USE OF ANALGESICS AND REYE'S SYNDROME

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ABSTRACT

Non-steroidal inflammatory drug are commonly used as an analgesic, antipyretics and also anti-inflammatory agents by many people at all ages in the world .Non-steroidal anti-inflammatory drugs are useful to relief for pain ,fever inflammation but they show only palliative therapy which also have common and /or rare adverse effects as well as therapeutic effects. Reye's syndrome is rare, but very severe and serious side effect related to this group drugs.

Therefore in the present study. Reye's syndrome was examined in detail especially in children. Its prognosis, sign symptoms and reasons, treatment and relationship between use of the drugs and Reye's Syndrome, were evaluated. According to evidences about this problem, it is clear that there is between some analgesic group relationship group drugs and RS. Additionally serious the role and duties of health personnel especially pharmacist to prevent or reduce the risk are emphasized in this study

Key word: Reye's syndrome, Nonsteroidal anti-inflammatory drugs.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) which is using primary or secondary inflammatory, fever and pain. NSAIDs are among the most widely used for relieving with prescription or nonprescription among pharmaceutical agents in all age groups, in every country. Today NSAIDs are consumed about at least 30 million people in the world. This drugs usage increased abnormally for about 20 years. NSAIDs are used palliative treatment for rheumatoid arthritis, osteoarthritis, infectious and inflammatory diseases, menstrual cramps, sprains, slightly or normal pain, dysmenorrhea, juvenile rheumatoid arthritis and like this diseases. Using NSAIDs without prescription is possible and they are using for many disease with fever, pain and inflammatory so NSAIDs are chosen primary drugs by people. These drugs are using widely but they have many important side effects. One of them is Reye's syndrome which has occurred with the use of NSAIDs especially salicylates while viral infection occurs in children.

Reye's syndrome is rare form of acute non-inflammatory encephalopathy which is mostly brain and liver that usually follows an acute viral illness in children who is under 18 ages, and usually results in death. Although Reye's syndrome was described as early as 1929, it was not recognized as specific entity until 1963, when Dr.R Douglas Reye, an Australian pathologists, reported it as syndrome. The etiology of Reye's syndrome is uncertain. Drugs, some toxins and metabolic diseases are responsible. Ingestion of acetylsalicylic acid during or after a viral illness significantly reason of Reye Syndrome. The viral infections are mostly influenza B, influenza A and varicella. Currently, there is no conclusive data as to whether other forms of salicylates are associated with the development of Reye's Syndrome but the National Reye's Syndrome Foundation recommend that aspirin and combination products containing aspirin not be taken by anyone during viral illness. Moreover it is obscure point whether other drugs from this group cause Reye's syndrome or not.

Therefore major aim of the present study was to evaluate relation between analgesics usage and Reye's syndrome. Reye's Syndrome's ethiopathology, prognosis, which analgesics cause to the syndrome, frequently its reasons, treatment were extensively investigated. All evidences were assessed. In order to reduce risk of Reye's Syndrome especially in children. Finally, moreover responsibility of pharmacist and other health staff were determined.

DESCRIPTION OF ANALGESICS

Analgesics is a number of drugs purposed to relieve pain and used to acquire analgesia without causing the loss of consciousness, inhibiting the conduction of nerve impulses or varying the sensory perception. The primary classes of analgesics are the narcotics including additional agents that are chemically based on morphine molecule but have minimal abuse potential; Nonsteroidal anti-inflammatory drugs (NSAIDs) that includes the salicylates and Acetaminophen. Other drugs, notably the tricyclic antidepressants and anti-epileptic agents such as Gabapentin, have been used to relieve pain, particularly neurologic pain but are not routinely classified as analgesics. NSAIDs are among the most common analgesic medication in the World which is mostly preferred to relieve and reduce pain, fever and inflammation. NSAIDs are also preferred as non-narcotic analgesics, anti-inflammatory NSAIDs and non-opioid analgesics that have analgesic, anti-pyretic and anti-inflammatory effect. They have different kinds of classes but all of them have same therapeutic effects and adverse effects. In additionally, chemical structures of NSAIDs are different from each other but all of them have weak organic acid structure. Narcotic analgesics are also known as opioids that are all derived from opium family. This group of analgesics contain morphine, codeine and a number of semi-synthetics including meperidine, propoxyphene and others. All Narcotic analgesics are

effective in treatment of visceral pain when used in adequate doses. Their side effects are associated with their doses because this type of analgesics are showed addictive property so they are controlled under federal and state laws. There are some differences between these two types of analgesics. NSAIDs act primary in peripheral tissues to inhibit the formation of pain-producing substances such as prostaglandins so they are also known as milder form of analgesics. On the other hand, opioid analgesics have quite different mechanism of action of the NSAIDs that play directly role on the central nervous system so they are not only inhibit the incoming conceptive signals to the brain but also act at higher brain centers and controlling the affective component of the pain. As a result of, NSAIDs are class of non-addicting medication and they have less adverse effects when compared to the opioid analgesics. Acetaminophen is quite different them these two classes because that is non-narcotic analgesic with no anti-inflammatory properties. It is generally preferred for treating to mild to moderate pain. This drug is well tolerated in normal doses. However, it has toxic activity at high doses. Acetaminophen, salicylates and other non-steroidal anti-inflammatory drugs are found alone or in combination with other medicines in the composition of hundreds of medicines sold without prescription and over the counter medicines.

Description and History of Reye's syndrome

Reye's syndrome (RS) is very rare but it is a very serious, risky and life-threating condition which is characterized by viral illness and encephalopathy and fatty degradation of liver. It is describes as biphasic disease. First phase of disease is related with a non-specific viral-like illness that are respiratory tract infection or gastroenteritis .Besides that, encephalopathy is emerged with second phase of the illness which starts unpredictably with sensorial vomiting and sensorial changes. Reye's syndrome is a disease of infancy, childhood, adolescence and in some condition that may affect the adults but it occurs mostly in children depending on excessively usage of aspirin and some other analgesics during viral illness. Most of mitochondria, brain and liver are damaged in Reye's syndrome and these damages cause brain death and liver lubrication. Reye's syndrome is clinically begins after influenza like viral infections, upper respiratory tract diseases or gastrointestinal symptoms which is seen mostly after influenza especially Influenza B or Varicella in U.S. The health condition deteriorates after few days and recurrent severe vomiting is the most prominent symptom of this disease. This vomiting is the initiation of the encephalopathy and this situation may lead to the patient to loss of consciousness. A lot of factors can contribute to the development of Reye's syndrome. Salicylates which is taken during viral infections is the most trigger factor of the disease.

Reye's syndrome was firstly described in 1963 in Australia by RDK Reye. The occurrence of syndrome may have first been reported in 1929. In 1964, investigation of an outbreak of Influenza B that explained 16 children who developed neurological problems four of whom had a profile remarkably similar to Reye Syndrome was issued by Dr George Johnson and colleagues. According to some researches, this syndrome was defined as Reye-Johnson Syndrome. Although, it is commonly known as Reye's syndrome. Besides that, RS became reportable disease in 1973 in United State. Some studies such as Ohio and Michigan was shown that this syndrome was triggered depending on the use of Aspirin during upper respiratory tract or chickenpox infection. Beginning in 1980, physicians and parents were warmed about the association between the Reye's syndrome and use of salicylates in children and teenagers were warmed about the association between the RS and use of salicylates in children and teenagers with chickenpox or virus-like illnesses. Besides that, peak incidence was reported in 1979-80. In 1982, an advisory was published by U.S Surgeon Geed and in 1986, Reye's syndrome related warming label was required by the Food and Drug Administration (FDA) for all Aspirin containing medications (Daniel et.al. 2017).

Etiology of Reye's syndrome

The etiology of Reye's syndrome is not fully understood. Drugs, toxins and metabolic diseases are responsible for this disease. Besides that, it. There is thought to be linked to a viral infection. The viral infection which includes both Influenza B and Varicella are well-explained but the development of RS which contains each of these viral interventions is not widespread and it is not fully explained why specific induvial develop the disease. Also, researches shows that there is a link between the RS and use of salicylates. The salicylates which is taken especially during viral infections is increased the risk of the Reye's syndrome (John et.al. 1981).

Heterogeneity of Reye's syndrome

Reye's syndrome infection is a syndrome that is contained in a number of heterogeneous disorders caused by metabolic poison or drug. This process with suspicion is a critical process in diagnostics and usual renaissance syndrome and this syndrome requires a differential diagnosis.

In experimental animal models and environmental toxins such as aflatoxins, pesticides, insecticides and many chemical substances can cause symptoms like RS. Drugs containing salicylate, phenothiazine, metoclopramide, zidovidine, valproic acid, didanosine and various antiemetic agents can cause Reye's syndrome.

The viral-activated defense mechanism results in the primary isoforms of the cytochrome P450 (CYP 450). Some people who are genetically predisposed many even result in clinical

irregulities, even monitoring the therapeutic doses of a drug metabolized via the P450 cytokine. As a result, mitochondrial disorders can cause some disturbances in metabolism.

This is not a distinguishing factor for the liver. Most of energy-loaded drug metabolism occurs in the brain and skeletal muscles (Morgan et.al. 1963).

Causes of Reye's syndrome

The reason for the formation of the Reye's syndrome is not fully known but a number of studies Show that acetylsalicylic acid used in viral infection increases the risk of the RS in children and most of the symptoms of this disease are hidden (NIH Consense statement 1981).

•Viral infections: Acetylsalicylic acid used in children is known to be the most common cause of RS. These viral infections are Influenza A, Influenza B, Varicella zoster which are generally caused RS. In such diseases, ASA and similar medicines are taken to relieve the symptoms and at this condition, RS and its symptoms do not reveal (Schrör et.al. 2007).

The main pathogen of gastroenteritis is the Rotavirus which is very common in infancy and childhood in winter. The relation between the RS and Rotavirus has been reported. In a study conducted in UK between 1981 and 1992, 57 patients with viral infection, 9 patient with influenza us and 3 patient with rotavirus were detected. Rotavirus gastroenteritis is believed to lead to RS, there is no evidence to support this situation. Large-scale epidemiological and pathological studies are required. Other viruses that lead to Reye-like syndrome are defined as measles, herpes simplex, rubella and human herpes virus (NHS, 2017).

•Drugs:

Salicylates: Salicylates are drugs that are classically associated with Reye's syndrome. Many epidemiological studies have revealed the association of Salicylates with disease. Reye's syndrome developed in 0.1% children receiving aspirin but more than 80% of patients who received aspirin in the last 3 weeks were diagnosed with Reye's syndrome (NHS, 2017).

Paracetamol, experided tetracyline, valproic acid, zidavudine, didanosine and antiemetics have been associated with the Reye and Reye-like syndrome. A report of a child receiving antiretroviral therapy (didanosine and sstavudine) at over 3 months of high doses resulted in Reye's syndrome (Medscape, 2017).

•External factors without drugs: Reye and Reye-like syndrome, insecticides, herbicides, aflatoxins, paint-thinners, hepatotoxic fungi and acne-berry hypoglycemia included herbal-remedies containing atractylocite (NHS, 2017). According to a study done by the New Brunswick, many children are not only Reye's syndrome due to influenza, varicella or viral infection. Genetic and environmental factors sometimes cause the Reye's syndrome. The main suspect factors are chemicals used in aerial forest spray programs at New Brunswick. In which

the active substance is an organophosphate insecticide known as phenothiodin (Devulapalli, 2000).

•**Genetic factor theory:** Genetic disorders constitute Reye-like syndromes. Mostly fatty acid oxidation disorders and urea cycle disorders are identified but at the same time, amino and primary carnitine organic acid deprivation, primary carnitine deficiency and carbohydrate metabolism irregulaties are found. Sudden disturbances and recurrence of symptoms are depended on dietary and metabolic changes. Genetic disorders occasion family members of these symptoms. The rate of patients with RS was 0.4%. The proportion of patients' brother/sister with RS is 2.3%.It is likely that some of these patients will be caught in RS (NHS, 2017).

According to a theory, a viral infection can change in the immune system of child born with yet unknown susceptibility or genetic differences or it can damage when a child with a genetic predisposition to the theory receives aspirin, one of the components that damage the aspirin salicylate activity has changed and can cause severe destruction of the damaged immune system and destruction result in attacking healthy liver cells in the immune system but there is no clinical evidence supporting this theory (John et.al. 1981).

Risk groups for Reye's syndrome

Reye's syndrome can be seen in all ages of children but that is most common between 6-9 ages and 10-14 ages. 6-7 ages are very important and critical ages because this disease is peaked in this period. There is no discrimination between sexes. RS can be seen both genders (Belay et.al. 1999).

Reye's syndrome is seen between 5-9 ages with Varicella. On the other hand, it is seen between 10-14 ages with Influenza especially Influenza B (Kramer, 2009). Besides that, RS is very rare for newborns and for people over 18 years (Belay et.al. 1999).

Incidence of Reye's syndrome

Disease Control Center (CDC) says that only 10% cases of Reye's syndrome are recorded. The incidence of RS has decreased dramatically after health warnings relate on-aspirin delivery to children in 1980s (Belay et.al. 1999). In 1980s, there were 52 cases per year in England and Ireland but in 1990s this number has fallen to 17 cases. 597 cases are reported in UK between in 1981-1996 (Belay et.al. 1999). Similar rates were recorded in other countries. The case of RS has not been recorded in England and Wales since 2001 (NHS, 2017). The incidence of disease was recorded as 0.6/100.000 children in 1979. On the other hand, this ratio was dropped to 0.1/100.000 children in 1989. Patients were not reported more than 36 in US between in 1987-1993 in one year and patients were not reported more than 2 between in 1994-1997 in

one year (Belay et.al. 1999). 1207 cases were detected in total under 18 years of age between 1980 and 1997 in US. The incidence rate was reported 0.15-0.88/1.000.000 children in this period per year (Belay et.al. 1999). The incidence of RS was defined 0.797/1.000.000 children between at 1995-1996 in France. The disease can be seen very extremely during the season (December to April) when viral infections are on rise. Incidence of disease is 1 or 2 decibels in summer (Belay et.al. 1999).

Diagnostic Criteria for Reye's syndrome

Reye's syndrome is very rare disease. Firstly, beginning step in diagnosis is removed some diseases which are seen rarely and have similar symptoms with RS.

These diseases are;

• Meningitis

• Aflatoxin poisoning

• Encephalitis

• Urea cycle disorders

• Fatty acid oxidation disorders

Besides that, urine and blood test can be performed to determine if a toxin or bacterium has an increase in blood and whether the liver function is normal or abnormal (Praxis, 1994).

Signs and Symptoms of Reye's syndrome

Some signs and symptoms of Reye's syndrome are occurred about three to five days after onset of a viral infection such as influenza or chickenpox or upper respiratory infection such as cold. These signs and symptoms are including;

SIGNS and Symptoms of Reye's syndrome

Diarrhea Hallucinations

Rapid breathing

Weakness or paralysis in the arms and legs

Persistent or continuous vomiting Seizure

Unusual sleepiness or lethargy Excessive lethargy

Irritable, aggressive or irrational behavior Consciousness

Confusion Delirium

Disorientation fluctuating personality changes

Hyperammonemia High level of alanine aminotransferase and aspartate aminotransferase

Diarrhea and rapid breathing are generally first signs and symptoms of RS especially for children younger than age 2. Besides that, persistent or continuous breathing and unusual sleepiness or lethargy are seen in older children and teenagers. If the conditions and complaints

progree, the signs and symptoms can dramatically increase and cause hazardous or fatal consequences such as delirium, coma and death may occur at the end of the this disease. Figure 9 has been demonstrated some symptoms of RS (The New York Times, 2017).

Stages of Reye's syndrome

Basically, Reye's syndrome can be categorized into 5 different stages which are ordered according to severity of disease. Lovejoy explains the evolution of stage 1 to 5. Besides that, Hurwitz is added unclinically stage which is called as phase 0. Finally, Disease Control Center is used the Hurwitz's classification and he is only added phase 6 to this classification (Anochie, 2013). These are;

Stage 0: Abnormal history associated with Reye's syndrome and laboratory findings, clinical uncertainty.

Stage 1: Vomiting, laboratory evidence of liver dysfunction, lethargic, sleepy and headache are general symptoms of this stage.

Stage2: Deeply lethargic, restless, confused, delirious, combative, hyperventilation and hyperreflexia are symptoms that are seen in stage 2.

Stage3: Obtunded or in a light-coma, decorticate rigidity are general symptoms of stage 3.

Stage4: Deeping coma, seizures, decerebrate, rigidity, fixed pupils and loss of oculovestibular reflexes are seen this stage.

Stage5: Seizures, deep coma, flaccid paralysis, abset deep tendon reflexes, respiratory arrset and fixed, dilated pupils are symptoms of the stage 5.

Stage6: Patient who are not classified, cuartive and they are trying to change the level of consciousness with other drugs.

Some Complications of Reye's syndrome

Many complications are developed irreversibly. These complications are;

Electrolyte abnormalities Hypoglycemia

Acid-base disorders

Fluid impairment or uncontrolled secretion of antidiuretic hormone

Low blood pressure Cardiac arrhythmia

Bleeding; especially gastrointestinal

Hemorrhage Pneumonia

Deterioration in thermoregulation Coma

Death 30% permanent disability and impairment of motor functions in survivors.

Prognosis of Reye's syndrome

Reye's syndrome should be treated urgently as it can rapidly damage the lungs and brain. A child with RS should immediately receive an intense look to continue body operations. Survival rate due to developments in the treatment RS and its treatment is now estimated at 80% but brain may damage after this disease in some children (Butterworth, 1998).

Reye's syndrome mortality rate has decreased to 50% to 20% in recent years. According to CDC reports, the mortality rate was 31% in 1997 (Anochie, 2013). Some patients did not complete. Patients who are younger than 5 years have a relative risk about 1.8.

The level of ammonia that best describes the duration of disease's progression. Despite that fact that most reports correlate with a slight increase of 900mcg/dl. In 1999, the belief that the level of 45mcg/dl ammonia was the most accurate improvement with a relative risk of 3.4.

Ammonia level at 45mcg/dl, approximately 3% patients have neural sequelae and 11% have simple sequelae.

The mortality rate for stage 0 is 15% but for stage 5 is 90%.Survivors have a high rate of having long-term neurological disease in those with ammonia levels of more than 45mcg/dl, those with stage 2-5 disease or those under 2 years of age (Anochie, 2013).

Treatment of Reye's syndrome

Reye's syndrome does not have specific treatment. The patient must be taken to intensive care unit urgently during the treatment of the RS. The purpose of the treatment is minimized the symptoms of RS and supported to vital functions such as blood circulation and respiration. The majority of brain-injured end points are very important in preventing permanent damage to the brain.

As a intravenously treatment;

Glucose or Insulin, corticosteroids, diuretics, chemicals, sodium benzoate/sodium phenyl acetate and ondansetron are preferred for intravenously treatment of the Reye's syndrome.

• Glucose or Insulin: used for increasing the blood glucose levels.

• Corticosteroids: preferred for reducing the brain edema.

• Chemicals: used to correct blood chemistry and given to provide nutrients (Butterworth, 1998).

• Sodium benzoate and Sodium phenyl acetate: They may be effective in treating hyper ammonia. Hemodialysis is preferred when the ammonia level is above 500-600 mg/dl. Sodium benzoate and Sodium phenyl acetate can be used before the onset of hemodialysis or in conjunction with hemodialysis. Antiemetic agents are administered to reduce the vomiting in patients during the usage of sodium benzoate and sodium phenyl acetate.

• Ondansetron: It is used with Sodium benzoate and Sodium phenyl acetate to control nausea and vomiting associated with Reye's syndrome. Besides that, it is a selective Serotonin (5-HT3) receptor antagonist which blocks peripheral and central serotonin. It prevents nausea and vomiting in people who have been administered with intravenously sodium benzoate and sodium phenyl acetate (Anochie, 2013).

Hemodialysis is the most appropriate treatment for elevated ammonia level. Hemodialysis is recommended in patients who initially responded to Sodium benzoate and Sodium phenyl acetate. Hyper ammonia treatment increases nitrogen elimination. FDA has accepted sodium benzoate and sodium phenyl acetate in the treatment of hyper ammonia due to urease cycling disorder (Anochie, 2013). If the RS continues to progress seriously and the patient needs help in breathing, the tooling may need for the patient (Langford, 2002). Other body functions should return to normal in few days if brain edema is absent and the patient can recover for several weeks.

Relationship of analgesic consumption to Reye's syndrome.

ASA is the best known chemical agent related to the RS. After many studies conducted in America and England during the 1980s, ASA was proposed as major reason in RS cases.

After limitations on the consumptions of ASA in the 1980s were established, a dramatic decrease in the RS incidence has occurred (Prior et.al. 2000).

Aspirin and Reye's syndrome

After the discovery of the Aspirin in the 1800s, the patients were simply advised to 'take two aspirins and go to bed'. Aspirin is regarded as a panacea for many diseases. Being used as antiplatelet agent for cardiovascular diseases is one of aspirin's major roles.

The obtainability of aspirin with or without a prescription has caused it to be a popular analgesic and an anti-inflammatory agent. Its low risk profile and the fact that it can be taken on high dosages are the reason why the aspirin is frequently preferred. However, aspirin is far from a good medicine. Gastrointestinal and cerebral hemorrhages are risks for the elderly population. The consumption of aspirin for young people has been associated with the Reye's syndrome.

International Reye's Syndrome Foundation has prohibited the consumption aspirin by children or the young population (Langford, 2002).

There several factors in the development of RS however, aspirin consumed during a viral infection is indicated as the main causer of the disease. Its relationship to salicylates has been clarified by several world-wide epidemiological studies. RS has only developed in 0.1% of children but 80% of the RS patients backgrounds show that the patients has consumed aspirin within the last 3 weeks (Anochie, 2013).

The relation between the salicylate and RS was thought to be a prejudgment and the studies were limited however; after the suggestion made by healthcare organizations on not treating children with salicylates, the RS incidence decreased suddenly and dramatically.

. The causality between the RS and salicylates has never been fully established. However, in vitro studies show that when the fibroblastic culture and control groups of RS children are compared, the salicylates cause a decrease in long chain fatty acids, palmitates and beta-oxidation.

Studies show that consuming aspirin to prevent a viral disease also increases the RS development. If there is a viral disease, aspirin or other medicines consisting of aspirin should not be taken (Anochie, 2013).

Acetaminophen and Reye's syndrome

Acetaminophen is an analgesic and antipyretic agent which, show chemical similarities to aspirin.

After FDA and International Reye Syndrome Institution banned aspirin for due to Reye's syndrome, acetaminophen began to be prescribed as an analgesic and antipyretic. Frequency of Reye's syndrome cases decreased after the use of acetaminophen. A study conducted in Sidney Hospital where Reye's syndrome was first diagnosed showed that only 4 (8%) out of 49 patients with Reye's syndrome took ASA. This finding is related to limited salicylate use for viral diseases in Australia where acetaminophen being prescribed mainly to be used on children with viral diseases. Clinical and epidemiologic studies show a relation between acetaminophen and RS, however small. For example, a study conducted in Australia showed that 24% of patients with RS took acetaminophen. 41% of age-matched viral infection patients who were prescribed acetaminophen did not develop RS.

Crocker et al. think that ASA and acetaminophen worsen the condition when used for viral infections and potentially help RS develop (Prior et.al. 2000).

Ibuprofen and Reye's syndrome

Aspirin is considered a major reason for RS. When ibuprofen was first marketed and prescribed for children, the possibility of this new agent increasing RS risk rose. In a Boston University study about illnesses conducted on 55000 children, a relation between the medication and the illness was not observed.

RS incidence data results between 1977 and 1997 show that the dramatic decrease of RS is in correlation with increased ibuprofen sales of 1989-1997.

As ibuprofen usage became widespread, the researchers decided that there was no relation between ibuprofen and RS (Langford, 2002).

Ways to protect from Reye's syndrome and Recommendations

Unless your doctor suggests, you do not give acetylsalicylic acid or other medicines that contains this active ingredient for treatment to children under age of 18.

Other preparations containing acetylsalicylic acid;

• Acetylsalicylate

• Salicylic acid

• Salicylate

If your child has a flu or viral disease, paracetamol and ibuprofen should be given to reduce the pain. Besides that, it is not recommended to use ibuprofen in children with asthma and liver damage. You should consult your doctor and pharmacist if you are not sure.

DISCUSSION and CONCLUSION

Analgesics are widely used throughout the world. They include a very broad class that can be used both prescription and non-prescription. Analgesics are generally safe and are often consumed by many get groups as they exhibit fewer side effects than other drug classes, but occasionally have some adverse effects due to analgesic use. One of the most spectacular multipliers of there is the RS which takes especially children into the risk group.

Reye's syndrome is a rare but this syndrome usually results in a dramatic outcome, and the outcome of the disease may be death. For this reason it is necessary to have more knowledge and awareness about RS both doctors and pharmacists need to have more information about this subject. This should include in-vocational programs, lectures congresses, conferences on the RS After that, doctors and pharmacists should ensure that the information which is receiving the most appropriate way and understanding it by public. At this point, there is a great deal of duties dedicated to pharmacists. These roles are;

- Pharmacist should warn people in the interval especially December and April when viral diseases are seen more often. We need to have a brochure about Reye's syndrome in our pharmacy especially during these months.
- If doctors are prescribing medicines containing aspirin or aspirin, pharmacist should definitely look at diagnosis especially children under the age of 18. If there is a viral disease, pharmacist contact the doctor immediately.
- Pharmacist have to ask who gets the illness who wants to take aspirin without prescription if the medicines are used for child under the age of 18, pharmacist must be warned to patient.

Media organizations a play other major and critical role about the RS because visual works or news delivered via TV, radio, newspaper or internet will attract more attention from the public and will require the public to take more precautions.

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