

Breath of Life

How a Jetlag Treatment Could Prevent Permanent Newborn Brain Damage

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A common jetlag treatment in a simple skin patch could be the key to improving the lives of babies all around the world.

Every year, four million babies are born starved of oxygen. The consequences of this compromised birth are severe. Half of the babies do not make it past the first days or weeks of life, and those who do survive will most likely be severely disabled.

But sometimes the simplest answer is the best. We have been researching the use of melatonin in a skin patch to prevent permanent brain damage in the hours after birth.

A healthy baby grows in the uterus for 9 months. From a single cell, this future human will grow exponentially in size and complexity. By 3 months the placenta is providing nutrients, removing waste and exchanging gases between the baby and the mother.

Once the baby is fully developed, hormonal changes start the process of childbirth. As the uterus contracts, blood supply to the placenta is halted for short periods of time, cutting off the supply of oxygen. During the first moments outside of the uterus after the baby is delivered, it will begin to breathe and is no longer reliant on the placenta or mother for oxygen.

Childbirth thus causes short periods of time without access to oxygen for the baby. But just like how you can hold your breath for seconds at a time without causing any damage, the baby can handle these periods. However, permanent damage can occur if something goes wrong and the oxygen supply is low for too long.

Birth asphyxia describes catastrophically low oxygen levels at the time of birth. This occurs if something goes wrong with the placenta, such as it separating from the wall of the womb early, or if the umbilical cord becomes knotted or wraps around the neck of the baby.

This starves the baby of energy. Its body attempts to compensate for this by redirecting blood, and therefore the little oxygen available, to important organs such as the brain. Even though the body attempts to prevent the brain from being starved, brain damage can still occur.

The newborn brain is at its growth peak. It weighs about 400 grams, which is one-quarter of what an adult brain weighs even though the baby only weighs about 5% of an average adult.

Already there are tens of billions of neurons firing off and controlling all aspects of the body. The connections between cells are developing, letting different parts of the brain talk to each other.

This requires huge amounts of energy to function properly. When energy is not available, things start to go wrong.

The lack of oxygen during birth asphyxia causes a change in equilibrium from aerobic metabolism, which uses oxygen for efficient energy production, to anaerobic metabolism requiring limited oxygen. Less energy is produced and there is a rapid depletion of energy storage and a build up of waste products. The cells are unable to function properly and brain cells will begin to die.



But the body is resourceful. Once the baby is born, doctors will resuscitate the baby, helping the transition from reliance on the placenta to a self-sufficient state where the baby is breathing on its own. A state of apparent “normal” will follow for the next few hours, but not everything is truly right.

During this period, damaging cellular processes begin escalating quickly after birth. With an ample supply of oxygen the body now starts to furiously obtain energy to restore levels. The powerhouses of the cells, the mitochondria, are adaptable and can increase energy production once oxygen has returned.

The side-effect of this is an excessive release of free radicals. In an unfortunate turn of events, the excess free radicals then attack the fats that make up the wall of the mitochondria and cause the further release of free radicals and other dangerous chemicals.

A newborn brain has large energy requirements and a high fat content, and is at an incredible risk of damage by free radicals.

Free radicals are chemicals that have unstable high-energy bonds. Just like metal oxidising and rusting when exposed in air, free radicals essentially cause fats and DNA to “rust”. To cope with this the body has its own defence system, antioxidants.

Antioxidants stabilise the high-energy bonds in free radicals. However, after birth asphyxia the body does not have the capacity to protect itself from the excessive amount of free radicals circulating. A newborn brain has large energy requirements and a high fat content, and is at an incredible risk of damage by free radicals.

We know that free radicals are one of the main culprits of brain damage. Could we give an antioxidant that could help deal with excessive free radicals?

We know that melatonin, a hormone that people all across the world use to help them overcome jetlag, is a really potent antioxidant. Melatonin is a natural hormone that all humans produce in one of the glands in the brain. It helps with jetlag because it resets your body clock, but it is also really good at stabilising the high-energy bonds in free radicals. It will even convert free radicals into forms that are not dangerous to the body.

Melatonin also helps the body to produce more of its own antioxidants. It helps the genes in your body that code for antioxidants to be activated and produce other antioxidants that help fight free radicals.

Meanwhile, and most importantly, it is safe to use. Adults use it for jetlag; children for behavioural problems. It has been used to treat pregnant mothers and newborn babies for other pregnancy-related problems.

But can't the baby produce melatonin? Before birth, the placenta is providing the baby with melatonin but once the baby is born it won't produce melatonin on its own until about 3 months of age. This is why the baby is at a high risk of developing permanent brain damage from free radicals during this period.

Could we test melatonin to treat babies who are born starved of oxygen? It is not ethical or practical to test medications on newborn babies. Instead, we have developed an experiment that used newborn lambs that have been born with low levels of oxygen. We then treated the animals with melatonin intravenously to treat the early stages of brain injury.

Babies that have been starved of oxygen are slow to start breathing on their own, and have abnormal movements of their arms and legs. Lambs that have suffered the same condition have similar behaviours. But when we treated lambs with melatonin they behaved like a typical lamb, standing and feeding quickly after birth.

We also placed lambs into an MRI scanner, which uses magnetic radiation to enable us look at the brain non-invasively – including energy production within the brain. We can measure the amount of lactic acid, a waste product produced during times of low oxygen. We can also look at how well the brain cells are functioning.

The MRI scans showed that melatonin reduces lactic acid levels in the brain and improved how well the brain cells were able to function and fire off.

So melatonin seemed to protect the brain of newborn lambs, but how could we give this drug to newborn babies all around the world? Many people use skin patches every day. One of the most common uses is a nicotine patch as an aid to quit smoking. The skin patch provides a constant stream of nicotine into the blood without the person having to think about tablets, gum or injections.

We are currently investigating the potential use of skin patches containing melatonin. It will provide a simple and cheap method of administering this protective hormone to babies all across the globe. Imagine if a baby born in rural Australia, hours away from hospitals that specialise in caring for sick newborn babies, could be given a simple skin patch that could help prevent permanent brain damage.

We are slowly putting the pieces of the puzzle together, with the hope of saving the lives of the four million babies who are born starved of oxygen every year.

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