

Reye Syndrome: Dangers of Aspirin Use in Children

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ABSTRACT

Reye syndrome is a rare and potentially fatal illness that affects the pediatric age group between 6 months - 18 years of age. It is characterized by encephalopathy and fatty degeneration of the liver. The cause is unknown but the disease is usually preceded by a viral illness or aspirin use. Aspirin use historically appears to be an important etiology in the development of Reye syndrome. We found and reviewed 7 published case reports of Reye syndrome after the use of Aspirin, of which six patients were male while one was female and the mean age of patients was 5.5 years (SD=4.25). Reye syndrome has different manifestations ranging from lethargy, irritability, confusion, seizures and death. Diagnosis of this syndrome can be made based on clinical signs and laboratory testing. There's no test specifically for Reye syndrome, however, liver function test shows elevated levels of liver enzymes (AST and ALT) with increased levels of ammonia. Liver biopsy is also useful in making a diagnosis, showing microvesicular fatty changes. The outcome of Reye Syndrome depends on the level of cerebral dysfunction, with about a third of patients suffering long term neurological deficits. However, when diagnosed and treated early, prognosis for survivors is good and recurrence is rare.

Keywords: Reye syndrome; aspirin; children

INTRODUCTION

Reye syndrome is a rare neurological disease with a predilection to affect children rather than adults. It is often associated with encephalopathy, amongst other symptoms. Aspirin, a common over the counter drug, may be administered to children with viral illnesses, thus precipitating this condition. In the diagnosis of Reye syndrome, the importance of good history taking cannot be over emphasized. Symptoms become

noticeable about 12 hours to 3 weeks after exposure to the trigger. Signs and symptoms include; lethargy, vomiting, disorientation, delirium and coma, depending on the degree of progression.[1] Other possible factors have been linked to the development of Reye syndrome; varicella, Epstein-Barr virus, cytomegalovirus, mycoplasma and shigella.

Of these, aspirin stands out as the most common and probable. [2] It is imperative to note that Reye is no longer a common condition. A feat attributable to a reduction in the use of aspirin in children due to public health educative efforts. Of note, improvement in diagnostic methods have also helped to pick out true cases of Reye syndrome, thus reducing the rate of misdiagnoses. [3] especially as some inborn errors of metabolism were previously misdiagnosed as Reye. [4]

METHODOLOGY

A literature review was performed for articles related to Reye syndrome and aspirin. We used PubMed to search for published articles, including case reports and case series. Searches through the references of retrieved articles were also performed.

After removing duplicates, we identified seven articles. The following keywords were used: Reye syndrome, aspirin, Microvesicular steatosis, salicylate and mitochondrial hepatopathy. Inclusion criteria consisted of case reports and case series that are available in English with complete laboratory investigative findings of Liver function tests and ammonia levels.

Exclusion criteria consisted of duplicates, abstracts, non-English articles, articles that did not include human subjects, and works that were unpublished or unrelated to the topic of interest.

TABLE 1: Case reports included in this review of published case reports.

AUTHOR	AGE	SEX	ALT (IU/L)	AST (IU/L)	AMMONI A(μ MOL/L)
Su Etal[5]	20 months	Female	255	461	214
Pessoa Etal[6]	7 years	Male	741	190	150
McGovern Et al[7]	12.5 years	Male	946	1113	181
McGovern Et al[7]	9 months	Male	1034	725	108
du Toit-Prinsloo Et al[8]	8 years	Male	1100	958	226
Cag Etal[9]	6 months	Male	Q75	402	80
Singh Etal[10]	8 years	Male	1118	554	142

RESULT

We identified 7 case reports from our search of the above named journals which fulfilled the inclusion criteria, six patients were male while one was female. The mean age of patients was 5.5 years.(SD=4.25)Markedly elevated liver enzymes was a consistent laboratory finding with a mean AST of 629IU/L and a mean ALT of 752IU/L.In Reye syndrome, hyperammonemia is the foremost aetiological factor in the mechanism of brain damage and encephalopathy and this was also markedly elevated in these patients with a mean of 157mmol/l.Other laboratory findings noted was raised prothrombin time and hypoglycemia.

DISCUSSION

Reye syndrome is a non-inflammatory condition that results in encephalopathy and liver failure due to mitochondrial insults and subsequent fatty degeneration of the liver. The first known and properly documented case of Reye syndrome was in 1963 by Reye et al. in Australia.[8] Reye syndrome has a fairly classic pattern as it affects children and is preceded by an upper respiratory tract infection (usually viral) that is treated with Aspirin [11]. Reye is thought to be due to aspirin mediated damage to the mitochondria in these young patients, hence preventing fatty acid oxidation in the liver. Inability of these fats to be oxidized leadsto fatty accumulation the classic histologic finding of microvesicular hepatic steatosis.Reye syndrome typically progressed through 5 stages according to the National Reye Syndrome Foundation[12,13,14]

Stage 1 includes symptoms such as vomiting, lethargy, confusion and nightmares. Fever is usually absent during this stage. The second stage presents with symptoms such as hyperactive reflexes, fatty liver on biopsy and hyperventilation in some patients. Stage 3 presents with possible coma as well as continuation of the symptoms seen in stage 1 and 2. Stage 4 worsens cerebral symptoms as patients may present with coma, dilated pupils with minimal light response. Stage 5 presents with multiple organ failure and even death.

Diagnosis of Reye syndrome usually includes a meticulous review of patient history to access for history of viral infection and subsequent aspirin treatment. The mainstay for definitive diagnosis is Electron Microscopy. Under the electron microscope, we see microvesicular steatosis. Markedly elevated liver enzymes such as AST and ALT are also useful in diagnosis.

Hyperammonemia is also a precipitating factor for Reye encephalopathy and is seen in most patients with encephalopathy. Other useful laboratory markers are prolonged prothrombin time due to liver damage and hypoglycemia. When diagnosing Reye syndrome, it is important to keep in mind a series of differential diagnosis such as viral encephalitis, drug overdose or poisonings, head trauma or liver failure.

CONCLUSION

From the above case reports,the dangers of aspirin has been emphasized.Aspirin has been found to be associated with the development of Reye syndrome. Acute encephalopathy and liver failure presenting after aspirin use in a child below the age of 19 should raise high suspicion of this syndrome.The incidence and prevalence of Reye syndrome has reduced in recent years and this is attributable to the reduction of aspirin use in children and improved diagnosis of inborn errors of metabolism.It is also important to ensure public health scrutiny to ensure continued surveillance of this disease especially in developing countries with poor health resources.

AUTHOR'S CONTRIBUTIONS

Each named author has substantially contributed to the underlying research and has approved the final manuscript.

CONFLICT OF INTEREST

This manuscript has not been published and is not under consideration for publication elsewhere. We have no funding and none of the authors have any conflict of interest, financially or otherwise.

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