or seriously surgical stress is thought to be one of the most important reasons for immune suppression, anaesthetic agents used in these patients also play a part in the modulation of immune response. There is reasonable evidence that analgesic agents can inhibit immune function, especially opioids. Our study demonstrated a remarkable Th2 differentiation after pretreatment with morphine or tramadol. IL-4 and IL-10 elevated significantly while IL-2 and IFN-γ decreased significantly compared with control groups. We also found that the suppression of cell-mediated immunity was dose dependent. It indicates that excessively high concentration of these drugs should be avoided in clinical applications in order to maintain a healthy Th1/Th2 balance.

Nair and colleagues reported that morphine could modulate mice T-helper cell differentiating in vitro, resulting in the rise of Th2 subsets that suppressed cell-mediated immunity. Our results provided evidence that both morphine and tramadol could direct human T-helper cell into Th2 and the effect of morphine was apparently more powerful than tramadol. Both drugs showed a dose-dependent Th2 differentiation response. T-helper cell differentiation is controlled by a number of factors. Th2 differentiation directed by morphine or tramadol was closely associated with the levels of corresponding cytokines, which was the cause of the immune alteration.

To summarize, our research indicated that after pretreatment with morphine or tramadol in vitro, human T-helper cells tended to differentiate into Th2 cells.

Y.-N. Qian*, W.-J. Jin, L. Wang, H.-J. Wang
Nanjing, China
*E-mail: yanning_qian@yahoo.com.cn or qianyn@jlonline.com


Laryngospasm during subarachnoid block

Editor—The case report by Subramani and Paul was quite perplexing. The authors proposed that the laryngospasm was secondary to an increased parasympathetic tone resulting from the subarachnoid block. There are a few points that the authors have not clarified. What was the method by which they tested the level of sensory blockade after injecting the drug in the subarachnoid space? Why did the patient recover rapidly after the stimulus (removal of dressing) was removed? How does an increased parasympathetic tone as a result of subarachnoid blockade explain the further uneventful course? It seems improbable that the laryngospasm responded to atropine and ephedrine.

I would like to put forth a rather simplistic explanation for the laryngospasm—a mere response to pain experienced by the patient. An apparently ‘adequate’ (in extent) spinal may fail because the block has been tested using a stimulus of significantly different modality or intensity than the planned surgery. A simple single stimulus such as pinprick or cold may be blocked, but spinal cord mechanisms may result in repeated stimuli (temporal summation) or stimuli from adjacent regions (spatial summation), evoking pain. The subarachnoid block was performed in the right lateral position. The onset of bilateral block has been shown to be slower with blocks performed in the lateral position. The authors have not made it clear if the block until T11 was bilateral. All these factors alone or in combination, can explain why the patient had laryngospasm.

M. G. Chincholkar
Whitehaven, UK
E-mail: cmahindra@gmail.com

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Reducing allogeneic transfusion in cardiac surgery

Editor—I welcome the study by Diprose and colleagues comparing aprotinin and tranexamic acid in patients undergoing first time cardiac surgery. The authors have nicely demonstrated that aprotinin used in addition to intraoperative cell salvage is the most efficacious pharmacological therapy for reducing patient
exposure to allogeneic transfusion. One of the most important factors in making blood conservation a reality during cardiac surgery, is the acceptance of normovolaemic haemodilution. However, the transfusion trigger during cardiac surgery continues to remain controversial.2 We have earlier shown that cell saver in combination with intraoperative autologous blood donation decreased transfusion requirements in a group of patients with a mean body weight of 45 kg.3 Seventy-eight per cent of these patients undergoing valve surgery did not require any blood transfusion. This was possibly attributable to acceptance of a haematocrit of 15% on bypass and 25% after bypass. We have also compared cell saver and low dose aprotinin in patients undergoing valve surgery and found them to be comparable in terms of reducing blood transfusion requirement.4 Aprotinin helps by decreasing the postoperative bleeding, whereas the cell saver helps by making the patient’s own blood available for transfusion.

While these blood conservation strategies can substantially decrease the transfusion of allogeneic red blood cells and coagulation products, the clinical application of these reports should be carefully chosen. The important concerns related to the use of aprotinin include graft occlusion in patients undergoing coronary artery bypass grafting (CABG), anaphylactic reaction, and risk of impaired renal function. The risk of graft thrombosis is real and well documented.5 6 As regards cell saver, there is some concern about transfusion of cytokines through autologous shed blood.7 In addition, these are expensive techniques and the use of cell saver also requires services of a trained technician. It seems that preoperative risk stratification is essential to allow for more rational resource allocation of costly blood conservation strategies and blood bank resources. One such model has been recently developed.8 According to this model, independent predictors of blood product usage in CABG patients were preoperative haemoglobin 12.0 g or less, emergent operation, renal failure, female sex, age 70 yr or older, left ventricular ejection fraction 0.40 or less, redo procedure and low body surface area. Since with careful surgery homologous blood transfusion can be avoided in most patients undergoing primary CABG, we prefer to use aprotinin only in patients who have increased risk of bleeding such as those on aspirin or thrombolytic therapy, redo surgery or those having rare blood type. A combined approach, as described by Diprose and colleagues can also be considered in these patients.

D. K. Tempe
New Delhi, India
E-mail: tempedeepak@hotmail.com

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