REVIEW ARTICLE Open Access

A Review Article: Clean Water Contamination as a Risk Factor for Acanthamoeba Keratitis

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ABSTRACT

Introduction: Infectious keratitis is one of the main causes of visual impairment. The incidence of acanthamoeba keratitis is relatively rare, while the prevalence is around 1 to 9 cases per 100.000. One of the factors supporting the occurrence of *acanthamoeba* keratitis is the increasing use of contact lenses around the world.

Content: When there is microtrauma to the cornea, it can cause the expression of the mannose on the surface. With the emergence of mannose in the form of glycoproteins, it will be a requirement for the attachment of *Acanthamoeba* spp.

Conclusion: Keratitis *Acanthamoeba* is an infectious disease of the cornea due to the use of contact lenses that are too long exposed to water which causes the entry of *Acanthamoeba*. This disease has a good prognosis with immediate drug administration within the first 3 weeks after the onset of symptoms

Keywords: Keratitis; *achantamoeba*; cornea infection

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Article history:
Received: 10 October 2022
Accepted: 15 November 2022
Published: 30 December 2022

Published by:
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Mobile number:
+62821 9721 0007

Email:
greenmedicaljournal@umi.ac.id

Introduction

Infectious keratitis is one of the main causes of visual impairment. Keratitis is a major cause of turbidity of the cornea. The main cause of keratitis in developing countries is due to work-related ocular trauma. Several occupations can have a high risk of contracting this disease, including divers and fishermen who work in aquatic environments[1]. Precise early diagnosis of the causative organism is important to provide appropriate therapy to the patient [2]. Incidence of acanthamoeba keratitis is relatively rare, while the prevalence is around 1 to 9 cases per 100.000 [3]. One of the factors supporting the occurrence of acanthamoeba keratitis is the increasing use of contact lenses around the world[4]. In the United States, the incidence of acanthamoeba keratitis is estimated at 1 to 2 new cases per 1 million contact lens wearers each year, whereas 16.7% of adults in the United States wear contact lenses.[5]Acanthamoeba keratitis was first discovered in South Texas, United States in 1973 by a farmer who washed his injured eye with tap water. When the infection is not treated promptly, the sequential spread of infection can occur to deeper parts of the eye structures and central nervous system which can manifest as granulomatous amoebic encephalitis.

One of the pathogens that can cause keratitis in coastal communities with the majority of work as divers and fishermen is *Acanthamoeba spp*. *Acanthamoeba* parasites can cause progressive infection of the cornea[8]. The main risk factor for *Acanthamoeba* (KA) is the use of contact lenses while swimming or diving. In 2 of the 8 species of *Acanthamoeba* there are 2 types of species that most often cause infection, namely *A. castellanii and A. polyphaga*. *Acanthamoeba* is an amoeba that is often found in swimming pools, sea water, rivers, tap water and contact lens fluid. A late diagnosis of KA can cause amoeba to penetratethe corneal stroma and affect the success of therapy so treatment will be more difficult [9]. Considering that the local content of the Faculty of Medicine, University of Mataram is Archipelagic Medicine, the authors are interested in discussing *Acanthamoeba* in Coastal Residents of West Nusa Tenggara.

Definition

Acanthamoeba keratitis (KA) is a pathological condition in the form of corneal infection of the eye caused by acanthamoeba[10]. A person who frequently uses contact lenses increases the risk of minimal trauma to the cornea so that acanthamoeba can enter through the eye.[1]

Epidemiology

According to research data from Basic Health Research in 2013, the prevalence of corneal opacities reached 5.5%.[12] The incidence rate of this incident was found to be high in groups with livelihoods of farmers/fishermen/laborers which may be related to a history of mechanical trauma or work accidents to

the eyebecause in Indonesia the use of personal protective equipment at work has not been optimally applied[13]. The research continued until 2019, it was found that around 5% of the incidence of KA was associated with the use of contact lenses caused by *Acanthamoeba spp*[14].

Pathophysiology

In general, humans have a high resistance to *Acanthamoeba spp* due to the high concentration of immunoglobulin A in the lacrimal fluid which functions as an anti-protozoal. *Acanthamoeba spp* can enter the cornea, one of which is when there is microtrauma from the corneal epithelial layer and contact with a polluted environment. Upon entering the eye, *Acanthamoeba spp.* will attach to the corneal epithelium through glycoproteins present in epithelial cells and *mannose* located on the trophozoite membrane. When there is microtrauma to the cornea, it can cause the expression of the *mannose* on the surface. With the emergence of *mannose* in the form of glycoproteins, it will be a requirement for the attachment *of Acanthamoeba spp*. When the number of expressions is greater, *Acanthamoeba spp* will become more virulent and release toxic factors. An important component of KA is the protease MIP133 (Mannose Induced Cytopathic Protein) which can damage keratocytes, epithelial cells, and endothelial cells, causing apoptosis of macrophages[7]. There are 2 stages in the life cycle of acanthamoeba namely, the vegetative trophozoite stage and the dormant cystic stage[1].

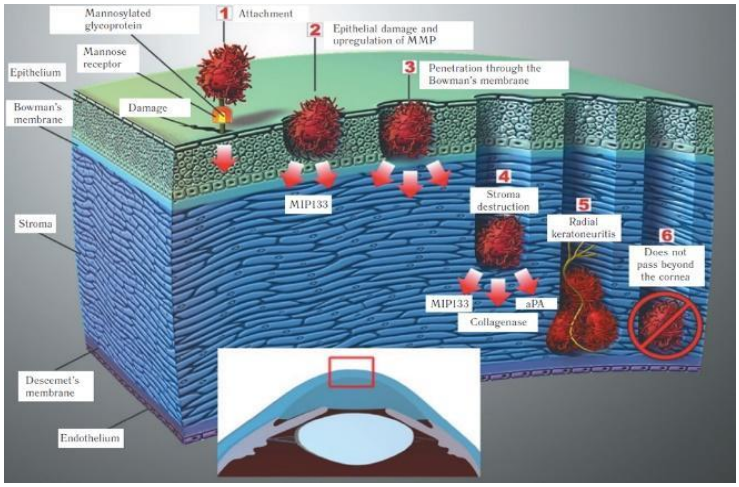

Figure 1. Pathogenesis of Acanthamoeba[7]

Clinical manifestations

Keratitis *Acanthamoeba* (KA) is often delayed or misdiagnosed with another infectious keratitis. The difficulty of diagnosis is because,in the early stages of the disease course, the clinical manifestations of KA are often non-specific and resemble the clinical manifestations of other corneal infections. Complaints of ocular irritation, blurred vision, and splitting are usually minimal. However, in KA there is a characteristic symptom in which the patient often complains of severe pain in the ocular or periocular area that is followingother clinical signs found. In addition, in KA the infection is almost always unilateral and will slowly progress from the epithelium to the stroma. Other complaints that may occur are eye redness, photophobia, discharge, and the sensation of a foreign body entering the eye[15].

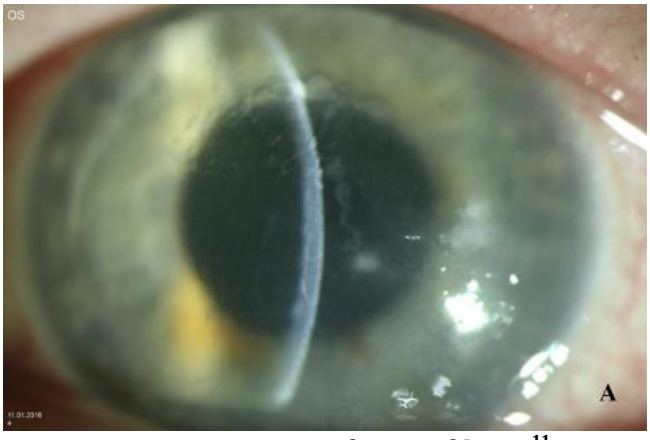

Figure 2. Overview of ring infiltrate[11]

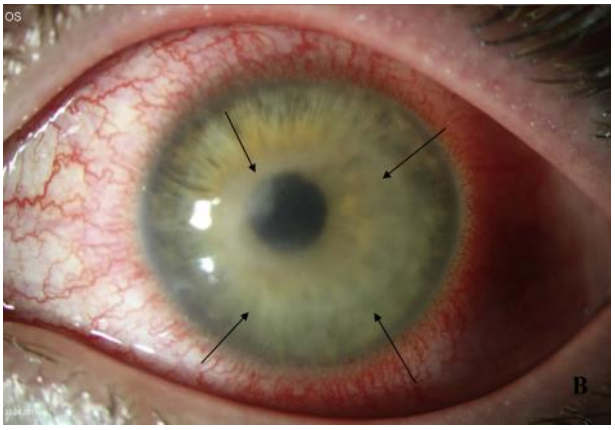

Figure 3. *Perineural infiltrate*[11]

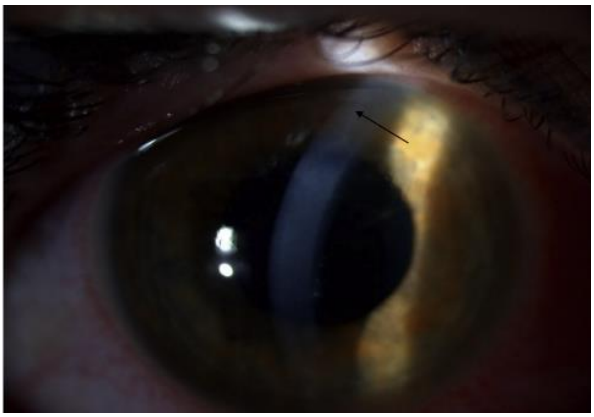

Figure 4. Features of scleritis, mature cataracts, iris atrophy, and persistent mydriasis[11]

Diagnosis

A thorough examination starting from the anamnesis data collection, physical examination, and supporting examinations is required in establishing the diagnosis of KA. In the history, it is necessary to obtain a history of using contact lenses, swimming or exposure to contaminated water or soil, as well as a history of trauma to the eye area which is the main risk factor for KA[14]. On physical examination, an in-depth ocular examination using a Slit Lamp. On this examination, chameleon-like epithelial changes or dirty epithelium in the first 2 weeks after the first symptoms appear. The dirty epithelium can be found in 50% of patients with KA. Furthermore, a ring infiltrate or Wessley immune ring will appear in the first 2 weeks to 1 month. The infiltration that occurs will continue and in the 6th week there will be a perineural infiltrate that can be found in 63% of cases of KA. If it is not treated in the following months, common complications of KA can occur in the form of mature cataracts, persistent endothelial defects, iris atrophy, secondary glaucoma, and other complications such as scleritis, sterile anterior uveitis, choriorenitis, and retinal vasculitis, which are less common happen[11].

Based on the depth of the lesion or defect that occurs in the cornea, infectious keratitis including KA is classified using grading as follows:

Table 1. Infectious keratitis grading[16]

Grade	Type of Infectious Keratitis
1	The defect occurs only in the epithelium
2	Mild thinning of the stromal layer, <50% corneal thinning
3	Thinning in the stromal layer, >50% corneal thinning
4	Descematocele (protrusion of intact Descemet's membrane)
5	Corneal perforation, defects

in all layers of the cornea

Investigations need to be done to ensure that the keratitis iscaused by *Acanthamoeba spp*. The supporting examination that has been consideredthe golden standard for establishing the diagnosis of KA is culture on agar media which is coated with *E. coli* bacteria. In addition, the high sensitivity (100%) and specificity (96%) of the polymerase chain reaction (PCR) examination shows the potential for PCR to become the golden standard for the diagnosis of KA in the future. IVCM (In Vivo Confocal Microscopy) has also been chosen because of its non-invasive procedure and high sensitivity (85.3%) and specificity (100%) [11].

Treatment

Conservative therapy of KA requires the use of a combination of two topical drugs. The combination of Polyhexamethylene biguanide (PHMB) with 0.02% chlorhexidine is a first-line therapy for KA which is quite effective to treat *Acanthamoeba spp* in trophpzite and cyst. Other combinations that can be chosen are the combination of chlorhexidine with natamicin or the combination of chlorhexidine with aromatic diamidines such as propamidine isethionate Brolene 0.1%, dibromopropamidine 0.15%, or hexamidine 0.1% [6]. During the first 3 days after corneal debridement, the selected combination of topical therapy was applied every hour. The frequency of application of the topical medication is then reduced to every 3 hours and continued for at least 3 - 4 weeks. If after 2 weeks of topical therapy there is no improvement in the condition of the cornea, surgical procedures such as corneal cryotherapy, amniotic membrane transplantation, or penetrating keratoplasty are necessary[11].

Prognosis

The severity of the disease and the time of initiation of therapy are two factors that greatly affect the prognosis. KA treated since the first 3 weeks after the appearance of symptoms mostly has a good prognosis. However, KA that is diagnosed late or that is accompanied by complications such as cataracts and scleritis is much more difficult to treat and has a poor prognosis. [17]

Conclusion

Keratitis *Acanthamoeba* (KA) is an infectious disease of the cornea due to prolonged use of contact lenses in water which causes the entry of *Acanthamoeba spp*. Symptoms that can be felt such as ocular irritation, blurred vision and splitting. The golden standard in the diagnosis of KA is to culture on agar media coated with *E. Coli*. This disease has a good prognosis with immediate drug administration within the first 3 weeks after the onset of symptoms.

Conflict of Interest

There is no conflict of interest

Funding Sources

There is no funding sources

Acknowledgment

There is no acknowledgment

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REVIEW ARTICLE Open Access

The Role of Reactive Oxygen Species in Muscle: Beneficial/Harmful

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ABSTRACT

Introduction: Skeletal muscle produces moderate quantities of oxidant species, such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), due to its contractile action, high oxygen consumption, and metabolic rate (RNS). Under normal physiological circumstances, the generation and removal of ROS/RNS are in dynamic equilibrium.

Content: The body reaches a condition of oxidative stress, however, when the oxidation products surpass the antioxidant defense capability. Increased oxidative stress has significant ramifications for the molecular, structural, and functional integrity of muscle. The release of reactive oxygen species (ROS) under pathological circumstances leads to cellular dysfunction and the progression of muscle disorders.

Conclusion: The antioxidants can put ROS in optimal concentrations to perform physiological signals in muscle. At appropriate concentrations, ROS and RNS can regulate intracellular signal transduction. Thus, moderate quantities of radicals are advantageous to muscle, but high doses of ROS are harmful. The aim of this review is to know about the role of ROS in muscle.

Keywords: Reactive oxygen species; muscle; skeletal; oxidative stress

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Article history:
Received: 17 October 2022
Accepted: 15 November 2022
Published: 30 December 2022

Published by:
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Mobile number:
+62821 9721 0007

Email:
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Introduction

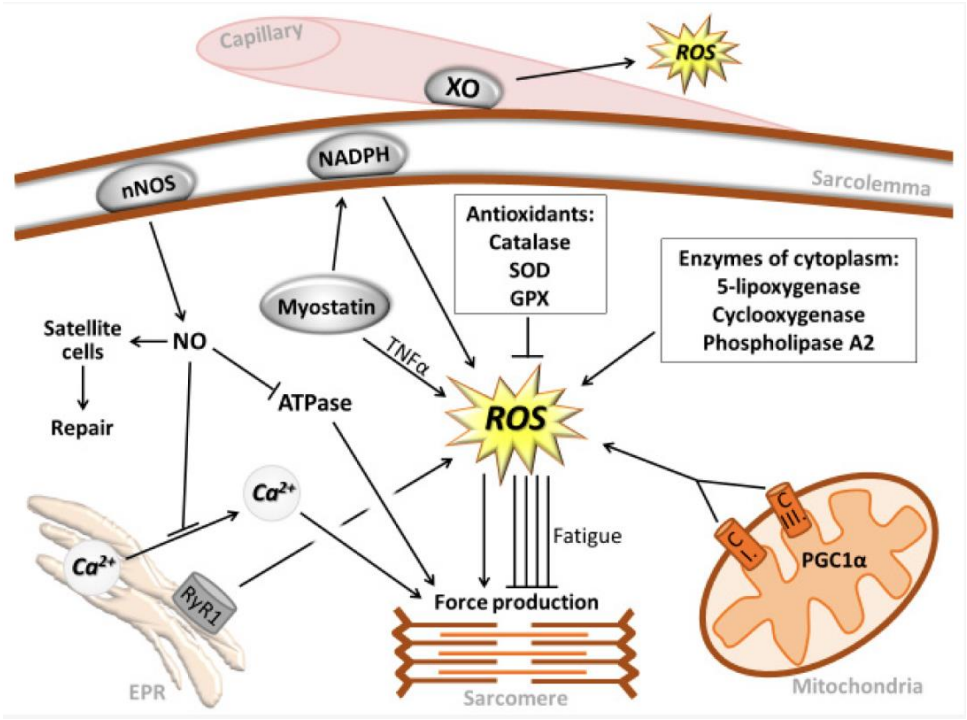
Cells suffer damage from oxidative stress (OS), which is characterized as a disruption in the pro/antioxidant balance since it causes an excessive amount of highly reactive oxygen species (ROS) and reactive nitrogen species to be produced (RNS). Cells generate and eliminate ROS/RNS to maintain redox equilibrium under typical physiological settings. OS participates in signal transmission and physiological adaptation, including the control of cell viability[1], but if the redox balance is upset, the ensuing sharp rise in ROS/RNS causes harmful alterations to cell components. As a consequence, inflammatory neutrophil infiltration, increased protease secretion, and the creation of many oxidation intermediates—all of which are thought to be significant players in aging and illness-occur [2].

The most prevalent tissue in the human body, accounting for 35–45% of its total mass, is striated skeletal muscle[3]. Skeletal muscle is a heterogeneous structure made up of muscle fibers, satellite cells of the basement membrane, and nerves[4], all of which are necessary for fundamental processes as breathing, movement, postural support, and thermogenesis.[4]

Skeletal muscles are remarkably capable of both adaptation and excellent regeneration. Loss of muscular function and a reduced capacity for muscle regeneration not only significantly lower quality of life, but may also have an impact on professional athletes' careers. Inflammation is present in non-inflammatory muscle ailments as well as inflammatory muscle illnesses, such as those that follow intense activity or different degrees of muscular injury. Such inflammation is mostly brought on by high ROS levels.

OS will result from an imbalance between the generation and removal of ROS and RNS, hence it is critical to comprehend the origins of these species. Living things emit ROS as a typical byproduct of cellular metabolism. RNS are chemicals created when reactive oxygen species and other components interact with NO. ROS and RNS may be divided into two categories based on their chemical makeup: the second category is made up of radical and non-radical molecules[5]. Superoxide (O2) and hydroxyl radicals (HO) are examples of radical ROS species, while hydrogen peroxide is an example of a non-radical one (H2O2). Nitric oxide (NO) and peroxynitrite (ONOO) are examples of RNS.

ROS Generation in Muscle



Figures 1. Source of ROS in Skeleta Muscle[6]

1. Mitochondria

The majority of ROS in organisms is generated by mitochondria. In most cell types, mitochondria play a part in various cellular activities, including oxidative phosphorylation. The mitochondria found in skeletal muscle cells are numerous, physiologically active, and highly prone to create ROS. Because skeletal muscle consumes a lot of oxygen, ROS produced as byproducts of mitochondrial oxidative phosphorylation are especially harmful to the genome of skeletal muscle. 90% of the oxygen the body consumes under physiological circumstances is oxidatively phosphorylated in the mitochondria, with just 1% to 2% of that oxygen escaping via the mitochondrial respiratory chain due to reactive oxygen species. Excessive exercise may injure muscles by producing increased ROS and RNS, which can impede muscular contraction[7]. In mammalian cells, the mitochondrial transport chain (ETC) is the primary source of ATP, and the ETC has many sites on both sides of the mitochondrial inner membrane where it may create O2[8].The ETC complexes I and III are the primary O2 producing sites under physiological circumstances[9]. The tricarboxylic acid (TCA) cycle enzymes 2-oxoglutarate dehydrogenase (OGDH), malate dehydrogenase (MDH), and pyruvate dehydrogenase (PDH) will be activated by coupled respiration on glutamate/malate or pyruvate/malate, and this maintains a low membrane potential while complex V is producing ATP [10]. The electrons ultimately reach complex III and IV as they go down the ETC. Complex II is succinate, a substrate for succinate dehydrogenase (SDH), an enzyme involved in the TCA cycle[11]. Additionally, electrons return via complex I during mitochondrial hyperpolarization to convert NAD+ to NADH.

Muscle fibers are primarily responsible for the contractile activity. Due to changes in mitochondrial contents between fast-glycolytic, fast oxidative/glycolytic, and slow fiber types, there are disparities in oxidative capability. The quantity of mitochondria in a muscle impacts how well its fibers can oxidize. Fast contractions depend on glycolysis, which takes place in the cytosol and allows for quick ATP synthesis but is ineffective. Through mitochondrial oxidative phosphorylation, which is slower but more effective, slow contractions create ATP [12]. Fast II muscle fibers are different from slow type muscle fibers in that they stimulate greater amounts of ROS production[13]. Additionally, researchers discovered that Tap63 is involved in the regulation of myoblast metabolism. It was demonstrated that knockdown of Tap63 expression results in mitochondrial respiration, as evidenced by a decrease in spare respiratory capacity and an increase in the rate of myoblast proliferation[14].

2. NADPH Oxidases

Neutrophils and macrophages, which may generate high levels of ROS during the inflammatory response and serve as the body's first line of defense against pathogens, were the first cells to be found to have NADPH oxidases (NOX). NOX is a complex made up of six subunits, of which gp91phox is the functional one. The other five are p22phox, p47phox, p67phox, p40phox, and Rac. Pg91phox homologs have been discovered in a variety of cell types, including NOX1, NOX2, NOX3, NOX4, NOX5, DUOX1 and DUOX2. The principal ROS sources in skeletal muscle cells during skeletal muscle contraction are NOX isoforms 2 and 4, which are found in the plasma membrane, transverse striatum, and sarcoplasmic reticulum and function to control calcium release[15].

3. Xantin Oxidase

As a cytosolic molybdoflavoenzyme that catalyzes the hydroxylation of hypoxanthine to xanthine and of xanthine to uric acid, xanthine oxidase (XO) is known as a crucial enzyme in purine catabolism[16]. Both the related endothelial cells and the cytosol of muscle contain XO. As a result of the large increase in XO activity brought on by contraction, there is an increase in lipid peroxidation, protein oxidation, muscle injury, and edema[17]. Hypoxanthine and xanthine levels increase during vigorous activity, which uses a lot of ATP, and they act as substrates for XO to produce ROS[18]. It's interesting to note that PGC-1, a peroxisome proliferator-activated receptor, appears to play a role in the regulation of exercise-induced mitochondrial biogenesis[19].

4. Myostatin

Myostatin isa muscle differentiation inhibitor, has recently been shown to signal muscle cell ROS generation via canonical Smad3, nuclear factor (NF)-B, and TNF- alpha[20]. Myostatin increases ROS generation in the absence of Smad3 by activating the p38 and ERK mitogen-activated protein kinase (MAPK) pathways, which are mediated by TNF-, IL-6, NOX, and XO [21].

5. Phospholipase A2

During muscular contraction, members of the phospholipase A2 (PLA2) family of enzymes also help to increase intra- and extracellular ROS. They the separate arachidonic acid from phospholipids in the mitochondrial, sarcoplasmic, and plasma membranes. Arachidonic acid is a crucial lipid signaling molecule and a source of ROS via its use as a substrate by lipoxygenases [22].

Antioxidant

All mammalian cells are equipped with regulatory mechanisms to maintain oxidation/reduction (redox) balance since it is essential for cellular health. The cellular antioxidant system is a crucial aspect of redox regulation. Antioxidants are often described as any chemical that considerably slows down or stops a substrate from oxidizing. Readers who want additional information about antioxidant systems are referred to more in-depth evaluations since a thorough study of cellular antioxidants is beyond the purview of this article. However, a short description of cellular antioxidant systems is given here to set the stage for further talks in this study. Antioxidants in cells, both enzymatic and non-enzymatic, function as a sophisticated regulatory network to regulate ROS levels. In order to reduce ROS and maintain redox equilibrium, antioxidants are, segregated throughout the cell in both organelles and the cytoplasm. Additionally, there are antioxidants in the blood and interstitial fluid, and these extracellular antioxidants are crucial in removing ROS from extracellular fluids.

Cells are shielded from harm caused by ROS via three main antioxidant techniques. First, cells and extracellular space both contain a large number of low-molecular-weight compounds that may scavenge ROS. Second, certain enzymatic antioxidants work by converting reactive oxygen species (ROS) into less reactive molecules, which suppresses oxidation and stops these ROS from changing into more harmful species. The binding of pro-oxidant transition metals, such as iron and copper, by metal binding proteins, which act as chelating molecules to stop these transition metals from contributing to the generation of ROS, is the last antioxidant method.

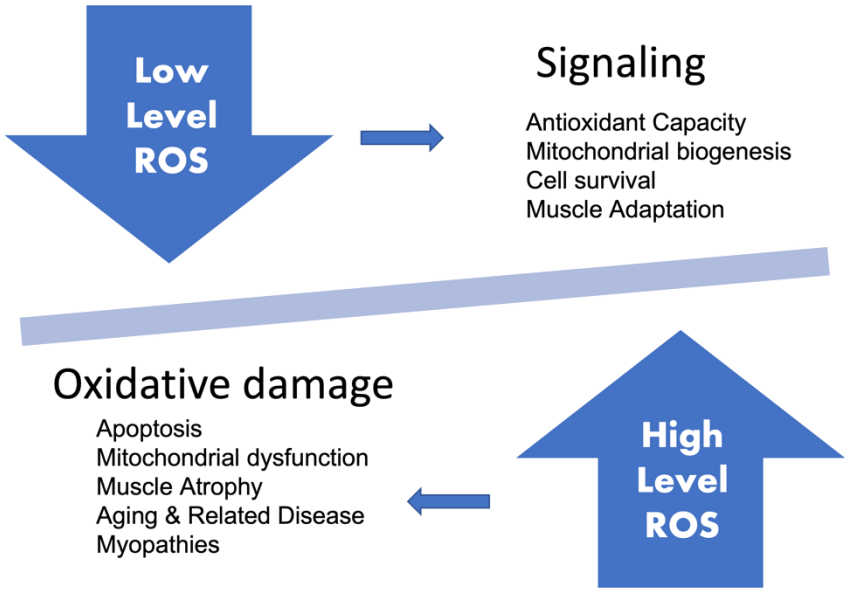
The Role of ROS in muscle

There is accumulating evidence that low levels of reactive oxygen species stimulate the production of antioxidant enzymes and other defensive systemsPhysical activity is connected with the formation of reactive oxygen species, which may play a crucial role in the positive benefits of physical activity. Endurance exercise induces oxidative, metabolic, and thermal stress on skeletal muscle, which triggers some cellular signaling pathways that result in advantageous muscle changes. Mitochondria and ROS generation are essential components of this system. Increased mitochondrial content (mitochondrial biogenesis) improves the regulation of energy metabolism, resulting in increased oxidation of fatty acids and decreased glycogen for ATP synthesis. In addition, endurance exercise may increase mitochondrial integrity through two mutually exclusive routes: changes in mitochondrial dynamics and selective autophagic destruction of mitochondria

(mitophagy). Increased mitophagy after exercise is advantageous because it improves overall mitochondrial quality by selectively eliminating damaged or malfunctioning mitochondria. It has been shown that long-term regular exercise in humans preserves functioning autophagy, ensuring that senior athletes have more muscle mass and strength than old inactive patients[23].

Under physiological settings, skeletal muscles probably engages an endogenous antioxidant defense mechanism to keep the ROS product at a "functional" level. Regular/moderate exercise has been demonstrated to increase the activity of endogenous antioxidant enzymes such as SOD, glutathione peroxidase, and catalase, hence inducing an antioxidant defense.

Muscle homeostasis factors nuclear factor-kappaB (NF-kB), activator protein-1 (AP-1), mitogene activated proteine kinases (MAPKs), heat shock transcriptional factor-1 (HSF-1) and insulin receptor kinase are sensitive to redox changes as well as typical biological components.[24,25] Notably, moderate exercise stimulates MAP kinases, which in turn activates NF-kB, which enhances the production of antioxidant enzymes such as superoxide dismutase (SOD) and ferritin heavy chain (FHC), counteracting ROS formation and promoting adaptation to exercise (eNOS and iNOS). [26]



Figures 2. The Role of ROS in Skeleta Muscle

Recent research has revealed skeletal muscle as an endocrine organ capable of producing, expressing, and releasing cytokines and other peptides, known as myokines, that exert paracrine, autocrine, or endocrine effects.[27] Incongruously, prolonged and hard exercise may cause oxidative damage to cellular elements, indicating that free radicals contribute to muscular tiredness under specific situations, such as eccentric labor (i.e. lengthening of contracted muscles like in running downhill or squatting with weights). It has been hypothesized that rigorous exercise might exacerbate disturbance of the cellular milieu via increased

oxidative damage and inflammatory process, which may have a detrimental synergic effect on the senescent muscle in particular.

Consequently, the exercise of severe length and intensity under likewise extreme circumstances, such as hypoxia, creates considerably larger quantities of free radicals that exceed cellular antioxidant defenses, resulting in protein carbonylation, DNA damage, and RNA oxidation. Notably, the elimination of excess ROS by enzymatic and nonenzymatic antioxidants reduces muscle exhaustion during submaximal contractions. [28]

Following excessive ROS generation, proinflammatory cytokines, and NF-kB the activation, the search for molecular explanations found that severe exercise inhibits pathways for preserving mitochondrial integrity. In addition, vigorous exercise in elderly participants decreased fusion (Mfn2) and fission (Drp1) proteins, which may lead to alterations in mitochondrial morphology. PGC-1, which is known to regulate mitochondrial biogenesis and be the major regulator of an oxidative phenotype inside contracting muscle, is another route in which the presence and balance of reactive oxygen and nitrogen species must be appropriately regulated.[29] Additionally, high ROS generation might disrupt calcium homeostasis. Ca2+ dysregulation may stimulate aberrant NF-kB transcriptional activity, resulting in activation of proteolytic systems and muscle atrophy. [30]Growing data suggest that excessive ROS generation may function as second messengers in cellular signal transduction pathways, activating proteolytic systems such as calpain and caspase. Different concentrations of ROS exhibit opposing effects, which may be explained by the idea of hormesis, in which a little dosage of a chemical is stimulatory and a large amount is inhibitory. Thus, modest concentrations of radicals are beneficial to muscle, but excessive dosages of ROS are detrimental.

Conclusion

ROS are not necessarily harmful to cells. Accumulating evidence has shown that antioxidants can put ROS in optimal concentrations to perform physiological signal in muscle. At appropriate concentrations, ROS and RNS can regulate intracellular signal transduction.

Conflict of Interest

There is no conflict of interest

Funding Sources

There is no funding sources

Acknowledgment

There is no acknowledgment

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REVIEW ARTICLE Open Access

Caisson Disease among Recreational Divers: Review Literature

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ABSTRACT

Introduction: Caisson disease is one of the most common emergencies in divers with very common signs and symptoms that clinicians must be careful to identify based on a complete history and physical examination. The disease also requires immediate and definitive management, usually hyperbaric therapy for a better prognosis.

Content: This article discussed the types, pathophysiology, and management of caisson disease caused by the release of nitrogen gas bubbles into the blood or tissues during or after a pressure drop in the environment. This is a disease that can be prevented by paying attention to existing risk factors.

Summary: Caisson disease or decompression sickness is a collection of symptoms that are often encountered in archipelagic countries and can affect anyone diving for seafood or recreational activities. The symptoms are common, but by knowing the pathophysiology, clinicians can identify the disease and immediately perform therapy, thereby preventing complications such as arterial a gas embolism (AGE) so the mortality and morbidity due to caisson disease can be reduced.

Keywords: Caisson disease; diving; partial pressure; nitrogen

Article history:
Received: 19 October 2022
Accepted: 15 November 2022
Published: 30 December 2022

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Published by:
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Mobile number:
+62821 9721 0007

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Introduction

Indonesia is an archipelago composed of approximately 17,508 large and small islands scattered around the equator with a tropical climate. Indonesia's marine area is estimated at 5.8 million km2 with a coastline of 81,000 km and is the country with the longest coastline in the world. Diving has become the activity of choice for local and foreign tourists to enjoy the beauty of the Indonesian sea. [1]

Tourist and those people who live in coastal areas or fishermen looking for marine creatures for their livelihoods by diving are at risk of causing decompression sickness. Decompression sickness is a syndrome associated with the formation and increase in the size of bubbles in tissues and/or blood when the partial pressure in gases in the blood and tissues exceeds the pressure outside the body (ambient).[2]

The incidence of decompression sickness for recreational diving is estimated at three cases per 10,000 dives, while for occupational diving slightly higher with a range from 1.5 to 10 cases per 10.000 dives. The incidence in Europe ranges from 10 to 100 cases per year, but in Indonesia, there was no data available. However, the number of fishermen in Indonesia who show symptoms of decompression sickness is 15.3%. Research in Kepulauan Seribu, DKI Jakarta documented that 6.91% of fishermen experienced decompression sickness, while research on Bungin Island, NTB, showed that 57.5% of divers showed symptoms of decompression sickness in the form of joint pain and mild hearing loss to deafness as much as 11.3%. [3]

Etiology and Risk Factors

A couple of factors are involved within the pathogenesis of the DCS. Divers with bronchial asthma, atrial septal illness, patent foramen ovale, or obesity are greater vulnerable to increase DCS. The intensity of the dive under the sea surface, the temperature of the water, and the rate of ascent are considered the main contributory factors to thedevelopment of DCS. when divers ascend at a velocity of nine–10 meters/min, they have minimum threat of growing DCS. If the ascent is faster (>19 meters/min), the chance of DCS is considerably higher.18 Caisson ailment takes place whilst a speedy discount in stress (e.g., throughout ascent from a dive, go out from a hyperbaric chamber, or ascent to altitude) causes gases previously dissolved in blood or tissue to form bubbles in blood vessels, it occurs in approximately 2 to 4/10,000 dives among leisure divers. The incidence is better amongst business divers exposed to greater depths and longer dive times with the subsequent risk factors: bloodless temperature diving, acting flight after diving, and long and or deep dives.[4,5]

Pathophysiology

Bubble formation is considered the number one mechanism of harm in decompression sickness. Divers take in inert gas (nitrogen whilst respiratory air) into tissues while respiratory compressed gasoline during a

dive, with greater fuel absorbed on deeper or longer dives. all through the ascent to sea degree, the partial pressure of dissolved gases in tissues can exceed ambient stress, leading to the formation of bubbles in the ones tissues or blood passing through them. this can additionally arise at some point of rapid ascent from sea degree to high altitude. The resulting venous gasoline emboli are small (19 to 700 μm) however very commonplace after diving or exposure to fast altitude. these emboli are generally filtered via the pulmonary capillaries and are asymptomatic. however, venous gasoline emboli can attain the arterial stream via overwhelming the filtering ability of the pulmonary capillary network or thru intrapulmonary or intracardiac proper-to-left shunts, which include atrial septal defects and patent foramen ovale (PFO).[6]

The presence of a PFO increases the chance of decompression sickness of the cerebrum, spinal wire, internal ear, and pores and skin, possibly due to small, arterialized venous gas emboli arriving in saturated tissue capillaries after diving springing up thru inward diffusion of a gas. The vulnerability of the brain, that is rather perfused (thus unexpectedly dissipating inert gasoline) and unlikely to saturate after diving, may additionally get up from publicity to high numbers of small arterialized venous fuel emboli, probably coalescing to shape larger bubbles, as has been suggested after a strongly wonderful bubble comparison take a look at for PFO.[6]

Bubble formation in the tissue might also motive mechanical disruption and focal hemorrhage, in particular inside the white remember of the mind. Even small intravascular bubbles may additionally have bodily outcomes, with inflammatory and thrombogenic host responses. Small doses of arterial gas may also provoke a progressive lower in cerebral blood waft, an impact abolished by means of neutrophil depletion. Intravascular bubbles can detach endothelial cells from the underlying basement membrane, ensuing in impaired regulation of vascular tone, plasma leakage, and hypovolemia. thru this mechanism, a excessive venous fuel embolism can injure pulmonary capillaries and induce pulmonary edema. Even without gross mechanical damage, bubble touch with the endothelium can provoke brief receptor capacity vanilloid ion channel commencing, calcium inflow, mitochondrial disorder, and cell death. adjustments inside the coagulation machine after decompression consist of a moderate lower in circulating platelets due to activation and extended consumption, in addition to an increase in circulating fibrin monomers.[6,7]

Manifestations of decompression illness in mice were decreased by way of pre-treatment with glycoprotein IIb/IIIa receptor antagonists. Male mice proof against decompression sickness have improved prothrombin time and reduced circulating issue X degrees. supplement activation has also been said. Circulating microparticle ranges increase after diving. The motive of this increase is uncertain, but micro debris may additionally play a pro-inflammatory function in decompression sickness.[7]

Fisiologis and Clinical Menifestation

Nitrogen is plenty greater soluble in fatty tissue than in different sorts; consequently, tissues with a

excessive-fat content (lipids) usually have a tendency to absorb more nitrogen than do special tissues. The frightened machine consists of about 60 percentage lipids. Bubbles forming within the brain, spinal cord, or peripheral nerves can motive paralysis and convulsions (divers' palsy), problems with muscle coordination and sensory abnormalities (divers' staggers), numbness, nausea, speech defects, and man or woman modifications. whilst bubbles collect within the joints, ache is typically excessive and mobility is limited. The term bends is derived from this discomfort, due to the fact the affected person generally is not capable of straighten joints. Small nitrogen bubbles trapped below neath the pores and skin may additionally reason a purple rash and an itching sensation known as divers' itches. Generally, those signs and symptoms via bypass in 10 to 20 minutes. excessive coughing and trouble respiratry, referred to as the chokes, imply nitrogen bubbles within the respiration gadget. different signs and symptoms embody chest ache, a burning sensation even as respiratory, and severe shock.[19]

Diagnosis

The diagnosis of decompression sickness depends on the patient's history and physical examination, with no reliance on specific supporting examinations. This is because magnetic resonance imaging (MRI) and computed tomography (CT) scans have low sensitivity in assisting the diagnosis of decompression sickness. The exception for thoracic plain photographs is considering would have taken a long time to perform the examination. A plain thoracic photograph is done to see if the patient has a pneumothorax which is a contraindication to pure O2 administration. Suspicion of decompression sickness can be inferred if the patient presents with symptoms of decompression sickness and a history of diving within the previous 24 hours. A thorough neurological examination should be performed in patients with suspicion of decompression sickness to look for other disorders that are not complained of during history taking.[8]

Based on severity, the symptoms of decompression sickness are divided into two groups, namely type 1 and type 2 decompression sickness symptoms. Decompression sickness symptoms consist of joint pain, muscle pain, muscle weakness, fatigue and, skin symptoms. Symptoms of type 2 decompression sickness involve abnormalities of the central nervous system (stroke), respiratory system, and cardiovascular system.[9] The most common symptoms are joint pain in 58% of cases, muscle pain in 35%, and low back pain in 7%. The anatomical locations of joint pain in order from most frequent to least frequent were shoulder, elbow, knee and ankle. The second most common symptom of decompression sickness was paresthesia as in 63.4% of cases. Other accompanying symptoms can include headache, fatigue, malaise, hives, purpura marmorata, chest pain, dyspnea, nausea and vomiting, anorexia, cramps, and spasms. [10] Decompression sickness can also cause thrombocytopenia due to the attachment of platelets to nitrogen gas bubbles. Possible neurological deficits can also occur in decompression sicknesses such as cognitive abnormalities, cranial nerve lesions, and spinal cord dysfunction due to the destruction of white matter due to the formation of micro thrombus in

the spinal circulation. Other manifestations may include hearing loss such as tinnitus and vertigo. The worst possibility of decompression sickness is paralysis or even death. [11]

Management

The selection of suitable remedy is based on by means of the severity of the medical findings and instances. important situations of treatment pathways are shown in the determine beneath. should we use severe manifestation in bracket (type II) and moderate manifestation (type I) characteristics.

Recompression in a hyperbaric chamber is the definitive remedy for decompression sickness. one of the dreams of recompression is to reduce the bubble extent, thereby lowering signs and symptoms as a result of mechanical disruption of tissues and disposing of ischemia. the usage of recompression has been acknowledged to be effective, in comparison to no recompression, since the overdue 1800s, specially whilst applied early after harm. but, if the partial pressure of nitrogen within the frame is better, it calls for an extended and greater gradual decompression.

Evaluation

All casualties requiring recompression therapy in a hyperbaric chamber should be referred to the hospital for evaluation and monitoring, even if the casualty appears fully conscious. Referral to the hospital should be done as soon as possible unless the patient is confirmed dead.

Prognosis and Complications

A commonplace hassle is arterial gas embolism (AGE). signs and symptoms of AGE develop unexpectedly and are regularly complained of heavily. In a examine conducted by using Leitch & inexperienced (1989), AGE signs and symptoms took place all through ascent to the surface, at the surface, or within five minutes of arriving on the surface in 107 of 116 dive instances (92%). Ascent to the floor is regularly speedy, with breath-keeping resulting from panic after an underwater coincidence. despite the fact that, AGE can arise throughout regular ascent. medical manifestations commonly imply brain involvement, with arterial fuel frequently disbursed in a couple of cerebrovascular territories, with multifocal manifestations. Inside the examine mentioned above, the most not unusual preliminary manifestation become a lack of recognition (in 39% of instances), accompanied by way of confusion (37%), dizziness and presyncope (30%), hemiplegia (27%), visible modifications (21%), headache (20%), dysphasia (eleven%), and seizures (eleven%). In about half of the cases, there are obvious signs of underlying pulmonary barotrauma, which include chest ache and hemoptysis. Symptomatic restoration happens in about 1/2 of the cases, however there may be recurrence in some of those cases.

Having a records of decompression sickness will increase the hazard of a comparable occasion inside the destiny. prognosis depends at the severity and additionally depends on factors which includes speed of

first treatment, get entry to a referral clinic and definitive remedy.[11,16]

Conclusion

Decompression sickness is a syndrome caused by the formation of air bubbles in tissues or blood vessels as a result of dissolved noble gases (generally nitrogen) not being completely expelled through the lungs. The main risk factors for decompression sickness in divers are dive depth, duration, frequency and rate of ascent to the surface. Decompression sickness is divided into two based on the symptoms present in divers, mild type or type 1 with symptoms of joint and muscle pain and skin abnormalities such as itching and blueness and severe type that reaches the central nervous system or type 2. The most common signs and symptoms of decompression sickness are joint pain, muscle pain, and tingling/paresthesia in the extremities. However, complications such as paralysis and even death can also occur. Management of decompression sickness begins with the administration of 100% oxygen at atmospheric pressure and if symptoms persist then definitive therapy should be given in the form of recompression with a hyperbaric chamber. That decompression sickness for drivers is preventable by educating them about safety stop and not rising to the surface quickly also avoiding the risk factors.

Conflict of Interest

There is no conflict of interest.

Funding Sources

There is no funding sources.

Acknowledgment

There is no acknowledgment.

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ORIGINAL ARTICLE **Open Access**

High Reliability Organization in Medical Technology in Health Service

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ABSTRACT

Introduction: Medical technology in health services is often regarded as a solution to the quality of health services. This is because medical technology is considered a solution in reducing errors in medical decision-making. Technology in the world of health aims to increase the effectiveness and efficiency in medical services. The purpose of doing this research is to find out how the benefits of HRO theory are in realizing work safety in hospitals.

Methods: This research used a qualitative design for collecting the data from information obtained through the skype instrument. The number of respondents in this study was 15 respondents where 1 respondent was a pilot respondent who was interviewed early to develop questions that approached the HRO theory developed.

Results: The purpose of this research is to see how reliable emergency room nurses in hospitals in the safety of patient care through questions created based on five basic principles of high-reliability organization. Safety programs in health services are developed through high-reliability organization theory and are used to enhance safety culture and guide organizations in Indonesia to learn from mistakes that have occurred but these cannot be measured as numbers.

(Continued on next page)

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Article history:
Received: 16 October 2022
Accepted: 15 November 2022
Published: 30 December 2022

Published by:
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
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Conclusion: High reliability organizations can assist in a comprehensive approach to assisting health service organizations in providing effective and reliable services and interventions. By using the principles in high reliability organization, an organization can take valid steps to support the sustainability of a system free from errors.

Keywords: Reproducibility of result; Safety management; reliability

Introduction

Health services in Indonesia are in dire need of reliable personnel to health services and equitable distribution of health workers. The government must create an equal distribution system for health workers including the needs of nurses and the welfare of nurses must be considered [6]. All Indonesian people must have health insurance that they can use without having to go through a very long and long-lasting bureaucracy. Nurses who work in health services must be tested and have certification and experience in their fields, and management who work in health services must be aware of the importance of inspection and improvement of the performance of nurses who work in their hospitals[7].

Good communication between health workers is an additional solution to create a work environment that has a high safety and work ethic. If irregularities are found in the health service, positive remedies and interventions must be carried out immediately to prevent the recurrence of the error[8]. Finally, there must be an evaluation of the performance of health services of all hospitals be it government hospitals or private hospitals so that the performance of hospital services can be generalized without the term that service at hospital X is better than at hospital Y even though patients are in the same class and same disease [9].

Safety performance in health care culture must adopt theories from HRO that have long been used in the nuclear and aviation world. The principles applied by HRO here are to improve safety performance by outlining the principles of HRO. The principle of HRO is used by breaking it down some questions related to the HRO principle to provide an in-depth overview of all parties involved in an organization and who have many roles to play in the organization's regulation. Every organization should have the design for the questions to be asked in determining the extent to which the organization is said to be reliable.

HRO in Medical technology in health services

Medical technology in health services is often regarded as a solution to the quality of health services. This is because medical technology is considered a solution to reducing errors in medical decision-making. Technology in the world of health aims to increase the effectiveness and efficiency of medical services.

However, technology is not the only solution to improving patient safety in health services, many other factors contribute to medical health services because many are found to lack adjustments to the software or technology used in many hospitals. Initially, the hospital staff reported the results of the service, is based on what was obtained from examinations issued by health technology, but the medical staff still had to pay attention to complaints or symptoms from patients because the status of the results of health technology did not always match what was experienced by the patient.

Methods

The design used in this study is a qualitative design in which the researcher collects primary data from information obtained through the skype instrument, namely through skype the researcher conducts direct interviews with respondents using questions adopted from the HRO theory developed by Karl E. Weick and Kathleen M. Sutcliffe in his book entitled "Managing the Unexpected". The number of respondents in this study was 15 respondents where 1 respondent was a pilot respondent who was interviewed early to develop questions that approached the HRO theory developed. Then the data collected will be analyzed using the SPSS method. The instrument used in this study was a questionnaire or questions that had been prepared based on the theory adopted from a book written by Karl E. Weick and Kathleen M. Sutcliffe entitled "Managing the Unexpected". Besides skype media is one of the social media that can record interviews between researchers and respondents clearly and accurately. Researchers chose to use Skype because they were very aware of how difficult it was to determine the time to meet with respondents because their time was very limited because they were faced with work and time with their families, so the method of interviewing through Skype was considered very effective for this study. In addition, with Skype, we can record conversations so that research results can be accurate and reduce bias for the results of this research.

The subjects used in this study were nurses who served in the hospital emergency room both permanent and non-permanent nurses. There are 3 permanent nurses and 11 temporary nurses, 1 pilot study is a non-permanent nurse. The hospital emergency room is chosen because the rhythm of work in the hospital emergency room must be fast and accurate and involves the life and death of patients, wrong medical action, the consequences, which can be fatal and even lead to death, as well as the delay in medical action, it can be fatal to patients,therefore HRO theory is very appropriate to be used for emergency room nurses.

The emergency room nurses are selected with permanent and non-permanent status to see how the two nurses view the hospital's performance in patient safety. Why is the number of non-permanent nurses more than non-permanent nurses because the number of non-permanent nurses in the hospital is indeed small and there are only 3 people working in the emergency room and the rest of the non-permanent nurse.

Result

Respondents selected in this study were nurses working in the Emergency Department (Emergency Installation) hospital which consists of two employment statuses, namely permanent employees and temporary employees. All respondents selected were respondents who had experience working in the hospital emergency room either old or new to look for comparisons between them.

The ER nurse was chosen as a respondent in this study because I worked at the hospital as an ER doctor since 2013 so it has been about six years and I have known the character and personality of the nurses working there. It is not easy to choose nurses who can be honest and open to telling the problems that occur at the hospital and again this interview risked their position as emergency room nurses where if their answers were slightly distorted or contrary to the reality of what happened it would cause them to be able to or considered to be making it up just because of frustration at the conditions they experienced while working in the emergency room.

In this study, emergency room nurses with permanent and non-permanent employees were selected as research respondents because we can see a more varied perspective between employees with permanent and non-permanent status in hospital management. This perspective can be influenced by income problems that are very lame between permanent employees and non-permanent employees, where the salaries of permanent employees and non-permanent employees are very much different. Another problem that can change their perspective is that non-permanent employees sometimes have no salary paid for three consecutive months.

Emergency room nurses were chosen as research respondents because emergency room nurses are role models in hospitals and are first-line staff who have more intense direct contact with patients compared to other hospital staff. For example, the patient first enters the nurse who checks first then the doctor, then the nurse reports the patient's condition to the doctor, after that the doctor checks and submits the next action to the nurse, and so on. In addition, emergency nurses can also represent how the regulation and performance of a hospital in patient medical services.

Discussion

Interview Preliminary Questions

All respondents in this study answered that they had heard about patient safety, but not all respondents were able to explain correctly what the patient was. As an example:

"In my opinion, after all, a safe patient is how we treats patients according to the SOP, the patient starts coming to the handler and the action must be following the SOP, because if we are not who our patient is, we don't know if there is any infectious disease or not" . (Respondent 4)

"Safe patients are usually patients who enter the hospital from the emergency room usually are infectious patients." (Respondent 8)

Respondents who answered were and can explain correctly there are 11 respondents and for respondents who answered ever but the explanation is less precise there are 2 respondents. Respondent who answered that they have never been able to explain what a safe patient is the respondent 6. Overall all respondents answered that they had heard about a safe patient.

The Selection of different shifts in this study is because the research respondents who are emergency room nurses not only work in one shift but in three shifts and between them are more dominant shift, then shifts are more dominant than each choice shift respondents at each interviewers. It is also known that the workload of the night shift is heavier than the morning shift and the afternoon shift because the night shift IGD nurses should take a break instead of having to perform medical services for patients who come in the middle of the night whose arrival hours are uncertain, it could be while they are asleep.

In addition, night shift nurses seldom getting the hospital management people down directly to the emergency room to look at the activities of nurses in the emergency room. This is because management people enter at 8 am and leave at 4 pm so only hospital shifts and afternoon shifts can be seen by hospital management people. Respondents who work on the night shift are 7 people, respondents who work on the morning shift are 6 people and respondents who work on the afternoon shift only amount to 1 person.

The training that was attended by respondents varied greatly but in general most of the respondents had participated in training related to safe patients. However, it was found 5 respondents had never participated in training and the rest had participated in training related to safe patients. 5 respondents had attended BTCLS (Basic Trauma Life Support) training or basic training in cardiac emergency. Some respondents who have attended ATLS (Advance Trauma Life Support) training or emergency training in trauma patients.

In addition, some respondents had attended PPDG (Emergency Care Education and Training) and also had attended training on how to use APAR (Light Fire Extinguisher). Another training that had been attended by the research respondents was BHD (Basic Life Support) training. Then finally, the training that was attended by respondents was PPI (Infection Prevention and Control) training. This is very much fulfilled by the high cost of training and the free time they have to attend the training.

For the second question, respondents who answered that they had seen the incident of their colleague in the emergency room had happened almost wrongly stabbed, almost wrongly given the medicine, and almost mistaken treatment of 10 people.

"Oh, yes, I have been in the midst of a change of service. So, the story is we are operands, and there are patients, that must be my friend. Coincidentally, I am just an official, but my shift friend is almost close, but fortunately the medicine has not been included, so the opera seems not to be too high, not too clear

because there are more patients. The one who just entered the emergency room was the one who was wrong, not the medicine, it turns out that the drug was injected and almost inserted, fortunately it didn't work "(Respondent 1).

For example, in a recent incident, one of my friends gave the wrong drug, not wrong, why is it wrong, he just wrote wrong, it turns out he put drugs into a baby patient that should not be for babies, just reading errors. Actually, including negligence" (Respondent 14).

This is probably due to several factors, one of which is the response of the patient when the emergency room nurse wants to take medical action such as a pediatric patient who is raging, thus breaking the concentration of the emergency room nurse in performing medical actions, operand patient information at the time of shifting inaccurate and less accurate fatigue from nurses resulting in decreased concentration in medical treatment.

Respondents who answered that they had never seen the incident were almost wrong punctured, almost wrongly given medicine, and almost wrong treatment was 4 people.

"During this time, while I was in the IGD there was never one wrong action, wrong giving medicine Thank God never sometimes not following the actual operational standards, sometimes not according to the theory carried out, the action is not according to theory and not according to SOP" (Respondents 5).

"If what I got so far, Alhamdulillah, it hasn't been there yet and hopefully it won't happen because we at IGD always have it applied. 7 patient safety targets and posted on the table at the nurse's table. So we always remember every action we check carefully First."(Respondent 9).

Communicate and exchange information, especially information relating to patient safety and emergency staff themselves. There were 12 respondents who answered.

"Usually, in one month, there are sometimes two to three small meetings in the emergency room to review events that have occurred in some time, good, actually if we from the staff of the IGD share information, so that other pressures can be known as the new information "(Respondent 3).

"If it's active, it's a doc to exchange information, usually every month we have a meeting to discuss what's lacking in the room, what's the problem, usually every month we have a meeting like that. Usually, it's not because in IGD we shift so we don't all come except only on official days because they must guard the emergency room "(Respondent 9).

Based on the results of interviews conducted by researchers, it can be concluded that the hospital has the ability to encourage staff to foster good communication related to patient safety and emergency staff themselves so that self-awareness is formed within the staff that is their initiative in conducting communication between peers whether it's during the watch shift or when they have free time if there are few or no patients. So they can more often exchange new information that can increase their knowledge.

The risk of lack of safety behavior where the emergency room is a place where speed is needed in an

act of handling patients and nurses must be able to keep working by following the applicable SOPs. This situation is very contradictory and as we know that work by following the SOP requires a long and long time. We also want to see how the actions of nurses who are able to work in accordance with the SOP while maintaining patient safety. The theory or concept of HRO applied in this study also looks at how risk behavior or nurses' risk behaviors in which emergency nurses work long hours tend to be easily exhausted so that for the next service where he is exhausted it can cause accidents in work which will have an effect in handling medical patients. Besides the character of the nurse herself who does not pay attention to how to work by following the SOP or is ignorant of the patient because of fatigue for example, there is one of the respondents who said that he did not listen to accident patients who come in the middle of the night who need immediate help because he is sleeping.

Position above Expertise

The fifth principle of the HRO we see is how the emergency room nurse will ask for referrals when faced with a difficult situation in performing the medical treatment in the emergency room if in that situation there are staff in higher positions but less skilled and there are staff in lower positions but experts, still found the respondents who are temporary employees will tend to ask for referrals from higher positions because employees do not remain afraid that if something happens or something goes wrong with their medical actions, people who have higher positions will be more able to overshadow them than if they ask for referrals to more an expert but his position is lower, because if they ask for a referral from an expert but his position is lower than if a mistake occurs then the nurse will not get stronger protection if he asks for a referral to a higher position but less expert.

The hospital is in the eyes of some nurses whose temporary status is highly upholding one's position. As long as you have a higher position that means you have more power. The hospital's leadership is not the head or director of the hospital but there is still the highest leader, namely the leadership of the organization that houses this hospital. This means that all forms of regulation in the hospital must be known to the highest leadership of the hospital.

The hospital saw how the emergency room nurse worked and whether it was following the SOP or not if it was following the SOP then this would be a special note for the hospital to then explain at the monthly meeting held every month and attended by all leaders of the room. The follow-up of the head of the room including the head of the ER will reprimand that if he made a mistake[14,15].

Poor patient safety can also be caused by the insensitivity of the emergency room to the situation of the patient. One of the respondents we interviewed was among those who said that they had once visited a patient where the patient's condition as usual was not dying and the complaint was not too significant, then the emergency room doctor performed the examination only with the naked eye by looking at the patient with the invisible eye the doctor said the patient was still safe and no investigations were carried out and

finally the patient was told to go home. The next day the patient returns with a worse condition the possibility of this patient suffering from certain diseases that worsen his condition due to not getting treatment. Only then the patient was treated.

Conclusion

In this study what has not been achieved is the lack of hospital samples used as a comparison. Further research needs to be done involving several hospitals both government-owned hospitals and private hospitals so that the results obtained can be more convincing that the same situation also occurs in the emergency department of other hospitals. Future research plans will carry out the same research using a larger sample of emergency nurses, nurses on duty in nursing or other parts of the hospital, and nurses on duty from several hospitals and comparing between government and private hospitals.

Conflicts of Interest

There is no conflict of interest

Funding sources

There is no funding sources

Acknowledgments

There is no acknowledgments

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CASE REPORT Open Access

McCune-Albright Syndrome: A-Rare-Case Report

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ABSTRACT

McCune-Albright syndrome (MAS) is a rare genetic disordered originally recognized by the triad of polyostotic fibrous dysplasia, precocious puberty, and cafe-au-late spots. We report a case of 2 years-11-month-old girl who came with complaints of menstruation 5 days ago. Breasts appear enlarged. On physical examination, it appears that the café au lait region of the abdomen and left femur resembles the "coast of Maine". There was an increase in the levels of FT4, estradiol, and alkaline phosphatase, and low TSHs, LH, and FSH levels. The radiological examination of the bones of the left hand corresponded to the bone age of 6 years. Bone survey photo showing multiple lytic and blastic lesions in the proximal 1/3 of the left femur. We are monitoring this patient, and planning to administer Tamoxifen and Zoledronic acid. Tamoxifen (an estrogen agonist/antagonist) or Letrozole (an aromatase inhibitor) have been used for the management of precocious puberty and rapid bone maturation. Despite differing in presentation, all patients with precocious puberty were successfully treated with Tamoxifen and/or Letrozole, to emphasize the significant progress of bone age. A systematic approach to diagnosis and management is essential to optimize outcomes for patients with MAS, especially with fibrous dysplasia. No medical therapy is able to change the course of the disease in fibrous dysplasia. However, screening and treatment for endocrinopathy can reduce some bone morbidities.

Keywords: Fibrous Dysplasia; polyostotic; puberty; precocious; aromatase inhibitors

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Article history:
Received: 16 October 2022
Accepted: 15 November 2022
Published: 30 December 2022

Published by:
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

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+62821 9721 0007

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Introduction

Multiple endocrinopathies, early puberty, polyostotic fibrous dysplasia, which causes deformities and pain in the legs, spine, and face, and skin alterations in the form of café au lait macules are all signs of McCune-Albright Syndrome.[1]

Although complete information on the prevalence of MAS is not yet known, it is estimated that it affects between 1/100,000 and 1/1,000,000 worldwide. Contrarily, information on skeletal abnormalities brought on by MAS in the form of fibrous dysplasia has been widely published; it is estimated that this condition accounts for more than 7% of benign bone tumor cases.[2,3]

The endocrinopathies seen in this condition today include several endocrine disorders, such as hyperthyroidism, acromegaly, phosphate wasting, and Cushing syndrome. A somatic activating mutation of the GNAS gene, which is found in many different tissue types, is the cause of the varied constellation of symptoms.[4] Here, we report one patient with McCune Albright Syndrome, a rare disease, who was treated at our institution.

Case

A-2 years and 11-month girl came with complaints of menstruation 5 days ago. The breasts appear enlarged 2 weeks before admission to the hospital. The patient had brown patches on the abdomen and left thigh which had been observed since birth with irregular shapes.

On physical examination, the breasts appeared to be enlarged, the *café au lait* region of the abdomen and left femur appeared to resemble the *coast of Maine* (Figure 1). Anthropometric status within normal limits.

Figure 1. Our patients with breast augmentation, and café au lait

On laboratory examination, there was an increase in alkaline phosphatase (317 U/L), an increase in FT4 (3.22 ng/dl), and increase in estradiol (37 pg/ml) was found. Decreased TSH (<0.05 mIU/ml), decreased LH (0.12 mIU/ml), decreased FSH (<0.1 mIU/ml), Vitamin D (39 ng/dl) and Calcium (8.3 mg/dl) were within normal limits. FT4 results in this patient initially increased, but after 3 months of monitoring, FT4 was found to be decreased and within normal limits.

On bone radiological examination, the patient's estimated bone age was 6 years old (according to Greulich and Pyle), and osteopenia with coarse trabeculae was consistent with the appearance of fibrous dysplasia. (Figure 2). The x-ray of the lower extremities also showed multiple lytic and blastic lesions in the proximal 1/3 of the left femur (Figure 3).

On thyroid ultrasound, it has the impression of bilateral nodular goiter involving the isthmus and bilateral colli regional lymphadenopathy level Ib, level II, level III, level IV, and level V. On abdominal ultrasound, there was an adnexal cyst sinistra.

Figure 2. Her bone age was 6 years old, and osteopenia with coarse trabeculae

Figure 3. Multiple lytic and blastic lesions in the proximal 1/3 of the left femur

The management of our patients is monitoring the general condition of the patient including subjective complaints and vital signs and also providing explanations to the family to understand the patient's condition and play a role in its management so that optimal growth and development can be achieved. We treat our patient with calcium and vitamin D supplementation for maintenance of calcium and vitamin D levels and plan to give Tamoxifen and Zoledronic acid. The management of hyperthyroidism in this patient is observation because, in monitoring, there is a decrease in FT4 levels, if under monitoring, FT4 increases again, hyperthyroidism therapy will be given.

Discussion

Our patient was diagnosed with McCune-Albright syndrome (MAS) based on physical examination, laboratory, and radiology examination. MAC is a rare mosaic disorder that presents along a broad clinical spectrum.[5] Historically, MAS has been described as the triad of fibrous dysplasia (FD) of the bones, café-au-lait skin color, and peripheral premature puberty (PP). Phosphate depletion, newborn hypercortisolism, excess growth hormone, and hyperthyroidism are other related hyperfunctioning endocrinopathies.[5,6]

The clinical manifestations of McCune-Albright syndrome vary greatly. Precocious puberty in girls is a typical early symptom, and repeated ovarian cysts can cause vaginal bleeding and breast development.[15] Precocious puberty, which manifests as penile growth, pubic and axillary hair, acne, body odor, and sexual behavior, is less common in boys. Like the patient who has enlarged breasts and menstrual complaints, Because of the activity of the luteinizing hormone, precocious puberty occurs (LH).[7,8]

Our patients also feature Café-au-lait. Café-au-lait spots are seen in 53-95% of MAS cases with the

characteristic macula being on one side, not crossing the midline of the body, and generally distributed in the chest, neck, and groin areas. Irregularly shaped blotchy edges resembling the coast of Maine. They are often the first clinically apparent manifestations of MAS, presenting at or shortly after birth[9,10]

Several other endocrinopathies and other tissue involvement have been reported in the literature.[1,7] Hyperthyroidism was present in our patient. Hyperthyroidism is common in 10%-30% of MAS patients. Hyperthyroidism in this syndrome occurs due to mutations in the G protein at the level of thyroid-stimulating hormone (TSH). Uncontrolled hyperthyroidism can lead to increased bone age.[11]

On radiological examination, our patient impression of fibrous dysplasia. On radiographs, fibrous dysplasia typically has a look that is referred to as "ground glass." Long bone lesions typically have a "lytic" appearance. As in our case, radiologically, multiple lytic and blastic lesions were found in the proximal 1/3 of the left femur.[12] The lesions typically start in the medulla and spread outward, replacing healthy bone and causing cortical thinning. Fibrous dysplasia of the bone is also a major manifestation of MAS.[11,13] The GNAS1 mutation makes adenyl cyclase chronically active, which boosts cAMP levels and promotes aberrant osteoblasts and hyperfunction of bone precursor cells. A gradual change from normal bone tissue to aberrant fibroosseos tissue distinguishes these dysplastic lesions. Pathological fracture, bone fragility, discomfort, and nerve compression are all consequences of this lesion's extension. The femur, tibia, humerus, and forearm are the bones most frequently fractured.[11]

MAS is managed by a diverse team of professionals based on the observed clinical indications. Women can utilize tamoxifen and aromatase inhibitors as the primary treatments for early puberty. Stable-state analogs of gonadotropin-releasing hormones are used to inhibit the hypothalamic-pituitary-gonadal axis in the case of the development of precocious puberty. Zoledronic acid has been used to treat patients with fibrous dysplasia, it can provide pain relief and reduction in bone turnover markers. Radioablation and antithyroid medications were originally used to treat hyperthyroidism. There are no set standards for fibrous dysplastic lesions. The emergence of discomfort, stress fractures, deformities, or functional loss is typical grounds for surgical stabilization, nevertheless.[14] The patient is receiving calcium and vitamin D supplementation. We plan to give Tamoxifen and Zoledronic acid, hypertiroidism undergoing monitoring and may receive drug therapy if hypertiroid progresses.

Conclusion

McCune Albright Syndrome (MAS) is a rare syndrome. Growth monitoring is necessary for patients with MAS. Pharmacotherapy should be considered for MAS that interferes with growth and worsens clinically.

Conflict of Interest

There is no conflict of interest

Funding Sources

There is no funding sources

Acknowledgments

There is no acknowledgment

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