Clinical Reports

Use of propofol for the prevention of chemotherapy-induced nausea and emesis in oncology patients

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Nausea and vomiting associated with antineoplastic chemotherapy are distressing and may keep patients from complying with chemotherapy protocols. No drug has emerged among many as an effective antiemetic. It has been speculated that propofol may have intrinsic antiemetic properties. We report the use of low-dose continuous infusion propofol in three oncology patients to treat chemotherapy-associated nausea and vomiting. A bolus of 0.1 mg · kg^{-1} followed by a continuous infusion of 1 mg · kg^{-1} · hr^{-1} was effective in both prevention and treatment of nausea and vomiting. All three patients were alert, reported low nausea scores by visual analogue scale, and had no episodes of vomiting. When the infusion was discontinued, nausea and vomiting were noted in two patients. Propofol, given in a subanaesthetic infusion, was safe and effective as an antiemetic in these three patients.

Les nausées et vomissements associés à la chimiothérapie antinéoplasique sont affligeants et peuvent empêcher les patients d'être fidèles aux protocoles de chimiothérapie. Aucun médicament ne s'est avéré être un antiémétique efficace. Il a été suggéré que le propofol peut avoir des propriétés intrinsèques antiémétiques. Nous rapportons l'utilisation d'une perfusion continue de propofol à bas dosage, chez trois patients oncologiques, afin de traiter les nausées et vomissements associés à la chimiothérapie. Un bolus de 0,1 mg · kg^{-1} suivi d'une infusion continue de 1 mg · kg^{-1} · h^{-1} était efficace pour la prévention et le traitement des nausées et vomissements. Les trois patients étaient alertes, avaient des pointages bas pour la nausée sur une échelle visuelle analogue et n'avaient aucun épisode de vomissement. Lorsque l'infusion a été cessée, des nausées et vomissements ont été notés chez deux patients. Le propofol, lorsque donné à l'aide d'une infusion subanesthésique, était sécuritaire et efficace en tant qu'antiémétique chez ces trois patients.

Key words
ANAESTHETIC, INTRAVENOUS: propofol;
VOMITING: antiemetics, incidence, nausea.

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Nausea and vomiting associated with chemotherapy are important deterrents to paediatric patients from complying with their chemotherapeutic protocols.[1] High-dose steroids, metoclopramide, dopamine D-2 receptor antagonists, and derivatives of cannabinoids are among the many drugs that are employed to address this problem.[2-4] None has emerged as the drug of choice to treat chemotherapy-induced nausea and vomiting and thus this clinical dilemma remains unresolved.

We have reported that following the introduction of propofol for induction of general anaesthesia in our paediatric oncology patients, the incidence of postoperative nausea and vomiting was reduced to less than 1%.[5] This observation led us to speculate that propofol has intrinsic antiemetic properties. We report our preliminary experience with the use of propofol for the treatment and prophylaxis of chemotherapy-induced nausea and vomiting in three patients.

Case #1

A 13-yr-old, 40 kg girl with osteogenic sarcoma of the humerus presented to our hospital after a night of intractable nausea and vomiting following high-dose metho-

trexate. After no relief was conferred by hydroxyzine and intravenous fluid, we were consulted.

Initially, the patient was asked to score her nausea on a scale of 1–100 (100 representing the worst imaginable nausea). She reported a score of 90, followed by an episode of emesis. The patient was given propofol 0.1 $mg \cdot kg^{-1}$ as an *iv* bolus followed by a continuous *iv* infusion of 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ (IVAC, San Diego, California). She reported only mild sedation and stated that she felt much better. Her nausea score was two and she experienced no further episodes of emesis. She spent the day napping and watching television. Within 15 min of the discontinuation of the propofol infusion, the patient began retching. She reported a nausea score of 70.

Case #2

A 14-yr-old, 35 kg boy with osteogenic sarcoma of the femur underwent preoperative chemotherapy followed by tumour resection and prosthesis insertion. Chemotherapy in the past was consistently complicated by multiple episodes of nausea and vomiting unrelieved by various antiemetic agents. On the day that the patient reported to the outpatient clinic to receive clyclophosphamide, our service was consulted to control emesis. Prior to the initiation of chemotherapy, the patient was comfortable and had a nausea score of two. Propofol was administered as a 0.1 $mg \cdot kg^{-1}$ bolus followed by an infusion of 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ (IVAC, San Diego, CA). Following the initiation of cyclophosphamide infusion, the patient continued to report a nausea score of less than ten, had no episodes of emesis, and remained alert. When the propofol was discontinued at the end of the day, the patient complained of severe nausea and had two episodes of vomiting.

Case #3

A 22-yr-old, 50 kg male with metastatic osteogenic sarcoma was receiving isophosphamide. Throughout his two years of chemotherapy he repeatedly experienced severe nausea and vomiting that usually necessitated admission to the hospital for hydration and symptomatic relief. At the time of our evaluation, he was found to be retching and severely distressed. He reported a nausea score of 100. After a bolus of *iv* propofol 0.1 $mg \cdot kg^{-1}$ the patient had less nausea and reported a nausea score of 60. An additional bolus of *iv* propofol 0.1 $mg \cdot kg^{-1}$ was given and continuous infusion of 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ (IVAC, San Diego, CA) was initiated following which he reported a nausea score of ten. During the infusion, the patient fell asleep but was easily awakened by verbal contact. When left undisturbed, he slept for most of the day. At the end of the day he did not require hospitalization and was given a prescription for an antiemetic. He was wide awake at discharge and reported a nausea score of 60 within minutes after the infusion was dicontinued.

In all three, continuous surveillance with one-on-one nursing was used. Patients and family members were instructed not to handle the infusion pumps. Resuscitative equipment was readily available but no other monitors were applied.

Discussion

The classical studies of Borison and Wang[6] in the 1950s attempted to define the anatomical components of the emetic reflex. They proposed that an area within the reticular formation of the medulla initiates vomiting when activated. Over 30 neurochemicals have been associated with this anatomical area.[7] It is well established that many anti-neoplastic agents release neurotransmitters outside the central nervous system, i.e., the gastrointestinal tract, that effect the central vomiting centre.[8] This complex neurochemistry illustrates the difficulty in developing effective antiemetics.

The effect of propofol on both central and peripheral neurotransmitters has not been well defined. Without well-designed studies, it would be premature to classify this drug as an antiemetic or to propose a mechanism of action in relation to previous work. In the three patients selected for treatment with propofol in this report previous antiemetic therapy had failed. The patient in the second case had never experienced a day of chemotherapy without nausea and vomiting. We chose to use propofol prophylactically here. For propofol to be useful as an antiemetic, the dose should be less than that known to cause sedation to avoid the need for intensive monitoring and nursing care. The dose we selected was well below sedative doses.[9] All three patients reported relief from nausea and had no vomiting while the infusion was maintained. Sedation was never greater than mild. We cannot describe, based on these three cases, the "antiemetic" dose of propofol. Blood samples were not obtained and no attempt was made to reduce the infusion rate when the patient had relief. In this report, no attempt was made to define if there was a component of anticipatory vomiting in these three patients. A placebo effect cannot be excluded without an organized investigation. We informed the patients and their families that the relief conferred by the propofol might last as long as the infusion was continued and that the patients would be discharged from the hospital with a prescription for an alternative antiemetic.

The administration of propofol in these patients attenuated the incidence of nausea and vomiting in three patients without the occurrence of serious side-effects. This observation has led to the development of a controlled study to determine the antiemetic efficacy of propofol in patients receiving chemotherapy in doses that

are likely to cause nausea and vomiting. As propofol is an anaesthetic with significant side-effects including apnoea and hypotension, we suggest that it should be used only by anaesthetists who are familiar with its use. Unlike other anaesthetic agents, e.g., volatile agents and narcotics, which promote nausea and vomiting, propofol may possess antiemetic properties in subanaesthetic doses.

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