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CLINICAL INFORMATION

Treatment of status migrainosus by general anesthesia: a case report

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Migraine disorder;
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Abstract

Background and objectives: The status migrainosus is a complication of migraine characterized by severe headache for more than 72 h that did not respond to treatment, with risk of stroke and suicide. Researches on treatment are directed to drugs that stimulate GABA receptors; propofol and isoflurane act on sub-GABA_A receptors and theoretically could be interesting. The first has been the subject of research in severe migraine. Opioids are employed in pain, and its use in chronic headache is debatable, but these agents are employed in acute cases. The goal is to present a case of refractory status migrainosus in that we decided to break the pain cycle by general anesthesia.

Case report: Female patient, aged 50 years, with status migrainosus, in the last five days with visits to the emergency department, medicated parenterally with various agents without result. Without comorbidities, dehydrated, described her pain as "well over 10" in Visual Numeric Scale (VNS). After consulting the literature, and given the apparent severity of the condition, we opted for a general anesthesia: induction with fentanyl, propofol, and vecuronium and maintenance with isoflurane and propofol for two hours. Following the treatment, in the postanesthetic recuperation (PAR), the patient related her pain as VNS 3, and was released after five hours with VNS 2. Subsequently, her preventive treatment was resumed.

Conclusion: Status migrainosus is a rare disabling complication and anesthetics have been the subject of research in its treatment; the option for general anesthesia with agents that stimulate GABA receptors, propofol and isoflurane, in association with fentanyl, proved effective and should encourage new research.

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PALAVRAS-CHAVE

Transtorno de enxaqueca;
Terapia combinada;
Anestesia geral

Tratamento do estado de mal-enxaquecoso pela anestesia geral: relato de caso**Resumo**

Justificativa e objetivos: O estado de mal-enxaquecoso é complicação da migrânea caracterizada por cefaleia severa por mais de 72 horas não responsiva à terapêutica com risco de AVC e suicídio. Pesquisas no tratamento se direcionam às drogas que estimulam receptores GABA; propofol e isoflurano atuam nos sub-receptores GABA_A e teoricamente poderiam ser interessantes. O primeiro já foi objeto de pesquisas na migrânea severa. Opioides são empregados em dor, seu uso crônico nas cefaleias é discutível, mas são empregados nos casos agudos. O objetivo é apresentar caso de estado de mal-enxaquecoso refratário em que se optou para quebrar o cicloálgico por uma anestesia geral.

Relato de caso: Paciente do sexo feminino com 50 anos em estado de mal-enxaquecoso havia cinco dias com passagens anteriores por serviço de urgências, medicada por via parenteral com vários agentes sem resultado. Sem comorbidades, desidratada, descrevia sua dor como "muito superior a 10" na ENV. Após consulta à literatura, face à gravidade aparente do quadro, optou-se pela feitura de uma anestesia geral; a indução foi com fentanil, propofol, vecurônio e manutenção com isoflurano e propofol por duas horas. No fim, na RPA, no primeiro contato classificou sua dor com ENV 3, teve alta após cinco horas com ENV 2. Ulteriormente retomou seu tratamento preventivo.

Conclusão: O mal-enxaquecoso é uma complicação rara incapacitante e anestésicos têm sido objeto de pesquisas no tratamento; a opção por uma anestesia geral com agentes que estimulam os receptores GABA, propofol e isoflurano, aliados ao fentanil, mostrou-se eficaz e deve incentivar pesquisas.

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Introduction

The state migrainosus is, according to the International Headache Society, a severe complication of migraine characterized by disabling pain crises, lasts for longer than 72 h and is presented in a continuous manner without remission and unresponsive to usual treatments.¹ It is a rare condition, but always an emergency and a challenge to primary care physicians. The risk of stroke and suicide attempts are part of the complications described in the literature^{2,3} and that should be considered. The pathophysiology responsible for this type of evolution is still subject to much controversy^{4,5} and due to the common failure of the usual treatment in such circumstances, various approaches in bouts of severe migraine with anesthetic drugs have been made, from local endovenous anesthetics⁶ to opioids,^{7,8} and also with hypnotics as propofol.⁹⁻¹¹ This latter strategy has come to very interesting results, and his alleged action would be the interaction with the central GABA receptors,⁹ with an mechanism similar to other anesthetic agents, including inhaled isoflurane,^{9,12,13} not necessarily in the same receptor subtypes. Therefore, other drugs with similar mechanism of action in these receptors also have been a target of research for the treatment of migraine.⁹ Some of the doses of propofol proposed in the literature^{10,11} were superior to those used in general anesthesia and, although intermittent, conducted to loss of consciousness and respiratory depression, reaching¹¹ a bispectral index (BIS) of 40. Given these assumptions in the literature, we report a case in which a general anesthetic was successful in an attempt to abort a crisis of severe status migrainosus which was present in the last five days, after the failure of several attempts with the first-line therapy.

Case report

Female patient, 50 years old, 1.75 m tall and with 70 kg, with a history of migraine since adolescence, with bouts of very variable frequency, without other comorbidities. The patient has had several irregular treatments, and at that occasion was being preventively medicated with amitriptyline 25 mg at night and atenolol 50 mg in the morning. During crises, the patient made use of triptans; in her visit, we suspected of abuse of that last medication. At that time, she was in a crisis of five days duration, and unresponsive to all treatment attempts, with several passages in the emergency department, with use of intravenous dipyrone 1 g, dexamethasone 4 and 8 mg, chlorpromazine 25 mg, haloperidol 5 mg, ketoprofen 100 mg, meperidine 30 mg and 40 mg, lidocaine 100 mg, sodium valproate 100 mg, and antiemetics, some of them more than once, all without any satisfactory result; without food for three days, no vomiting, but had nausea and photophobia, was dehydrated and described her pain, with difficulty, as "far superior" to 10 in the Visual Numeric Scale (VNS)! In consultation with a member of the Pain Clinic of the institution in search of a solution, a literature survey was conducted and found the use of propofol and opioids in refractory migraine and similarities of action of the first drug with inhalational anesthetics. Given the failure of previous therapies, the description in the literature of drugs, doses and procedures which, in the view of an anesthesiologist, configured an approach that practically was an anesthesia, even with loss of consciousness and airway obstruction, and that were conducted in an induction of anesthesia ward or anesthesia recovery room with all available and habitual anesthetic monitoring present,^{8,9} we considered to accomplish a general anesthesia as a last

attempt to stop the pain status. After careful explanation to the patient, and verifying her fasting status, we obtained her informed consent, proceeding with a clinical exam: blood pressure was 150 × 90 mmHg, heart rate = 104 bpm, with no other noteworthy findings. The patient was taken to the operating room, with ECG monitoring with similar DII, pulse oximetry and noninvasive blood pressure determination and inducted with fentanyl 200 µg, propofol 150 mg and vecuronium 7 mg after ventilation by mask with O₂ 100%. The patient was intubated and underwent controlled mechanical ventilation keeping saturation always above 98% and capnometry with values between 34 and 36 mmHg. Maintenance of anesthesia was performed with isoflurane 0.5% in oxygen 40% and continuous infusion of propofol 1 mg kg⁻¹ h for two hours. The patient remained hemodynamically stable throughout this period. After that, the patient was decuritized, awakened, extubated and taken to the postanesthesia recovery room. Once the first contact was possible, the patient quantified and described considerable improvement her headache, having rated her pain as VAS = 3. After five hours, the patient was discharged. Before that, the patient drank water, remained without nausea and rated her pain as VNS = 2. A week after her discharge, the patient reported that her headache had stabilized, with a pattern alike the circumstances preceding the status migrainosus crisis, which allowed the reintroduction of the usual preventive medication by her attending doctor.

Discussion

It is estimated that migraine has a prevalence of 15% in the general population¹⁴; of this percentage, 1.4–2.2% is present in the form of chronic migraine,¹⁵ that, in adulthood, affects women twice, as compared with men.¹⁶ The treatment of migraine is targeted at relieving the symptoms by administration of analgesics, nonsteroid anti-inflammatory drugs, ergot alkaloids, triptans, antiemetics and opioids. Preventive therapy makes frequent use of beta-blockers, antidepressants and antiepileptic drugs, but a number of patients demonstrate refractoriness, and that is a major challenge. During crises, the absorption of the oral medication becomes affected,¹¹ and the parenteral via is preferred. Status migrainosus is a complication of its evolution and, although considered rare, a prospective study¹⁷ of 2006 showed that at some point of their lives about 20% of patients with chronic migraine experienced pain for longer than 72 h. Modifications of neurotransmission occur in migraine and studies have shown that these patients have an alteration in the metabolism of serotonin (5-HT). Potent agonists of 5-HT receptors with antimigraine activity have their effects explained by the reduction of vasogenic inflammation and partly by the vasoconstrictor effects on meninges, upon stimulation of 5-HT receptors.¹¹ By 1985 it was demonstrated that GABA would exert an inhibitory control over serotonergic neurons¹⁸ and that drugs effective in fighting migraine have their effects mediated by the agonism of GABA_A receptors, increase of GABA in the brain and decrease in the frequency of stimulation of the dorsal raphe serotonergic cells.¹⁹ Since 1996, with the work of Cutrer and Moskowitz,²⁰ it is known that the prospect of new drugs for migraine treatment was in the study of agents

with high affinity for GABA_A receptor and their modulation sites. Given the difficulty of overcome the pain in severe conditions, perhaps the first idea of using anesthetics arose in 1999 with the work of Ponnudurai et al.,²¹ who observed a protective effect of propofol (an hypnotic agent) against postoperative headache in a particular group of patients. Since then, several investigations with the use of anesthetic agents have been conducted. Propofol is a hypnotic agent for use in anesthetic procedures, have antiemetic properties and its efficacy has been demonstrated in cases of severe migraine. This agent would act through its agonist activity at the GABA_A receptor subunits β1, activating chloride channels and inhibiting synaptic transmission.¹¹ Opioids are agents that provide relief from pain, and are widely used in anesthesia and often in great number of painful conditions. Then, their use in refractory migraine is not surprising. Their continued use is, however, a matter of controversy. Some authors found no significant improvement in the long term in 74% of cases,²² while others emphasize their benefit,^{7,8} and methadone is the most widely used drug in these circumstances. The GABA_A subreceptor is an important target of inhalational anesthetics,¹² and these drugs, as well as intravenous agents, stimulate the receptor^{23,24} in a mechanism similar to that of the drugs currently studied for the treatment of migraine, which justifies this mention in the literature⁹ and the interest in this case. General anesthesia with propofol, fentanyl and isoflurane was an extreme option in an extreme case unsolved for a several days, and its use had its foundations with the knowledge of literature, and should be investigated further for more definitive conclusions. For this purpose, a protocol was subsequently presented to the Ethics Research Committee and approval was obtained.

Conflicts of interest

The authors declare no conflicts of interest.

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