Could a Medication Help With Bleeding Between the Skull and the Brain?

Chari, A

http://hdl.handle.net/10026.1/19778

10.3389/frym.2022.789786
Frontiers for Young Minds
Frontiers Media

All content in PEARL is protected by copyright law. Author manuscripts are made available in accordance with publisher policies. Please cite only the published version using the details provided on the item record or document. In the absence of an open licence (e.g. Creative Commons), permissions for further reuse of content should be sought from the publisher or author.
COULD A MEDICATION HELP WITH BLEEDING BETWEEN THE SKULL AND THE BRAIN?

Aswin Chari1,2*, Keng Siang Lee3, Alexander Alamri4, Peter J. A. Hutchinson5, Angelos G. Kolias5 and Ellie Edlmann6,7

1Department of Neurosurgery, Great Ormond Street Hospital, London, United Kingdom
2Developmental Neurosciences, Great Ormond Street Institute of Child Health, University College London, London, United Kingdom
3Faculty of Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom
4Department of Neurosurgery, St George’s, University of London, London, United Kingdom
5Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom
6Department of Neurosurgery, South West Neurosurgical Centre, University Hospitals Plymouth, Plymouth, United Kingdom
7Faculty of Health, Peninsula Medical School, University of Plymouth, Plymouth, United Kingdom

Chronic subdural haematoma is the medical name for bleeding that occurs between the skull and the brain. It usually happens to older people, like grandparents. If it causes serious symptoms, brain surgeons will operate. However, even after surgery, chronic subdural haematomas can come back, and further operations may be needed. We tested whether a medication called dexamethasone could prevent chronic subdural haematomas from coming back by performing a study of 750 people, in which half received the medication and half did not. The results showed that dexamethasone was good at stopping brain bleeds from coming back, but it had other
effects that caused patients to have a more difficult recovery than did those who did not take it. These results are really important to stop doctors from giving this medication—it shows that, at the moment, surgery alone is the best treatment.

**INTRODUCTION**

**Chronic subdural haematoma**, commonly called a brain bleed, is a condition in which bleeding occurs on the brain surface, between the skull and the brain. It most commonly affects older people such as grandparents (Figure 1). A brain bleed can put pressure on the brain and stop it from working well. People with subdural haematomas often feel unsteady, confused, or weak on one side of the body. These problems can develop gradually over days or weeks and are generally noticed by the person’s family, including their children and grandchildren.

**WHY DOES CHRONIC SUBDURAL HAEMATOMA NEED BRAIN SURGERY?**

Brain surgeons are usually the doctors who treat brain bleeds. The main form of surgery used to treat chronic subdural haematoma is called a **burr hole evacuation**. In this operation, surgeons drill some small holes in the skull, which allow them to wash out the blood (Figure 2). This surgery is necessary because the skull is a closed box that is just the right size to fit the brain. It does a great job of protecting the brain too! However, when blood or fluid gets into the skull, this puts pressure on the brain, stopping it from working normally. Opening up the closed box of the skull and washing out the blood relieves the pressure on the brain, allowing it to work normally again.
To treat chronic subdural haematomas, brain surgeons commonly use a drill to make two holes in the skull, through which the blood is washed away. This relieves the pressure on the brain and helps the patient get better!

Burr hole evacuations usually take 30–60 min and the surgery is pretty straightforward! Most people get better very quickly after this operation, but the blood can return in up to two of every 10 patients, requiring another operation.

Scientists have been looking for drugs that might prevent the bleeding from coming back. In the 1970s, some doctors thought that a medication called dexamethasone (the same medication used to treat COVID-19) worked well [1]. Doctors in the US, the Netherlands and Spain used dexamethasone with some success, but their studies could not say for sure that the drug was always helpful [2, 3]. So, in 2013, we designed a large study that would allow doctors to be certain whether dexamethasone worked to prevent return of chronic subdural haematomas, and whether it improved recovery for patients with these brain bleeds.

**DESIGNING MEDICAL STUDIES**

Doctors and researchers use lots of different types of study to find out if one way of treating a condition is better than another way. Some of these studies are better than others. The best type of study is called a randomized controlled trial, in which people with a certain medical conditions are randomly chosen to receive one treatment or another. Randomized controlled trials reduce bias in medical studies; for example, without the random choosing process, doctors might choose people who are more likely to benefit from one of the treatments, so the study might incorrectly show that that treatment is better.
When designing randomized controlled trials, there are three other critical things to consider:

- Who do we include or exclude?
- How do we judge which treatment is better? It is important to pick a measure that is important to both the doctors and the patients.
- How many people do we need? To determine this, we often need the help of experts in medical statistics.

**OUR RANDOMIZED CONTROLLED STUDY**

The previous studies using dexamethasone for chronic subdural haematoma were not randomized controlled trials, so we thought that it was necessary to conduct such a study before recommending the use of this drug for patients with brain bleeds. We designed a randomized controlled trial to test whether people who received dexamethasone along with surgery for a chronic subdural haematoma did better than those who took no medication [4]. It took just over 3 years to recruit 750 patients to the study from around the UK. Half of the patients got dexamethasone and the other half got a placebo, which is a pill or treatment that looks just like the medication but does not contain the active ingredient. We followed up with the patients for 6 months to see how well they recovered from their operations and whether their chronic subdural haematomas came back (Figure 3A) [5].

As we expected, chronic subdural haematomas were much less likely to come back if dexamethasone was given, with only 2% of patients in the dexamethasone group needing repeat surgery compared to 7% in the placebo group. However, surprisingly, the patients who were given dexamethasone still made a worse recovery overall compared to the placebo group (Figure 3B). This means that, despite helping with the brain bleed, the dexamethasone caused complications that made patients more ill. These complications included infections and high blood sugar, which made it harder for patients to make a full recovery.
CONCLUSION

Randomized controlled trials are important to accurately compare two treatments. In our randomized controlled trial, we showed that, although dexamethasone reduces the need for further operations in patients with chronic subdural haematoma, it is associated with more complications during recovery. This study was really important for providing a definitive answer about whether dexamethasone was a good medical treatment for people with brain bleeds. It showed that, even though previous scientific studies suggested dexamethasone was effective, the only way to know for sure was to do a large, randomized controlled trial like we did. Because of our work, dexamethasone is no longer given for brain bleeds—our results changed the practices of doctors around the world.

Unfortunately, chronic subdural haematoma is becoming more common [6]. Future research will hopefully improve treatment. For example, other randomized controlled trials have shown the importance of inserting a small drain under the skull for a few days after surgery [7]. In the future, we hope that patients will be able to have less invasive surgeries or even avoid surgery altogether!

FUNDING

The Dex-CSDH trial was funded by the National Institute for Health Research Health Technology Assessment Programme (Dex-CSDH ISRCTN number, ISRCTN80782810).

ORIGINAL SOURCE ARTICLE


REFERENCES


kids.frontiersin.org October 2022 | Volume 10 | Article 789786 | 5
treatment in chronic subdural haematoma. Neurocirugia.

SUBMITTED: 05 October 2021; ACCEPTED: 15 September 2022; PUBLISHED ONLINE: 03 October 2022.

EDITOR: Atsushi Asakura, University of Minnesota Twin Cities, United States

SCIENCE MENTORS: Demetrios A. Arvanitis and Beatrice Ugiliweneza


CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

COPYRIGHT © 2022 Chari, Lee, Alamri, Hutchinson, Kolias and Edlmann. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

YOUNG REVIEWERS

ELISA, AGE: 12
Elisa is a young girl with a curious mind. She is very passionate about science, especially related to health. She is interested in research and would like to start getting involved in conducting her own explorations in high school. She hopes that, with her critical thinking, her love for health discoveries and her drive, she will be able to contribute to science through journal review.
KALOMOIRA MARIA, AGE: 11
I love nature (coniferous forests and lakes), games, books and music (especially piano). I enjoy English and Maths. Science is the latest addition to my interests. My favorite book series is the Pages & Co. and my favorite book heroines are Tilly from the Bookwanderers, Anne of Green Gables and the renown Hermione Granger from the Harry Potter Series.

AUTHORS

ASWIN CHARI
Dr. Aswin Chari is a resident neurosurgical doctor in London, UK. He is currently completing a Ph.D., investigating why some children are cured and others are not following brain surgery for epilepsy. *aswin.chari.18@ucl.ac.uk

KENG SIANG LEE
Keng Siang Lee is a medical student, researcher, and talented artist based in Bristol, UK. When he grows up, he definitely wants to be a neurosurgeon!

ALEXANDER ALAMRI
Dr. Alexander Alamri is a resident neurosurgical doctor in London, UK. He has just started a Ph.D., investigating patients undergoing deep-brain stimulation and spinal cord stimulation for severe pain.

PETER J. A. HUTCHINSON
Professor Peter J. Hutchinson is a professor of neurosurgery in Cambridge, UK. His main research involves improving our understanding and outcomes of patients with brain injuries. He is also the director of the NIHR Global Health Research Group on Acquired Brain and Spine Injury, which aims to improve care and access to care for patients with brain and spine injuries around the world.

ANGELOS G. KOLIAS
Dr. Angelos G. Kolias is a neurosurgeon and researcher in Cambridge, UK. His main interests are surgery for brain tumours, spine surgery, neurotrauma, and general neurosurgery. He has an interest in optimising the design of neurosurgical randomised trials.

ELLIE EEDLMANN
Dr. Ellie Edlmann is a resident neurosurgical doctor and researcher in Plymouth, UK. Her main interests are in brain injury, specifically chronic subdural haematoma.