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Educational case report

Pregabalin as adjunct in a multimodal pain therapy after traumatic foot amputation – A case report of a 4-year-old girl

Stephanie Wössner[a,b], Kirsten Weber[c], Anna C. Steinbeck[d], Markus Oberhauser[a,b], Matthias Feuerecker[a,b,e,*]

[a] Department of Anaesthesiology, Kantonsspital St. Gallen, Rorschacher Strasse 95, CH-9007 St. Gallen, Switzerland
[b] Paediatric Anaesthesia, Ostschweizer Kinderspital, Claudiusstrasse 6, 9006 St. Gallen, Switzerland
[c] Department of Paediatric Surgery, Ostschweizer Kinderspital, Claudiusstrasse 6, 9006 St. Gallen, Switzerland
[d] Department of Paediatric Cardiology, Klinikum Großhadern, University of Munich, Marchioninistraße 15, 81377 Munich, Germany
[e] Department of Anaesthesiology, Klinikum Großhadern, University of Munich, Marchioninistraße 15, 81377 Munich, Germany

HIGHLIGHTS

- Case report on traumatic fore-foot amputation in a 4 year old child.
- Multimodal post traumatic pain therapy.
- Adjunct pain therapy with pregabalin.

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ABSTRACT

Background and purpose: The purpose of this case report is to describe a multimodal pain therapeutic concept including the adjunct use of pregabalin in a 4.5 year-old child after forefoot amputation.

Phantom limb pain and sensation is a complex pain syndrome that is difficult to treat and prevent. 70–75% of all children develop such a pain syndrome after amputation. We describe here a paediatric patient who underwent forefoot amputation following traumatic foot injury and received multimodal pain therapy including pregabalin.

Methods: A 4.5 year-old otherwise healthy girl suffered severe injuries of the right foot and lower leg during a motor vehicle accident. Due to development of severe necrosis, forefoot amputation had to be performed during the hospital stay.

Results: Initial pain therapy included paracetamol, ibuprofen, metamizol, morphine and fentanyl. With mounting pain and anxiety, regional anaesthesia of the distal sciatic nerve was administered in combination with a ketamine and morphine patient controlled analgesia pump (PCA). The peripheral blockade of the distal sciatic nerve was placed with the guidance of ultrasound and nerve stimulator. The PCA concept included a continuous basal rate combined with a bolus function. Although the regional anaesthesia was well positioned and functioning, there was inadequate pain control. The pain was described by the patient as short, highly intense and sharp sensations with intensity on the visual analogue scale (VAS) of 10 (out of 10). Furthermore, she suffered from anxiety episodes and sleep disturbance. The medical team decided to treat with pregabalin to resolve these issues while awaiting amputation (Lisfranc line). She received psychological counselling as adjunct treatment. This multimodal concept enabled an early and efficient pain reduction pre- and post-amputation and allowed for the possibility of a hospital discharge without any opioid pain medication.

Conclusion: The multimodal pain therapy including pregabalin was well tolerated, safe and highly effective in this case of traumatic limb injury and subsequent amputation. The use of pregabalin allowed significant pain and anxiety reduction for the patient.

Abbreviations: ATLS, advanced trauma life support; i.v., intravenous; K-wire, Kirschner wire; NSAIDs, Nonsteroidal Anti-Inflammatory Drugs; OR, operating room; PCA-pump, patient controlled analgesia pump; p.o., per os; PLP, Phantom limb pain; pt, post trauma; q8 h, every 8 hours; VAS, visual analogue scale.

* Corresponding author at: Department of Anaesthesiology, University of Munich, Marchioninistrasse 15, 81377 Munich, Germany.
E-mail address: matthias.feuerecker@med.uni-muenchen.de (M. Feuerecker).

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Implications: Pregabalin is frequently used in adult patients for severe complex pain syndromes. There are only few reports of such adjunct medication (pregabalin) in paediatric pain syndromes. These reports focus mainly on the paediatric oncologic population. The case reported here encourages physicians to consider adjunct medications when treating complex pain, which are well established in the adult population. The benefits of such therapy in complex pain and anxiety can be extended to the paediatric population in select cases. Of course, one must always take into account that many routine medications used in children are well established but are off-label use. The authors are well aware of this problem and have conducted a critical literature review prior to pregabalin administration, including the search for randomized trials examining safety and tolerability. The parents or legal guardians of a minor must be thoroughly informed and consent to such a constellation of medical treatment.

1. Introduction

Traumatic partial or total limb amputation can lead to complex pain sensations. There is a high prevalence of phantom limb pain (PLP) in patients post amputation. Overall prevalence of PLP ranges between 40% and 80% depending on the amputation site and the patient collective. The elapsed time after amputation also plays an important role in its development [1–3]. In the paediatric population, the incidence of PLP seems to be generally lower, though it is described that 70–75% of the children complain about this specific type of pain [4,5]. PLP is most commonly described as a sharp and sudden type of pain in children [4]. Until now, the exact pathophysiology remains unclear. PLP was historically thought to be of psychological nature, recent research however, showed that both neurological (peripheral as well as central nervous system) and psychological components are at play in PLP [6]. Hence, PLP is one of the hardest chronic pain syndromes to treat.

2. Case presentation

A 4.5 year old healthy girl (body weight 20 kg) ran into oncoming traffic while playing with her friends. She sustained severe crush injuries of the right foot and lower leg from the back wheel of a truck (Fig. 1). First aid on site included the sterile bandage of the sub-amputated right foot and leg as well as fentanyl given by the emergency physician. Her vital signs remained stable throughout the transport to hospital and in the emergency room. After an initial advanced trauma life support (ATLS) evaluation in the emergency room, she was immediately transferred to the operating room (OR). General anaesthesia (propofol, remifentanil, fentanyl) was given in combination with a caudal block using ropivacaine and clonidine. Surgical procedures included a degloving-refixation and temporary Kirschner-wire (K-wire) fixation of the right foot. Postoperative analgesic therapy was ordered with paracetamol (12.5 mg/kg every 8 h (q8 h), per os (p.o.) or rectal), ibuprofen (5 mg/kg q8 h, p.o.), metamizol (20 mg/kg q8 h, intravenous (i.v.)) and morphine (0.1 mg/kg q3–4 h, i.v.) on demand. The first wound inspection under midazolam sedation was done on day 1 post trauma (pt) and from then on, on a daily basis. Due to the loss of the regional perfusion, venous stasis and increment dry necrosis of the toes and forefoot with mummification, surgical debridement and lateral decompression cuts were performed on day 6 pt under general anaesthesia (propofol, isoflurane, fentanyl, caudal anaesthesia with ropivacaine and clonidine). The postoperative analgesic regime was continued as the patient did not complain about pain in the resting state until the night of day 8 pt. On this night a morphine bolus of 2 mg i.v. had to be given twice with a time interval of four hours. From day 9 pt on the patient was transferred daily to the OR for dressing changes under general anaesthesia (propofol, isoflurane, fentanyl). Due to increasing intensity and frequency of pain (short, stabbing extreme pain sensations in the right foot, especially at night), a catheter-based peripheral blockade of the distal sciatic nerve was initiated on day 9 pt (0.2 mg/kg/h ropivacaine, regional). Catheter placement was performed under ultrasound guidance and nerve stimulation. Despite a functioning and well placed catheter, we additionally gave an i.v. Patient Controlled Analgesia (PCA) – pump containing a hospital standard solution of ketamine and morphine ([0.5 mg/ml] respectively) with a continuous infusion rate of 10 μg/kg/h and a bolus of 15 μg/kg available every 8 min. This allows the patient to self administer additional medication from the pump on top of the basal rate. The pump is programmed to administer a bolus in at least 8 min intervals, meaning pushing the button more often than every 8 min will not result in further bolus application. The maximum injectable amount of the PCA solution allowed was 16 boluses over 4 h (240 μg/kg). In addition to the above described therapy with nonsteroidal anti-inflammatory medication, the pain was well controlled. Prior to the planned forefoot amputation (Lisfranc line) on day 14 pt we started a concurrent prophylactic neuropathic pain therapy with pregabalin on day 13 pt with 1.25 mg/kg p.o (25 mg capsule). The

Fig. 1. Development of the traumatic foot injury.

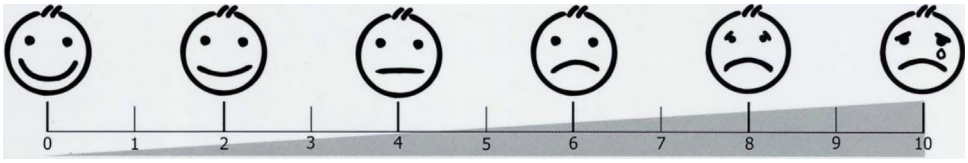

Fig. 2. Applied visual analogue scale.

girl was able to swallow the capsules without any problems. In the next few days we increased the dose to 2.5 mg/kg/d p.o (50 mg capsule). Aside from drowsiness during the first 48 h, there were no other side effects of pregabalin. The patient was adequately alert, while the pain and anxiety episodes dramatically subsided. Throughout the hospital stay, pain was assessed using a visual analogue scale with the tool shown in Fig. 2. The VAS allows a consistent assessment on a numeric scale, with the help of parents or nurses. Overall VAS was below 3 following pregabalin therapy, a significant reduction. From day 16 pt onwards, the bolus function of the PCA was not needed. Her forefoot and lower right leg were covered with mashed skin grafts from both thighs 6 days after amputation. On day 22 pt we were able to stop the sciatic nerve catheter and to reduce the continuous i.v. PCA infusion (5 μg/kg/h). The next day metamizol was prescribed on demand and per os. After 20 days (on day 29 pt the PCA therapy), morphine and ketamine was also discontinued. 37 days after the trauma we were able to discharge the patient in a pain free state with the following medications: ibuprofen 10 mg/kg p.o. on demand up to 3 times/d, metamizol 12.5 mg/kg p.o. on demand up to 3 times/d, pregabalin 2.5 mg/kg p.o. The multimodal pain therapy also included early psychological trauma interventions as well as art-, learning- and physio-therapy.

3. Discussion

This case describes a 4.5 year old girl who underwent a traumatic foot amputation, an initial re-fixation of the foot followed by surgical amputation 14 days later due to necrosis. Of particular note in this report is the specific character of the evolving pain and escalation of pain therapy. By the end of the first week in hospital, the patient developed maximal sudden and sharp pain sensations in the right foot mainly at night. The pain was neuropathic in character, which was increasingly more difficult to control with NSAIDs and morphine. With an inadvertent amputation, the pain medication regimen was definitely lacking, especially in anticipation of possible PLP. With overall inadequate pain management and mounting neuropathic pain, we intensified the therapy with the placement of a sciatic nerve catheter and a morphine/ketamine PCA-pump to reduce the risk of PLP. Fisher and Meller [7] have reported on a postoperative placement of a continuous sciatic nerve blockade in patients undergoing lower limb amputation and its beneficial effect of opioid reduction. We decided to combine the nerve block with the morphine/ketamine PCA-pump as a result. Hayes et al. [8] were able to show in a randomized controlled trial that continuous administration of ketamine in the perioperative period decreases the incidence of PLP from 71% to 47% (control versus ketamine group). Though ketamine is broadly used in the postoperative pain therapy, one has to be aware that it is only approved for pain therapy in mechanically ventilated (intubated) patients. Whereas Wu et al. [9] demonstrated the effectiveness of i.v. morphine in the treatment of PLP compared to placebo or i.v. lidocaine. Another important aspect during her hospitalization was the increasing anxiety and bad dreams of the accident. Despite psychological trauma counselling, we decided to start treatment with pregabalin.

Pregabalin is originally an add-on anticonvulsant drug for the therapy of refractory seizures in adults. It is also effective and beneficial as a medication for neuropathic pain and generalized anxiety disorders [10]. Its safety and tolerability in children ageing 1 month to 16 years has been shown in a phase I randomized controlled study as a powerful and safe drug in the treatment of refractory partial seizures (doses up to 15 mg/kg/day) [11]. Few reports are available in the treatment of neuropathic pain and complex regional pain syndrome with pregabalin in children [12,13].

There are no previous reports on limb amputation in children and subsequent pain management with pregabalin. Our patient profited greatly from the multimodal pain therapy including pregabalin. The latter was well tolerated and had a remarkable effect on the reduction of overall pain medication use.

4. Conclusions

Prevention and treatment of phantom limb pain is a clinically challenging situation, especially in the paediatric population. The medical team should strive for a well-established multimodal pain concept and early pain reduction. Newer adjunct medications such as pregabalin are safe in children and can be a very useful addition in a multimodal pain concept.

Consent

For this publication, a written informed consent was obtained from the patient's parents who are the legal representatives. The consent also includes the publication of images of the injured extremity. A copy of the written consent is available for review by the Editor-in-Chief of this Journal.

Conflict of interest

All authors declare that there is no competing interest.

Authors' contributions

SW, KW, MO, MF carried out the treatment and the critical literature review for the use of pregabalin. SW, AS, MO, MF drafted the manuscript. Specific and very significant advice regarding therapy was given by AS. All authors carefully approved the final manuscript.

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