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Other aspects of nitrous oxide-related neuromyelopathy



The point is well made that the “work-up” of suspected nitrous oxide (NO₂) myelopathy should include, not only serum vitamin B12 (i.e., cobalamin) measurement, but also documentation of serum homocysteine, methylmalonic acid (MMA), and folate levels [1]. The rationale is that some patients in whom cobalamin derangements are implicated in the aetiopathogenesis of NO₂-related neurotoxicity may, nevertheless, have serum cobalamin levels within the normal range [2]. In one such patient (case 1) NO₂-related neuropathy was initially mistaken for Guillain-Barre syndrome, arguably because there was no concurrent spinal cord demyelination and, hence, no abnormality detected on magnetic resonance imaging (MRI) of the entire spinal cord. On the basis of the provisional diagnosis of Guillain-Barre syndrome that patient was prescribed a 5 days course of intravenous immunoglobulin. The correct diagnosis was made only after eliciting a history of NO₂ recreational use, and also after documentation of a serum MMA level of 29,653 mmol/l (normal < 280 mmol/l). He gradually improved after he was prescribed vitamin B12 injections [2]. In the same series there was a patient (case 3), with NO₂-related myelopathy, in whom a normal serum vitamin B12 level coexisted with an elevated serum homocysteine level [2]. That patient experienced a complete recovery after a course of vitamin B12 injections [2].

NO₂-related neuropathy in the absence of abnormalities on MRI imaging of the spinal cord has been documented in anecdotal reports [2–4] and also in a retrospective study of 33 patients evaluated in one institution over a period of 10 years [5]. In the latter study the coexistence of myelopathy was confirmed using clinical manifestations or T2 hyperintensity on spinal cord MRI. Fifteen patients were evaluated by spinal cord MRI, among whom seven had T2 hyperintensity of the posterior columns. Overall 20

patients exhibited clinical features or MRI abnormalities suggestive of myelopathy [5]. A pseudo Guillain-Barre presentation similar to the one in case 2 [2] was documented in one anecdotal case report of NO₂ neurotoxicity [6]. This was a patient who initially experienced flaccid bilateral foot drop and sensory deficits in a stocking distribution. MRI of the lumbar spine was normal. The cerebrospinal fluid showed a protein concentration of 72 mg/dl and no pleocytosis. Within 24–48 h paresthesiae ascended to the nipple line, and he experienced clumsiness of fine finger movements. MRI of the cervical spine was then performed, and this showed focal nonenhancing posterior T2 lesion at C2–C6. He experienced significant improvement after a course of vitamin B12 injections [6].

The normal levels of serum vitamin B12 documented in cases 1 and 3 [2], and in other anecdotal reports [3,4] exemplify so-called “functional” cobalamin deficiency, the latter characterised by coexistence of normal serum cobalamin levels and accumulation of substrates of the reactions catalysed by cobalamin, namely, MMA and homocysteine [2–4]. In all subtypes of cobalamin deficiency the toxicity of NO₂ is mediated by the inactivation of vitamin B12 as a result of oxidation by NO₂. This leads to a reduction in the conversion of homocysteine to methionine [3], the latter a precursor of S-adenosylmethionine, which is necessary for myelin production in the central and in the peripheral nervous system [7,8].

Patients at risk of NO₂-related myelopathy are, reportedly, also those in whom NO₂ is administered as a general anaesthetic in the presence of predisposing factors for cobalamin deficiency, such as old age, inflammatory bowel disease, and vegetarianism [1]. Previous bariatric surgery should also be included in that list, given the fact that it, too, is a risk factor for cobalamin deficiency [9].

When NO₂ is administered as a general anaesthetic NO₂-related neurotoxicity may also occur in the presence of 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency [10]. This occurred in a 3 month old child who had good physical status prior to administration of NO₂ as a general anaesthetic, the latter for the purpose of enabling resection of a mass in the left leg. On the 25th postoperative day he experienced seizures, and was found to be hypotonic and arreflexive. The plasma homocysteine level was elevated at 0.6 mg/decilitre (normal value < 0.01) and the vitamin B12 level was normal. Genomic DNA-sequence analysis revealed that MTHFR deficiency was caused by a novel MTHFR mutation which changes the conserved methionine at position 581 of the enzyme to isoleucine. The consequence was that NO₂-related inactivation of methionine synthetase was superimposed on MTHFR deficiency, the combined derangements giving rise to an excessive accumulation of homocysteine [10], which, in turn, has well documented neurotoxic potential in its own right [11,12].

Misgivings that anesthesiologists have about using NO₂ as an anaesthetic agent have been articulated in a recent review which concluded that it was incumbent upon anesthesiologists to evaluate their patients for risk factors that might predispose them to NO₂-related myelopathy, and to avoid NO₂ if such risk factors are present [13].

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Novel information and communication technology system to improve surge capacity and information management in the initial hospital response to major incidents



The initial response of local hospitals to major incidents involving natural and anthropogenic hazards is crucial [1–6]. When a major incident is recognized by a hospital's headquarters, it is necessary to

increase medical surge capacity and capability before external supports arrive. Thus, the hospital must communicate a variety of information to multiple staff, including those who are off-duty [1, 7]; staffing is key to increasing surge capacity [8–12].

Few investigations of emergency staffing have been conducted [13]. Hospitals have reported using an emergency telephone contact system—a so-called “phone tree”—or automatic assembly according to predetermined criteria [14]. However, phone trees necessitate direct verbal communication and the information is only communicated to one staff member at a time. In the automatic assembly method, health-care providers are required to collect the necessary information by themselves. Moreover, subsequent information management, such as personnel assignment after emergency staffing, is an essential element in the initial hospital response. Despite this, rarely have effective information management systems been developed [8, 15].

The recent development of information and communication technology (ICT) has been remarkable [16–19]. ICT could be used for emergency staffing and subsequent information management [15]. Specifically, we hypothesized that, compared with existing methods, an ICT system would enable prompter and more accurate information transfer with more effective utilization. We developed a new ICT system with three functions: (1) simultaneous notification, (2) response and arrival status management, and (3) personnel assignment and verified its effectiveness in simulation tests (Figs. 1–2 and details [Supplementary data]).

In simulation test 1 (information transmission), our ICT system transmitted information to the staff and back to headquarters significantly more rapidly than the conventional phone tree approach ($P < 0.01$; Fig. 3). The ICT system transmitted information to study participants significantly more accurately than the phone tree approach ($P < 0.05$; Fig. 4A–C).

In simulation test 2 (the information management of the personnel assignment function), all study participants successfully completed

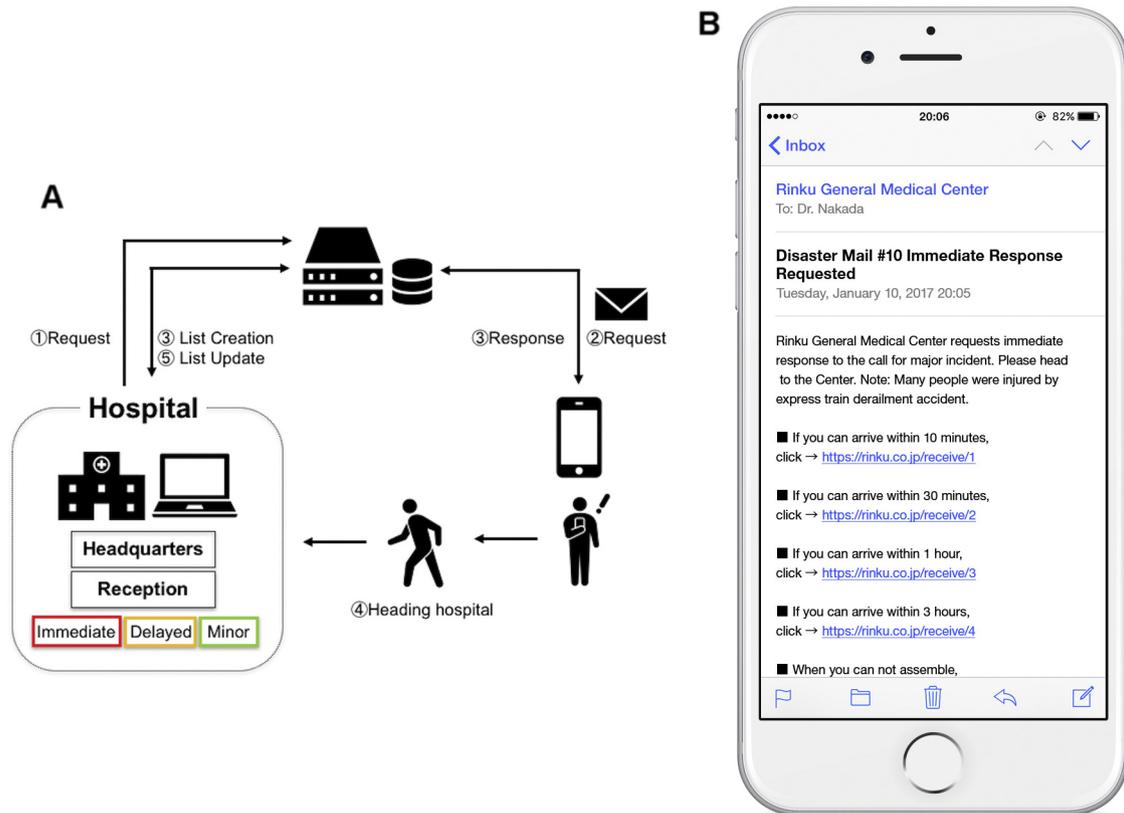


Fig. 1. Panel A: Schematic diagram of procedure. A headquarters in the hospital activates the system by filling in a request form. The request is securely transferred to a cloud server via the internet. The cloud-based software automatically creates an e-mail based on the content of the request; it then sends the e-mail to staff mobile phones. Responses from staff outside the hospital are transferred to the cloud server, where a record of current response status is created and updated at all times. After staff members arrive, the ICT system can add information regarding their assigned area to aid personnel assignment. Panel B: Received mail text in mobile phone of staff outside hospital.