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The Modern-Day Use of Thalidomide

Is Thalidomide Ethical to Use in the Modern Era?

– Tiffany Alder | Zach Armstrong | Asher Frayn |

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Abstract

This paper explores the ethicality of using Thalidomide in the modern day by assessing different continents' historical experiences with the drug, but also the current use of the medication and the restrictions surrounding its use.

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Introduction

Thalidomide is a drug that was first introduced to the commercial market around 1957 as a non-toxic and safe sedative and muscle relaxant. It soon became prevalent in Germany due to its apparently non-toxic properties and its ease of availability, being an over-the-counter drug. The lack of prescription needed, combined with its advertisement of being non-toxic and safe for pregnant women, quickly made it the first-choice drug for people suffering from severe morning sickness. The first signs of the embryopathy (a developmental abnormality in embryo caused by drug exposure) would arise in descriptions in 1959, but it would be another 6 years before it would be withdrawn from commercial use globally. By this time, an estimated 10,000 infants had been impacted worldwide (Macpherson & Figg, 2004). However, in 1964, the use of Thalidomide began increasing once again, this time in the use of exceptional, humanitarian cases, for the treatment of Hansen's disease, also known as Leprosy. Then in 1992, when conducting research into macular degeneration, it was discovered that Thalidomide could be effective in restricting the growth of blood vessels, possibly acting as a treatment for certain types of cancer. Since then, there has been a broadening in the attitudes of the general population. In 2002, Thalidomide once again became the wonder drug it was originally advertised as. This time, however, in the treatment of Hansen's disease, myeloma and some complications of HIV/AIDS.

With the continual rise and fall of Thalidomide since its discovery, it is necessary to address the widening use of the drug in the modern era (2002 onwards), given the potentially harmful side-effects that have been noted since the 1950s.

A Brief history of Thalidomide in Europe

Throughout the 1950s and early 60's in Europe, thalidomide was being used very broadly as an over-the-counter drug in Germany, to help with sedation and symptoms of morning sickness (Franks et al., 2004). The drug had never been tested on pregnant animals, and the sole reason it was marketed as the "safer alternative" to its competitors, was based on the premise that no matter how much of the drug was given to the rat, it would not die. For developing or testing a drug that is going to be circulated in the human market, especially a drug that was marketed towards pregnant women, more rigorous testing would have been advisable.

Some experts claim that worldwide thalidomide would lead to the death of approximately 2,000 children, and result in around 10,000 children being born with birth defects (Knightley, 1979; Medical xpress, 2010). Once the danger was realised, however, it was pulled from the market and the use was highly regulated (Magazanik, 2015). In 1968, the Medicines Act was passed as a direct result of the Thalidomide Scandal in Europe. This created strict restrictions between what types of drugs could be available for general sale, and what had to be prescribed by medical professionals. The Grünenthal executives and senior staff were put on trial for negligent manslaughter and other crimes associated with the thalidomide scandal. The trial continued for two years and was discontinued in December 1970.

Overall, it is likely due to the turbulent history of the drug usage in Europe, resulting in around 10,000 children being impacted by the drug, that there is a question surrounding the morality of its use today.

Current uses in Europe

As of 2022, thalidomide is only prescribed in the UK under strict regulations. Anyone who is prescribed the drug is made to undergo counselling where the risks are discussed. Any women who are taking thalidomide are required to take two types of birth control, and men are required to use contraception (Macmillan Cancer Support, 2015). Here it is clear that the measures implemented have had a significant impact on the rate of babies born with birth defects. In 1961 Britain, it was estimated by Leck and Millar (1962) that over 800 children were born with abnormalities attributed to thalidomide, compared to zero since 1970.

Ultimately, Europe witnessed the outcomes of using thalidomide and deemed it unsafe for general, unregulated use. Following the serious fallout that the Thalidomide epidemic of the 1950s and 60s resulted in, most European countries decided that continuing to allow widespread unchecked usage would be negligent and unethical.

A Brief history of Thalidomide in South America

Unlike its history in Europe, Thalidomide was not used for morning sickness in South America. It wasn't until Shekin Jacobs' 1964 discovery that Thalidomide could be used as an effective treatment for Hansen's disease, that the drug's popularity began to flourish in leprosy-prone areas of Brazil (Silverman, 2002). Since then, Thalidomide has been the first-choice recovery plan for many Brazilian physicians in the treatment of patients with severe complications of Hansen's disease. Following 1994 legislation, Thalidomide was put under tighter regulation in Brazil, and its production quickly became strictly regulated. Nevertheless, numbers of Thalidomide embryopathy would continue to rise, with some estimates suggesting that there were 100 potential cases between the years 2005 and 2010 (Crawford, 2013). Partially due to the prevalence of Hansen's disease and the availability of Thalidomide; between 2005 and 2010 over 5.8 million thalidomide pills were distributed throughout Brazil (Crawford, 2013). The majority of these pills had been distributed to impoverished Brazilians who had poor access to healthcare, where strict measures could not be enforced (Luiz Vinna & Lopez-Camelo, 2011).

Likely due to a combination of the prevalence of Hansen's disease in the years following 1968 in South America, and the lack of national healthcare systems until 2005, the prevalence of Thalidomide embryopathy have continued to be a persisting memory for many South Americans (Medical xpress, 2010). Therefore, the widespread unregulated Thalidomide prescriptions could be considered highly unethical.

Current uses in South America

Currently in South America thalidomide is mainly used in the treatment of symptoms associated with Hansen's disease. According to the World Health Organisation (2020), there were 127,558 cases of Hansen's disease reported in South America, 94% of which were reported in Brazil (*Leprosy*, 2022) . Furthermore, controlling the use of the drug in pregnant women is a continually difficult task to undertake, with the intake of the drug in early pregnancy being especially hard to manage , due to the unintended nature of most pregnancies. Following a case-reference approach, there have been 34 registered thalidomide embryopathy cases in South America since 1965 (Schüler, 1996). This is however, most likely unrepresentative of the true number, with monitoring systems having a low population coverage and a lack of defined phenotypes being monitored (Schüler, 1996). Dr Lavinia Schuler-Faccini, a professor at Universidade Federal do Rio Grande do Sul, estimated that there have been, "about 100 cases in these six years similar to Thalidomide syndrome" (Crawford, 2013). Elsewhere in South America there have been reported cases of several illiterate people misunderstanding the warning symbol that is required by law to be on the packaging. According to Claudia, Marques Maximino, the president of the Brazilian Association of Thalidomide Syndrome Victims, several pregnant women have purposely consumed the drug, as "they thought it was an abortion drug".

Overall, due to the prominence of Hansen's disease, and inability to appropriately regulate the use of the drug in early pregnancies and due to a lack of public awareness, the rate of thalidomide embryopathy continues to rise. This makes the morality of such widespread use of Thalidomide questionable.

Thalidomide in Asia

There is very limited research into the impact of Thalidomide in Asia, historical or modern. There has been some research on the historical impact of Thalidomide in Japan, and so this paper will focus on Japan within the Asian continent.

From 1959 to 1964 there were 309 victims of children born in Japan with Thalidomide embryopathy, but unlike their European counterparts, Japan reacted significantly quicker (Hinoshita, 2015). By September 1962, the drug was banned, and it wouldn't be until 2008 that the ban was lifted.

Although current research about the impact of modern uses in Japan is limited, Japan is responsible for much of the modern understanding of why Thalidomide causes the birth deformities. Such research includes Sakamoto (2009) and T.Ito (2010) who have conducted research about a recent development in sub-micrometre magnetic beads.

Thalidomide in North America

As with Asia, there is limited research into the impact of Thalidomide in North America, with the exception of the US.

Following reported cases of nerve damage in Europe, Dr Frances Kelsey at the Food and Drug Administration(FDA) refused to permit the public sale of Thalidomide in the US due to her questions surrounding the drug's safety for foetuses. The decision to not release the drug would significantly influence the US relationship with Thalidomide; there have only been 17 confirmed cases of Thalidomide syndrome in the US (H, 2002). Several months following Dr Kelseys' decision, evidence was found that Thalidomide was responsible for the severe malformations Europe had experienced and was linked to the death of three babies.

Since July of 1998, the FDA of the United States authorised the use of Thalidomide in the treatment of certain Hansen's disease complications. This would soon be expanded upon,.By October 2006, Thalidomide was also authorised in the use of patients with multiple myeloma. The decision to authorise the use of the drug was not taken lightly. Similarly to the European response, Thalidomide is only accessible via a prescription from a Risk Evaluation and Mitigation Strategy certified official (Thalidomide Today | Thalidomide, no date). This program ensures that people who are prescribed the medication are making an informed decision, and that there is strict control for pre-menopausal women . If prescribed in this situation, the physician must check for pregnancy during the treatment.

In the context of the US history with Thalidomide, and the current regulation surrounding its modern prescription, an argument can be made that the use of the drug is an ethical decision. Due to a cautious authorisation process, and not releasing the drug to the United States public, there were only 17 confirmed cases of infants being born with Thalidomide Syndrome. This same cautious authorisation process, has deemed the drug to be safe to use under specific conditions, and as a result America has not had a Thalidomide birth since the early 1960s.

Thalidomide in Australasia

The Australian response to the danger posed by Thalidomide is one of the most criticised. Despite this criticism, there is a lack of recent research on the impact of Thalidomide in Australasia. Within the continent there were a total of 124 cases of Thalidomide syndrome during the early 1960s.

This is partly due to an Australian doctor being the first to make the connection between Thalidomide and the increasing number of birth defects. In June 1961, Dr McBride wrote to The Lancet to warn them of the deformities he was noticing, and in December of that same year, the Australian government was warned of these findings by the drug manufacturers. Unlike in the US, following the governmental knowledge there was no media campaign to warn Australians of the dangers. Furthermore, there were no efforts to recall the drug from homes. In a BBC interview (Thalidomide scandal: How Australia's response has 'lagged behind', 2019) Ms McManus, a survivor herself, and lobbyist for other survivors claimed that "of 124 known Australian thalidomide survivors, between

20 and 30 were conceived in that timeframe where the government knew about thalidomide's atrocities, but did nothing".

The abundant government inaction in the case of Australia demonstrates the dangers of a complicit government and a lack of restrictions. This creates questions surrounding the moral philosophy of using the drug today (Taylor, 2018). Although Thalidomide was withdrawn in the Australian market in late 1961 and banned the sale of the drug entirely in August of 1961. In 2001 it would become authorised in the treatment of complications of Hansen's disease and certain bone marrow cancers (Taylor, 2018). Despite the resurgence of the drug in Australia, it would only be in October of 2020 that the Australian government would issue an apology (The Australian Government, 2020).

A notable legal case is Lynette Rowe, born on the 2nd of March 1962 with no limbs after her mother took Thalidomide during pregnancy. Rowe led a class action lawsuit against three parties: the German drugmaker Grünenthal, a UK-based Distillers Company which sold the drug in Australia, and Diageo Scotland, the successor company to Distillers. The claims were mainly situated around the idea that the Grünenthal drug manufacturers should have been aware that Thalidomide was linked to birth defects and the compensation they should receive for the pain, suffering and medical care. In 2013, after decades of international legal battles, numerous Thalidomide survivors won compensation of AUD$89 million (Coopes, 2013).

Discussion

In regards to the available literature documented in this paper, it is appropriate to conclude that given the proper restrictions, the use of Thalidomide as a modern medication is ethically justifiable. Despite the undeniable damage the drug has caused, resulting in over 10,000 children being born with severe developmental malformations, the hope it offers those suffering with myeloma and other chronic conditions, where other effective treatment opportunities are limited, is invaluable. Thus if properly regulated, with the correct procedure, the modern use of the medication is not only ethical, but essential in the place of no other treatment options.

The history concerning Thalidomide in each of these countries has made it apparent that regulations were a necessity. These regulations in Europe, North America and Australasia have led to a significant decrease in the detrimental side effects caused by Thalidomide. Many of the countries that were impacted by Thalidomide in the 1950-60s, have produced modern reports into how they are using Thalidomide currently and the successes they have had. However, this is not the case for many Asian countries that have been affected by Thalidomide. Despite Japan being one of the most impacted countries for cases of Thalidomide syndrome, there is a deficit in the number of modern research papers on the current uses of the drug. It is the belief of this paper, that this is an area in which more research is required.

Elsewhere, primarily in South America, the dangers of using the drug without the proper precautions in place can be seen. Partially due to the prevalence of Hansen's disease, Brazil in particular has seen

a resurgence in the number of infants being born with Thalidomide syndrome. Since 1965 there have been 34 verified cases, though the real number is predicted to be far greater. These cases demonstrate that the ethicality of the modern use of the drug is only justifiable when the correct provisions are in place.

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