

Synopsis on the paper "Acute migraine in pregnancy: Therapeutic opportunities"

Sinopse do artigo "Migrânea aguda na gravidez: oportunidades terapêuticas"

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ABSTRACT

Acute migraine is a debilitating pain crisis for which there are several therapeutic options, although no single universally effective prescription. When the migraine attack occurs in pregnant women, the pharmacological treatment options are very limited and a complex situation arises, in which to do or not to do have potential implications. The fear of possible damage to the fetus by the mother or the physician and the effect of recurrent and severe pain on the pregnant woman do not have a unidirectional response. For most drugs, the real risk potential in pregnancy has not been established, and suffering from chronic or recurrent pain also has potential adverse effects on pregnancy. This often leads to inaction or to the prescription of medication that is not necessarily useful. Pain should be treated effectively in all circumstances and pregnancy is no exception. This paper reviews the available options for the treatment of migraine attacks that may be used in pregnant women.

RESUMEN

La migraña aguda es una crisis de dolor discapacitante para la cual hay opciones terapéuticas pero no hay una única prescripción eficaz universal. Cuando la crisis migrañosa se produce en la mujer gestante son muy limitadas las opciones terapéuticas farmacológicas y se plantea una compleja situación en la que hacer o no hacer tienen su consecuencia potencial. El temor al daño posible del feto por parte de la madre o el médico y el efecto del dolor recurrente y severo sobre la mujer embarazada no tiene una respuesta unidireccional. En la mayoría de las medicaciones no está establecido el riesgo potencial real en el embarazo y presentar dolor crónico o recurrente tiene potenciales efectos nocivos sobre el embarazo. Esto lleva muchas veces a la inacción o

prescripción de medicación que no necesariamente es útil. El dolor debería tratarse eficazmente en todas las circunstancias y esta no es la excepción. El presente trabajo revisa las opciones de tratamiento de la crisis de migraña con posibilidad de uso en la mujer embarazada.

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SYNOPSIS

Buonanotte & Buonanotte started explaining epidemiological aspects of migraine which affects on average 11% to 14% of the adult population with a clear female predominance. Headache improvement in 2nd and 3rd quarters of pregnancy is explained as related to women with menstrual migraine before pregnancy. Even though, some women migraines get worse during pregnancy, and there are also complications such as preeclampsia, and coagulation disorders.

The authors go into a delicate terrain: the neurophobia in dealing with such women. This is a worldwide fact. The

scenario is more complicated when we consider the medical act and the principle of beneficence of seeking the patient well-being. There is the fear of medical legal consequences in this case, by action or omission, which in practice leads to considering that nothing could be pharmacologically prescribed in this clinical context. There is also the neurophobia by the fear of a secondary headache, added to the logical fear of potential harm to the fetus. This is associated with the existence of few safe drugs or medicines which safety is known but studies cannot be performed, thus tables are based on case reports.

Also, we must remember that 2 to 7% of migraines in pregnancy are "de novo" and it is necessary to think of secondary headaches, and that 35% of pregnant patients in the doctor's waiting room have secondary headache. Neuroimaging procedures are essential in the ancillary investigation of those patients, and tomography and magnetic resonance bring a minimal risk for both pregnant women and fetus – as long as an intravenous contrast enhancement is not used.

Secondary headaches to be considered in pregnancy are hypertensive syndromes associated with pregnancy: eclampsia and preeclampsia; posterior reversible encephalopathy; hemolysis, increased liver enzymes, and low platelets syndrome (HELLP); reversible cerebral vasoconstriction syndrome; pituitary apoplexy; venous thrombosis; brain hemorrhage: aneurysmal or AVM; artery dissection; idiopathic intracranial hypertension; and meningitis.

And then, the authors described the treatment of migraines in pregnancy, giving emphasis to non-pharmacological management. As for drugs, in acute pain not every medication can be taken, and this should be taken into account by migraineurs before becoming pregnant.

Further, the paper elegantly addresses the need to prevent migraine chronification, and discusses that among the modifiable factors are overweight, snoring, sleep apnea and insomnia, excessive consumption of caffeine, high frequency of headaches, frequent use of analgesics, other associated pains, neck trauma, emotional disturbances, and social, labour or affective changes.

In this review, products such as riboflavin and magnesium are emphasized with level of evidence B. Topical products like capsaicin with mint prepared with ethyl alcohol solution and topic acetaminophen are interesting to be prescribed to pregnant women. And here this review brought a novelty to the physicians who treat their pregnant migraineur patients.

The paper defines teratogenicity which is the structural or functional defect in organogenesis, involving from 3rd to 8th gestational weeks. The teratogenic action produced by medicines varies along the timeline related to the different periods of susceptibility to the injury. The risk of teratogenicity is not known in more than 90 % of the drugs approved by the FDA.

The prescription should balance or consider aspects which are very easy to be considered, even though difficult to be performed or to act. This is because no controlled studies are available, and the use of drugs would not be recommended.

Considering the risk and benefit includes to evaluate the gestational age and teratogenic risk at this stage, the effectiveness of the medication, the risk categories of this drug, and the will of the pregnant to use medication, to decide to bear the pain (which I do not agree particularly), to take the risk of the drug, to face the possibility of the route of administration, and to take the effects of pain on the body and on pregnancy, and the adverse effects of the available medicines.

There is not enough evidence to recommend a specific protocol in the treatment of acute migraine in any given situation. This absence obliges the physician to make a decision in each case where the indication does not necessarily correlate to the prescription (in this situation I name it as the 'art of medicine with little evidence').

Yet, the paper describes the options in acute migraine during pregnancy considering the principles of beneficence and nonmaleficence.

Acetaminophen - no established risk, mothers often use in pregnancy.

Anti-inflammatories - can be used diclofenac (50 mg), ibuprofen (400mg), naproxen (500 - 1,000 mg), piroxicam and indomethacin, which are categorized as risk B. Aspirin in doses of 900 - 1,000 mg shown efficacy in relief from migraine, and the risk is C. Avoid in the first quarter and in the woman who plans to become pregnant due to the possibility to prevent ovulation, implantation of the egg, or abortion. It is not recommended to use cyclooxygenase-2 inhibitors.

Triptans - a recent meta-analysis study concluded that the use of sumatriptan in pregnancy does not show increased risk of prematurity or birth malformations, and this sporadic use in pregnancy is acceptable because of low-risk.

Opioids - the risk is C, as the triptans, but opioids are associated with numerous complications in both the fetus

and the mother (physical dependence and withdrawal, growth retardation, neonatal respiratory depression and malformations). In general they are safe.

Magnesium - the infusion of 1 g of magnesium sulfate demonstrated efficacy in controlling migrainous attacks. Usage is safe in pregnancy and should not be administered for more than 3 consecutive days since the prolonged use may be associated with neonatal hypocalcemia and osteopenia. For that reason it was reclassified as risk D.

It is interesting this reclassification of magnesium, and this is another prominent aspect in this paper.

Antihistamines

Steroids - Steroids should not be prescribed more than 6 times. Dexamethasone has risk C and prednisone is B.

Dipyron - It is as safe as the acetaminophen.

Antiemetics

Nerve Blocks

Acupuncture

The authors conclude by making the remark that to decide a specific action on pregnant with migraine attacks is a complex choice, in which multiple factors are present. A strategy should be proposed for each particular case, considering the opportunities, and evaluating the lower risk; and the pain should always be treated.

The paper is very complete and brings some interesting news. More and more papers of this nature with regard to pregnant women are needed, since in this setting double-blind randomized studies cannot be performed.

REFERENCES

Buonanotte CF, Buonanotte MC. Migraña aguda en embarazo: oportunidades terapéuticas. *Neurol Arg.* 2016. <http://dx.doi.org/10.1016/j.neuarg.2016.05.004>

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