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Mass Casualty Training held in 2012 by Jordanian level 3 hospital-starbase, UN Mission in Liberia, discussion and review

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From the Editor

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This is the fourth issue this year and has various papers from the Region which includes collaborative work of some authors in Africa.

ALhasan M.Z et al investigated mass causality training by Jordanian level 3 hospital in Liberia. The authors stressed that mass casualties had associated with high risk of violence and injuries. They adapted guidelines from who's community emergency preparedness : a manual for managers and policy makers(who 1999). They analyzed the situation through breaking the problem into its components to examine risks, their causes, possible preventive strategies, response and recovery strategies and trigger events for these strategies. They identified the required resources for response and recovery strategies , resources available ,discrepancy between requirement and availability, and responsibility roles and responsibilities designation: to individuals and organizations. The final written emergency plan will consist of outputs of each step of the process.

Alqahtani, S investigated the perception and parent's Knowledge about High Body Temperatures in Children and Treatment Methods at Home. The objective of the study was to gauge the knowledge of parents about fever in their children and what treatment methods they do at home to treat it through a questionnaire. The study involved random selection of Saudi parents who have encountered having febrile children. A total of 353 parents completed the questionnaires. The study sample consisted mainly of mothers (62.3%). Fifty four percent of the parents are working (192) while the other forty five percent are not (161). A total of 38% of the parents believed that the best place to take the temperature of child is the ear (tympanic) followed by armpit (axilla) 37.1%. The rest of the parents took temperature orally (21%) and rectally (4%) respectively. In this study, about 43% believed that 37 degrees Celsius is the normal body temperature of a child followed by 36 degrees Celsius (20.4%). Approximately 30% of the parents considered a child with a temperature of 38-38.4 degrees Celsius as feverish followed by 38.5-39.90 degrees Celsius (26.3%).This study shows that parents should be more aware about high body temperatures and its consequences. There should be more health teaching among parents to correct the misconceptions they have about fever. Also, parents should be informed about different home treatments and its consequences. There is a need to develop programs that educate parents and provide them with information they need to better address the fever of their children.

Helvaci MR et al; tried to understand whether or not there are some relationships between rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) according to mean age of onset, frequency, and gender distribution in society. The study was performed in Medical Faculty of the Mustafa Kemal University between March 2007 and April 2016. All patients applying to the Internal Medicine Policlinic were included into the study. The study included 223 males and 210 females, totally. Mean ages of them were 30.4 versus 30.3 years, respectively ($p>0.05$). SLE was diagnosed in 6.0% of them (24 females and two males), and 92.3% of the SLE patients were female. Mean age of the SLE cases was 37.0 ± 13.6 (17-58) years. On the other hand, RA was diagnosed in 2.7% of them, so SLE was much more frequent in the society ($p<0.001$). Beside that 50.0% of the RA patients were female (six females and six males), so female predominance of the SLE was higher than RA ($p<0.001$). Mean age of the RA patients was 44.5 ± 7.6 (30-57) years, so RA patients were significantly elder than the SLE patients ($p= 0.038$). The authors concluded that because of the similar clinical presentation types, similar treatment agents, similar prognosis, and difficulties in differential diagnosis, RA may be one step further of the SLE due to its lower prevalence in the society (2.7% versus 6.0%, $p<0.001$), similar prevalences in both genders (50.0% versus 92.3% in females, $p<0.001$), and higher mean age of onset (44.5 versus 37.0 years, $p= 0.038$).

Helvaci MR et al; tried to understand effects of hydroxyurea on sexual performance in sickle cell diseases (SCDs). The study was performed between March 2007 and September 2013.The study included 337 patients (169 females). Mean number of painful crises per year was decreased with hydroxyurea (10.3 versus 1.7 crises per year, $p<0.000$). Mean severity of painful crises was decreased, too (7.8/10 versus 2.2/10, $p<0.001$). Although mean body weight, hematocrit (Hct) value, and mean corpuscular volume (MCV) increased, white blood cell (WBC) and platelet (PLT) counts and direct bilirubin, total bilirubin, and lactate dehydrogenase (LDH) values of serum decreased ($p<0.000$ for all). Parallel to these improvements, the mean number of sexual intercourse per month increased, significantly (2.0 versus 6.8, $p<0.001$). We detected hepatotoxicity in 13 acute painful crises among 1.211 episodes, totally (1.0%). All of them healed completely with withdrawal of all of the medications but not hydroxyurea alone. The solitary adverse effect of hydroxyurea was prominent anemia in higher dosages in 16 patients (4.7%), and they completely healed with transient withdrawal and decreased dosages thereafter. The authors concluded that Hydroxyurea decreases frequency and severity of painful crises, WBC and PLT counts, direct and total bilirubin, and LDH values of serum, whereas it increases mean body weight, Hct value, and MCV. Parallel to these physical and clinical improvements, mean number of sexual intercourse per month and chance of fertility increase in both genders in hydroxyurea users.

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Perception and Parent's Knowledge about High Body Temperatures in Children and Treatment Methods at Home

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Abstract

Background: Fever is one of the most common medical problems in children that needs immediate medical attention. The objective of the study was to gauge the knowledge of parents about fever in their children and what treatment methods they do at home to treat it through a questionnaire.

Patients and Methods: The study involved random selection of Saudi parents who have had febrile children. Parents were interviewed using a standard questionnaire to obtain sociodemographic information and to assess their knowledge about fever. The study also determined methods that the parents were using at home to treat fever.

Results: A total of 353 parents completed the questionnaires. The study sample consisted mainly of mothers (62.3%). Most of the parents who participated in the study have one child (47.3%) followed by parents who have two children (42.8%). There were only three parents who have more than four children (.8%). Most of the parents were between 18-30 years old (46.7%) followed by parents between 31-40 years old (40.5%). There were only seven parents who were older than fifty years (2%). Most of the parents attained a college/university degree (47.9%) followed by parents who had secondary certificate (34.6%). Interestingly, eight parents had a post graduate degree (2.3%). Fifty four percent of the parents are working (192) while the other forty five percent are not (161). A total of 38% of the parents believed that the best place to take the temperature of the child is the ear (tympanic) followed by armpit (axilla) 37.1%. The rest of the parents took temperature orally (21%) and rectally (4%) . In this study, about 43% believed that 37 degrees Celsius is the normal body temperature of a child followed by 36 degrees Celsius (20.4%). Approximately 30% of the parents considered a child with a temperature of 38-38.4 degrees Celsius as feverish followed by 38.5-39.90 degrees Celsius (26.3%).

In this study, 73.1% of the parents did not believe that alternating drugs is useful in cases where the temperature did not lower after administering an antipyretic drug. Almost 50% of the parents believed that seizure is the complication of fever followed by brain damage, dehydration, coma, and death. Parents' most frequently reported measurement of a child's temperature was best by using an electronic thermometer (34.8%) followed by an ear thermometer (28.3%). Other parents measured the temperature of their child by using their hands and with a mercurial thermometer. Most parents measured the temperature every 30 minutes to 1 hour (37.4%) followed by every 15 to 30 minutes (23.2%). When asked about the drug usually given to the child to reduce fever, the majority of the parents reported giving paracetamol (80%) while the others gave antibiotics (9.3%), ibuprofen (4.8%), and aspirin (1.1%). We also found that most of the parents use physical methods to relieve and treat fever such as tepid sponge bath with cold water (38.8%), cold showering (24.9%), tepid sponge bath with hot water (21.5%) and other methods. In order to determine the right dose of the antipyretic drug administered to the feverish child, 85% of the parents used a specific measuring spoon or syringe containing the drug. Others used a regular teaspoon or tablespoon.

Most of the parents when asked how the right fever lowering drugs and doses was decided, they indicated that they would follow the previous advice from the pediatrician (43.6%, 39.4%). Others consulted a pharmacist, or others, or relied on information gathered from media.

Conclusions: This study shows that parents should be more aware about high body temperatures and its consequences. There should be more health education among parents to correct the misconceptions they have about fever. Also, parents should be informed about different home treatments and their consequences. There is a need to develop programs that educate parents and provide them with information they need to better address the fever of their children.

Key Words: Fever, Methods, High body temperature

Introduction

Our body temperature is controlled by the hypothalamus. There are two types of signals being received by the hypothalamus. These signals are assimilated by the thermoregulatory center of the hypothalamus to maintain normal temperature. The human metabolic rate produces more heat than is necessary to maintain the core body temperature in the range of 36.5–37.5°C (97.7–99.5°F) in a neutral temperature environment (1, 2).

Fever is defined as an elevation of the body temperature above the normal variation. Normal temperature in children is about 98.6°F (37°C) when taken by mouth and 99.6°F (37.5°C) when taken by anus. Many doctors define a fever as an oral temperature above 99.5°F (37.5°C) or a rectal temperature above 100.4°F (38°C).(3)

Body temperature measurement is most commonly done to confirm the presence or absence of fever. Many decisions concerning the investigation of children are based on the results of the temperature measurement alone. An incorrect temperature measurement could result in delayed detection of a serious illness or alternatively an unnecessary infection.

A number of researchers published in the international literature have reported that parents have different conceptions, often erroneous, in relation to the exact temperature values considered as fever in childhood. Thus, concerns about fever are composed of incorrect associations between the peak of the fever and severity of the disease.

Concerns about fever by parents may be real or imagined and therefore assessment and monitoring of temperature is essential for decision making at home and in hospital settings (4).

There are different methods in taking the temperature of children. You can get the most accurate temperature reading by taking their temperature rectally. According to Harrison et al., rectal temperatures are generally 0.4°C (0.7°F) higher than oral readings. The lower oral readings are probably attributable to mouth breathing, which is a factor in patients with respiratory infections and rapid breathing. Lower-esophageal temperatures closely reflect core temperature. Tympanic membrane thermometers measure radiant heat from the tympanic membrane and nearby ear canal and display that absolute value (unadjusted mode) or a value automatically calculated from the absolute reading on the basis of nomograms relating to the radiant temperature measured to actual core temperatures obtained in clinical studies (adjusted mode). These measurements, although convenient, may be more variable than directly determined oral or rectal values. Studies in adults show that readings are lower with unadjusted-mode than with adjusted-mode tympanic membrane thermometers and that unadjusted-mode tympanic membrane values are 0.8°C (1.6°F) lower than rectal temperatures.(2)

The study was made to assess the understanding of the parents with children regarding high body temperatures and to know the methods they use at home as treatment aside from giving medications.

Results

Demographic Data

A total of 353 parents completed the questionnaires. The distribution of the socio- demographic characteristics of the parents who participated in the study is shown in Table 1.

The study sample consisted mainly of mothers (62.3%). Most of the parents who participated in the study have one child (47.3%) followed by parents who have two children (42.8%). There are only three parents who have more than four children (.8%). Most of the parents are between 18-30 years old (46.7%) followed by parents between 31-40 years old (40.5%). There were only seven parents who are greater than fifty years old (2%). Most of the parents attained a college/university degree (47.9%) followed by parents who had secondary certificate (34.6%). Interestingly, eight parents had post graduate degree (2.3%). Fifty four percent of the parents are working (192) while the other forty five percent are not (161).

Parent's Beliefs about Fever and Its Treatment

Table 2 shows that 38% of the parents believed that the best place to take the temperature of child is the ear (tympanic) followed by armpit (axilla) 37.1%. The rest of the parents took temperature orally (21%) and rectally (4%) respectively. In this study, about 43% believed that 37 degrees Celsius is the normal body temperature of a child followed by 36 degrees Celsius (20.4%). Approximately 30% of the parents considered a child with a temperature of 38-38.4 degrees Celsius as feverish followed by 38.5-39.90 degrees Celsius (26.3%).

In this study, 73.1% of the parents did not believe that alternating drugs is useful in cases where the temperature did not lower after administering an antipyretic drug. Almost 50% of the parents believed that seizure is the complication of fever followed by brain damage, dehydration, coma, and death.

Parents' Methods in Managing Fever

As shown in Table 3, parents' most frequently reported measure of child's temperature was by using an electronic thermometer (34.8%) followed by an ear thermometer (28.3%). Other parents measured the temperature of their child by using their hands and mercurial thermometer. Most parents measured the temperature every 30 minutes to 1 hour (37.4%) followed by every 15 to 30 minutes (23.2%). When asked about the drug usually given to the child to reduce fever, the majority of the parents reported giving Panadol/Fevadol (80%) while the others gave antibiotics (9.3%), ibuprofen (4.8%), and aspirin (1.1%). We also found that most of the parents use physical methods to relieve and treat fever such as tepid sponge bath with cold water (38.8%), cold showering (24.9%), tepid sponge bath with hot water (21.5%) and others.

In order to determine the right dose of the antipyretic drug administered to the feverish child, 85% of the parents used a specific measuring spoon or syringe containing the drug. Others used regular teaspoon or tablespoon.

Parents' Practices in Managing Fever

Most of the parents when asked how the right fever lowering drugs and doses were decided indicated that they would follow the previous advice from the pediatrician (43.6%, 39.4%). Others consulted a pharmacist, consulted others, or relied on information gathered from media.

Predictors of Some Practices of Fever Management

Overall, the prevalence of administering fever-lowering medications orally among this study sample of parents was 63% (Table 4). The route used to administer fever-lowering drugs was found to be significantly associated with age, gender, and number of children.

Table 1: Socio-demographic data of parents participating in the study

Variable	Frequency	Percentages
Number of Children		
1	167	47.3
2	151	42.8
3	32	9.1
4+	3	.8
Age of Parents		
<18	2	.6
18 – 30	165	46.7
31 – 40	143	40.5
41 – 50	36	10.2
>50	7	2.0
Educational Level		
Illiterate	13	3.7
Less than secondary	14	11.6
Secondary Certificate	122	34.6
College/University degree	169	47.9
Postgraduate degree	8	2.3
Working		
Yes	192	54.4
No	161	45.6

Table 2: Beliefs about fever and its treatment as reported by parents (N=353)

Variable	Frequency	Percentages
Belief about the best place where temperature is taken		
Ear	134	38.0
Armpit	131	37.1
Mouth	74	21.0
Rectum	14	4.0
Belief about the normal body temperature		
36º	72	20.4
37º	151	42.8
38º	53	15.0
39º	53	15.0
40º	16	4.5
I do not know	8	2.3
Belief about the high fever temperature		
37 – 37.4º	17	4.8
37.5 - 37.9º	71	20.1
38 – 38.4º	107	30.3
38.5 – 39.90º	93	26.3
40º	56	15.9
I do not know	9	2.5
Belief about the usefulness of alternating drugs		
Yes	95	26.9
No	258	73.1
Beliefs about the side effects of fever		
Seizure	173	49.0
Brain damage	91	25.8
Dehydration	44	12.5
Coma	19	5.4
Death	16	4.5
Nothing will happen	10	2.8

Table 3: Parent's methods in managing childhood fever (N=353)

Variable	Frequency	Percentages
Methods to measure the temperature		
Electronic thermometer	123	34.8
Hand	79	22.4
Ear thermometer	100	28.3
Mercury thermometer	30	8.5
I do not measure	8	2.3
I do not know	18	3.7
Frequency of measuring the temperature		
Less than 15 minutes	39	11.0
From 15 to 30 minutes	82	23.2
From 30 minutes to 1 hour	132	37.4
From 1 to 2 hours	69	19.5
More than 2 hours	31	8.8
Drug administered for fever		
Panadol/Fevadol	283	80.2
Antibiotics	35	9.3
Ibufrofen/Voltaren	17	4.8
Aspirin	4	1.1
Nothing	16	4.5
Remedies used in addition to drugs		
Tepid sponge with cold water	137	38.8
Cold showering	88	24.9
Tepid sponge with hot water	76	21.5
Using medications only	29	8.2
Using ice cubes	17	4.8
Others	6	1.7
Site of medication administration		
Oral	228	64.6
Rectally	125	35.4
Instrument used to administer the medication		
Regular tablespoon or teaspoon	33	9.3
Specific measuring spoon or syringe of the drug	300	85.0
Measuring spoon or syringe of other drug	20	5.7

Table 4: Demographic of parents by route of administering fever lowering medication (N=353)

Variable	Total N = 353 (%)	Administer		Chi-square P value
		Orally N = 199 (63.0%) (Row%)	Rectally N = 117 (37.0%) (Row%)	
Sex				.024*
Male	133 (37.7)	95 (71.4)	38 (28.6)	
Female	220 (62.3)	133 (60.5)	87 (39.5)	
Educational Level				.046*
Illiterate	13 (3.7)	11 (84.6)	2 (15.4)	
Less than secondary	14 (11.6)	31 (75.6)	10 (24.4)	
Secondary Certificate	122 (34.6)	79 (64.8)	43 (35.2)	
College/University degree	169 (47.9)	100 (62.1)	61 (37.9)	
Postgraduate degree	8 (2.3)	7 (87.5)	1 (12.5)	

* Statistically Significant

Discussion

The level of knowledge about high body temperatures and methods used by parents to treat fever at home were identified through the questionnaire provided to them.

The data gathered indicates that the parents had a good level of understanding regarding high body temperatures. Most of the parents who answered the questionnaire knew the correct normal body temperature and can determine whether their child is febrile or not. Parents expressed that taking temperature alone was sometimes the basis for administering medications especially antipyretics. Most of the parents believed that giving antipyretics is necessary when there is high grade fever.(5) For them, if high grade fever is not treated accordingly, it will result in complications such as seizures, coma, and even death, as similar to previous research.(11,12) These results are similar to study findings in other countries such as Kuwait and Palestine. However, it is not evident that the parents are aware that lowering the body temperature or giving medications for fever such as antipyretics guarantees the prevention of convulsions (6,7,8,9). Although febrile convulsions are terrifying to parents, they do not affect the neurological function and will not cause disabilities(10). Also, no parents were able to mention any side effects of taking antipyretics. A study in Denmark showed that parents were hesitant in giving medication to their febrile children due to some side effects (13). Lack of awareness and misinformation about the inability of antipyretics to prevent convulsions, and that these medications have side effects may be the reason for the significant use of antipyretics (14). Medication histories of the respondents revealed that most of the children were given antipyretics. According to Okposio, intake of antipyretics and antimalarials is only by perception of the mother regarding fever (15). Some of the parents give antipyretics even when there is minimal or no fever because they believe that a child must always maintain a normal temperature (16). Out of 353 parents, only 79 use hands in determining if their children have fever. Therefore, it is not the preferred method for assessing body temperature. Similar results have been seen in some other studies. A 33% PPV (Positive Predictive Value) for touch technique was declared unreliable as found by Katz-Sidlow (17). In an Indian study by Chatuverdi, only 38% PPV endorsed that the tactile technique is an unreliable screening test for fever. It is recommended that the use of thermometer should be encouraged in assessing fever (18).

Studies found that there are home treatments used by parents when it comes to fever, such as showering, cold sponge bath, ice bag application and even rubbing the body with alcohol. These methods may actually increase fever and can result in shaking, shivering and may lead to coma (19)(20) However, more than 90% of parents in the study answered that they use these methods to reduce their child's fever.

This study shows that parents should be more aware about high body temperature and its consequences. There should be more health education among parents to correct the misconceptions they have about fever. Also, parents should be informed regarding different home treatments and their consequences. There is a need to develop programs that educate parents and provide them with information they need to better address the fever of their children.

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An investigation into the outcomes of biliary atresia in Sulaimani, Iraq

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Abstract

Background and objective: Biliary atresia (BA) is a rare childhood disease that is associated with renal failure, cirrhosis, and death. This disease is typically treated through Kasai portoenterostomy which can be associated with some preoperative and postoperative complications. In this regard, the present study was aimed at investigating the relationship between early diagnosis of biliary atresia and its outcomes and complications following Kasai portoenterostomy.

Methods: In a retrospective study, 20 infants with biliary atresia who were treated through Kasai portoenterostomy or who did not receive treatment, were investigated. Required data were collected from their files and analyzed using Pearson Chi-square test through SPSS 20.0.

Results: The results of the present study indicated liver biopsy was an accurate method to diagnose biliary atresia. Stool color was found to be an important clinical indicator on presentation of BA. It was also seen that both groups of infants who received Kasai treatment did not develop cholangitis. Also, liver cirrhosis and portal hypertension were complications that were seen in both groups of patients who received and did not receive Kasai treatment. There was a significant relationship between early diagnosis of BA and survival more than 6 months. However, there was no significant relationship between receiving Kasai treatment and mortality rate.

Conclusion: Infants with biliary atresia survive more in cases of early diagnosis and referral for surgery; therefore, pediatric centers are highly recommended to perform evaluations for BA once they notice neonatal jaundice lasting more than 2 weeks. Effective postoperative care is also recommended for favorable outcomes of Kasai portoenterostomy.

Key words: biliary atresia, Kasai portoenterostomy, renal failure, retrospective study, the Kurdistan Region of Iraq

Introduction

Biliary atresia (BA) is a rare pediatric cholangio-destructive disease that has adverse effects on both the extra- and intra-hepatic biliary tract, and if it is not treated in a timely manner, renal failure, cirrhosis, and death can be among its outcomes [1, 2]. The prevalence of this disease has been reported to vary from 1 out of 8,000 to 1 out of 18,000 live births [3]. BA is usually non-syndromic and has an isolated anomaly [4]; however, it is sometimes associated with various congenital anomalies such as absence of cardiac defects, retro-hepatic inferior vena cava, preduodenal portal vein, situs inversus, asplenia, or polysplenia [5, 6]. Development of BA has been related to different factors; however, recent studies have reported that it is likely to be related to gene mutations [7]. During the first weeks of life, children with BA do not have any clinical signs, but 2-6 weeks after birth, they become increasingly jaundiced [8]. Other clinical signs of BA can include liver growth in size and firmness, anemia, malnutrition diarrhea, prolonged bleeding from the umbilical stump, and splenomegaly [9]. Numerous methods have been proposed and tried for the diagnosis of BA in neonates; however, very few of them have acceptable accuracy. Liver biopsy has been reported as the most helpful examination for BA with a diagnostic accuracy of >90%. It should also be noted that liver biopsy is most accurate if it is performed after 6 weeks of age because most features of BA may be absent before this age, and in that case, an intra-operative cholangiogram may be required [10].

Kasai portoenterostomy, also called hepatoportoenterostomy, was proposed by Morio Kasai in 1959 as an operative treatment for biliary obstruction in infants with non-correctable atresia [11]. In order to stimulate bile flow, reduce hepatic inflammation, prevent postoperative cholangitis, and decrease progressive fibrosis associated with BA, adjuvant medical therapy is commonly conducted after Kasai portoenterostomy [12]. Liver transplantation is used as a treatment method for those cases where the liver is severely impaired due to delayed diagnosis [13].

Although Kasai portoenterostomy is reported to be the most preferred treatment for BA, it has been associated with some preoperative complications such as ventilator associated pneumonia, electrolyte imbalance, DIC, hemorrhage, and sepsis [14] and postoperative complications including portal hypertension, liver failure, upper gastrointestinal bleed, and cholangitis [15].

The present study was carried out in the Pediatrics Teaching Hospital, Shar Hospital, and Shorsh Hospital in Sulaimani, the Kurdistan Region of Iraq, to examine the relationship between early diagnosis of biliary atresia and its outcomes and complications following Kasai portoenterostomy.

Patients and methods

The present investigation was a retrospective study that was carried out on 20 infants with biliary atresia hospitalized in the Pediatrics Teaching Hospital of Sulaimani, the Kurdistan Region of Iraq. Data collection was carried out from September 1, 2012 to September 1, 2016.

Convenience sampling was utilized to select the study sample. Both groups of infants who had received Kasai portoenterostomy (Kasai group) and those who had received no treatment (no-treatment group) were included in the study. After the selection of the infants, their demographic and pediatric characteristics including age, sex, place of residence, weight at the time of diagnosis, associated congenital abnormalities, age at the time of evaluation, color of stool, and color of urine were obtained from their files; as well as data on their liver enzymes at diagnosis time, ultrasonographic findings, and liver biopsy findings. In addition, data on complications and outcomes of BA were obtained from the patients who had undergone Kasai portoenterostomy and from those who had not. All required data of the surviving infants were obtained from the GIT department in the Pediatrics Teaching Hospital and Pediatric Surgical Department in Shar Hospital of Sulaimani, the Kurdistan Region of Iraq. Moreover, data of the infants who had died were obtained from the Histopathological Department of Shorsh Hospital, Sulaimani.

The collected data were analyzed using Pearson Chi-square test through Statistics Package for Social Science (SPSS) version 21. The results are expressed in form of numbers and percentages. The level of statistical significance was set at $p<0.05$.

The study was approved by the Ethics and Scientific Committee of College of Medicine, University of Sulaimani. Moreover, the infants' parents were contacted to obtain their verbal consent for participation in the study.

Results

The results of the present study revealed that of the 20 infants with BA, 14 were female (70%) and 6 were male (30%). They also showed that the infants' age during liver biopsy was less than 1 month (1 infant), 1-2 months (6 infants), and more than 2 months (13 infants). Moreover, it was seen that 14 infants weighed more than 3.5 kg and 6 less than 3.5 kg (See Table 1).

Regarding the patients' clinical characteristics, the results indicated that 3 infants had clinical presentation before 6 weeks of age (15%) and 17 after 6 weeks of life (85%). It was also observed that the stool color was pale in 18 infants (90%) and normal in 2 patients (10%). Moreover, the urine color was dark in 11 infants (55%) and normal in 9 patients (9%) (See Table 2).

Table 1: The infants' demographic characteristics

Variable		N.	%
Sex	Male	6	30.0
	Female	14	70.0
	Total	20	100.0
Age on liver biopsy	< 1 month	1	5.0
	1-2 months	6	30.0
	> 2 months	13	65.0
	Total	20	100.0
Weight	> 3.5 kg	14	70.0
	< 3.5 kg	6	30.0
	Total	20	100.0

Table 2: The infants' clinical features

Variable		N.	%
Clinical presentation	< 6 weeks	3	15.0
	> 6 weeks	17	85.0
	Total	20	100.0
Stool color	Pale	18	90.0
	Normal	2	10.0
	Total	20	100.0
Urine color	Dark	11	55.0
	Normal	9	45.0
	Total	20	100.0

Table 3: The infants' laboratory findings

Variable		N.	%
Elevation degree of liver enzymes	> 2 fold	16	80.0
	< 2 fold	4	20.0
	Total	20	100.0
Ultrasound findings	Triangular cord	7	35.0
	Gallbladder < 1.5cm	13	65.0
	Total	20	100.0
Lee Score liver biopsy finding	> 7	14	70.0
	Unknown	6	30.0
	Total	20	100.0

With regard to the laboratory findings of the patients, the results demonstrated that liver enzymes increased 2 fold in 16 infants (80%) and less than 2 fold in 4 cases (20%). The ultrasound findings revealed that 7 infants had triangular cords (35%) and 13 had gallbladder of shorter than 1.5 cm (65%). In addition, liver biopsy findings showed that Lee Index score was more than 7 in 14 infants (70%) and unknown in 6 patients (30%) (See Table 3).

According to the results, of the 8 infants who had received Kasai portoenterostomy, 7 had cholangitis as a postoperative complication. On the other hand, none of the infants who did not receive Kasai portoenterostomy developed postoperative cholangitis. In this regard, the two groups were significantly different (p=0.000). The two groups were not significantly different in terms of developing liver cirrhosis; 6 infants in the Kasai group and 11 in the no-treatment group had it (p=0.306). Also, the two groups were not significantly different in terms of portal hypertension; 4 patients in the Kasai group and 9 in the no-treatment group had it (p=0.251). The results also indicated that the two groups were not different in the two groups regarding failure to thrive; 5 patients in each group failed to thrive (p=0.361). Moreover, 7 infants in the Kasai group and 12 in the no-treatment group died, but this difference was not significant (p=0.209) (See Table 4).

The results also indicated that in the group with Kasai treatment, 4 infants survived 4-6 months and 6 more than 6 months, and in the group without Kasai treatment, 11 patients survived 4-6 months and 1 more than 6 months. The two groups were significantly different in this regard

Table 4: BA outcomes and complications in the two groups

Variable		Procedure		Total	P-value
		With Kasai	Without Kasai		
Cholangitis	Yes	7	0	7	0.000
	No	1	12	13	
	Total	8	12	20	
Liver cirrhosis	Yes	6	11	17	0.306
	No	2	1	3	
	Total	8	12	20	
Portal hypertension	Yes	4	9	13	0.251
	No	4	3	7	
	Total	8	12	20	
Failure to thrive	Yes	5	5	10	0.361
	No	3	7	10	
	Total	8	12	20	
Death	Yes	7	12	19	0.209
	No	1	0	1	
	Total	8	12	20	

Table 5: Survival duration in the two groups

Variable		Survival duration		Total	P-value
		4-6 months	> 6 months		
Kasai procedure	Yes	4	4	8	0.035
	No	11	1	12	
	Total	15	5	20	

Table 6: Association between survival duration and late/early diagnosis

Variable		Survival duration		Total	P-value
		4-6 months	> 6 months		
Age at diagnosis	1-2 months	0	3	3	0.028
	> 2 months	4	1	5	
	Total	4	4	8	

Table 7: Association between survival duration and weight during Kasai treatment

Variable		Survival duration		Total	P-value
		4-6 months	> 6 months		
Weight during Kasai procedure	> 3.5 kg	3	0	3	0.408
	< 3.5 kg	4	1	5	
	Total	7	1	8	

($p<0.05$), and the infants who received Kasai treatment survived longer (See Table 5).

According to the results regarding the association between early/late diagnosis of BA and the patients' survival duration, all of the patients who were diagnosed during 1-2 months of age survived beyond 6 months, while only 1 of the 4 infants who were diagnosed after 2 months of age survived more than 6 months. This difference was significant ($p<0.05$) (See Table 6).

Furthermore, regarding the association between the infants' weight during Kasai treatment and their mortality, the results revealed that none of the 3 patients who weighed over 3.5 kg died, while 1 of the 4 weighing less than 3.5 kg died; however, this difference was not significant ($p>0.05$) (See Table 7).

Discussion

As revealed by the results of the present study, of the 20 infants, 14 were female (70%) and 6 were male (30%). Similarly, other studies have also reported that the number of females with biliary atresia was more than males [16, 17]. It was observed that evaluation and follow-up were initiated after 6 weeks of age for most of the infants. In their study, Shneider et al. (2006) reported that initial evaluation happened at the mean age of 54 days [16]. Narsimhan (2001) also stated that 60% of patients with BA referred for surgery after 90 days of age [18].

Stool color was an important tool for clinical identification and presentation of BA. This tool revealed BA in 18 patients (90%). Stool color was also introduced by other studies carried out in Taiwan [19] and Japan [20] as a significant clinical sign of BA. The results also showed that 16 infants (80%) experienced increase in their liver enzymes by 2 fold. This finding is in agreement with those of the study carried out in Taiwan by Tang et al. (2007) who stated that elevation of liver enzymes can be utilized to differentiate between biliary atresia and neonatal hepatitis [21].

In the present study, 7 infants (35%) had ultrasound triangular cord sign and 13 (65%) had gallbladder length of less than 1.5 cm. This finding is different from that of the study conducted by Kanegawa et al. (2003) who reported that 27 out of 29 patients (93%) had triangular cord and only 5 patients (17.24%) had small gallbladder shorter than 1.5 cm [22]. This difference may be because of difference in technical facilities and the experience of the practitioners in the center in Japan compared to the different centers in the present study.

In the present study, liver biopsy especially was used for the final decisive diagnosis of BA, and it was used with Lee scoring index to diagnose BA in 14 patients and without Lee scoring index in 6 patients, which proves the accuracy of this diagnostic method. This finding is in line with that of the study conducted by Lee (2009) who reported that the overall diagnostic accuracy of liver biopsy was 92% with Lee scoring system and 88% without the Lee scoring index [23].

The results of the present study indicated that there was a significant relationship between early diagnosis and referral for surgery (1-2 months) and the patients' survival beyond 6 months after Kasai portoenterostomy. Similar results were reported by Narsimhan (2001) [18]. In addition, the results of the present study revealed that there was not a significant association between weight of more than 3.5 kg and prolonged survival after Kasai treatment. This finding was not in agreement with the one reported by Al-Kawaz (2014) who reported that 21 out of 25 patients weighing over 3.5 kg survived longterm and only 4 died [24].

Cholangitis, as the most common complication following Kasai procedure, was observed in 7 out of 8 patients. This finding is similar to the one reported by Lee et al. (2014) who reported that 64% of the patients in their study developed cholangitis after Kasai treatment [25]. But, it is not very similar to the results reported by Ramachandran et al. (2016) who reported a prevalence rate of 35.5% for development of cholangitis after Kasai procedure [26].

The results of the present study revealed that regardless of receiving Kasai treatment or not, most of the patients experienced liver cirrhosis and portal hypertension, but this correlation was not significant. Similarly, in their study, Lee et al. (2009) reported that 47 out of 57 patients with BA developed liver cirrhosis and only 7 had portal hypertension [27].

According to the present study, 19 out of 20 patients with BA died, and there was no significant relationship between mortality and reception or non-reception of Kasai procedure; however, those who underwent Kasai treatment had a longer survival period. In their study carried out in Malaysia, Lee et al. (2009) reported that 34 out of 57 patients died; 9 without any treatment, 23 after Kasai procedure, and 2 after liver transplantation [27]. Unlike the present study, Al-Kawaz (2014) reported that only 10 out of 34 patients (29.4%) who had received Kasai treatment died [24]. This difference can be attributed to various factors including experience of the surgical centers, late diagnosis, postoperative complications, and follow-up measures.

Conclusion

According to the results of the present study, liver biopsy was used to diagnose biliary atresia after the age of 2 months in most of the patients. It was seen that infants who were treated through Kasai procedure had a longer survival duration. Moreover, patients who were diagnosed earlier survived for a longer time. Also, cholangitis was the most common complication of BA regardless of receiving Kasai treatment or not. Therefore, pediatric practitioners are recommended to perform BA evaluations for infants if their neonatal jaundice lasts more than 2 weeks. Moreover, measures should be taken for early diagnosis once the slightest symptoms of BA were observed. In addition, pediatricians are recommended to provide infants with BA with appropriate postoperative care. Finally, pediatric centers should be equipped with advanced facilities, and pediatricians are recommended to develop their experience regarding biliary atresia.

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Rheumatoid arthritis may be one step further of systemic lupus erythematosus

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Abstract

Background: We tried to understand whether or not there are some relationships between rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) according to mean age of onset, frequency, and gender distribution in society.

Methods: The study was performed in Medical Faculty of the Mustafa Kemal University between March 2007 and April 2016. All patients applying to the Internal Medicine Policlinic were included in the study.

Results: The study included 223 males and 210 females, totally. Their mean ages were 30.4 versus 30.3 years, respectively ($p>0.05$). SLE was diagnosed in 6.0% of them (24 females and two males), and 92.3% of the SLE patients were female. Mean age of the SLE cases was 37.0 ± 13.6 (17-58) years. On the other hand, RA was diagnosed in 2.7% of them, so SLE was much more frequent in society ($p<0.001$). Beside that 50.0% of the RA patients were female (six females and six males), so female predominance of the SLE was higher than RA ($p<0.001$). Mean age of the RA patients was 44.5 ± 7.6 (30-57) years, so RA patients were significantly older than the SLE patients ($p= 0.038$).

Conclusion: Because of the similar clinical presentation types, similar treatment agents, similar prognosis, and difficulties in differential diagnosis, RA may be one step further of the SLE due to its lower prevalence in society (2.7% versus 6.0%, $p<0.001$), similar prevalence in both genders (50.0% versus 92.3% in females, $p<0.001$), and higher mean age of onset (44.5 versus 37.0 years, $p= 0.038$).

Key words: Rheumatoid arthritis,
systemic lupus erythematosus, chronic endothelial damage, atherosclerosis, metabolic syndrome

Introduction

Chronic endothelial damage may be the major cause of aging and associated morbidity and mortalities by causing tissue hypoxia and infarctions all over the body. Much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause, and probably whole afferent vasculature including capillaries are mainly involved in the process. Some of the well-known accelerator factors of the inflammatory process are physical inactivity, excess weight, smoking, alcohol, chronic inflammation and infections, and cancers for the development of irreversible consequences including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary artery disease (CAD), mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and premature death. They were researched under the title of metabolic syndrome in the literature, extensively (1, 2). The syndrome is characterized by a chronic low-grade inflammatory process on vascular endothelium all over the body (3, 4). The syndrome has become so common all over the world, for example 50 million people in the United States were affected (5). Physical inactivity induced excess weight may be one of the major underlying causes of the syndrome. Excess weight is a disorder characterized by increased mass of adipose tissue. The chronic inflammation induced endothelial dysfunction may be the action of excess weight for the increased atherogenicity (6-9). Probably chronic vascular endothelial inflammation including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) may also accelerate the premature aging process, and terminate with end-organ insufficiency and premature death. We tried to understand whether or not there are some relationships between RA and SLE according to the mean age of onset, frequency, and gender distribution in society.

Material and methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and April 2016. All patients applying to the Internal Medicine Polyclinic were included into the study. Patients with a history of one pack-year were accepted as smokers, and one drink-year were accepted as drinkers. A complete physical examination was performed by the same internist. Cases with another inflammatory event were treated at first, and the laboratory tests and clinical measurements were performed on the silent phase. A check up procedure including serum iron, iron binding capacity, ferritin, creatinine, hepatic function tests, markers of hepatitis viruses A, B, C and human immunodeficiency virus, a posterior-anterior chest X-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves and to measure systolic BP of pulmonary artery, and an abdominal ultrasonography was performed. Patients with RA were classified with the criteria of early rheumatoid arthritis (ERA) (10). The ERA criteria include a morning stiffness of 30 minutes or longer, arthritis of three or more joint areas, arthritis of hand joints, positivity of rheumatoid factor (RF), and positivity of anti-cyclic citrullinated peptide antibody (anti-CCP). RA is defined by the presence of three or more of the criteria. SLE is classified with the criteria of the American College of Rheumatology of 1997 including discoid rash, immunologic features, photosensitivity, neurologic disorders (headache, depression, seizures, and psychosis), oral ulcers, malar rash, arthritis, serositis, hematologic disorders (leukopenia, lymphopenia, thrombocytopenia, and hemolytic anemia), antinuclear antibodies (ANA), and renal involvement (proteinuria, low complement, red blood cell casts, granular casts) (11). Four of them are required for classification but not for diagnosis. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (12). Systolic BP of the pulmonary artery of 40 mmHg or higher is accepted as pulmonary hypertension (13). CRD is diagnosed with a persistent serum creatinine level of 1.3 mg/dL in males and 1.2 mg/dL in females. Cirrhosis is diagnosed with physical examination, liver function tests, ultrasonographic evaluation, and tissue samples in case of indication. An exercise electrocardiogram is performed just in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken just for the exercise electrocardiogram positive cases. So CAD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders in the cardiac walls. Eventually prevalence, mean ages of onset, and gender distributions of RA and SLE were detected in society and compared in between. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 223 males and 210 females, totally. Their mean ages were 30.4 versus 30.3 years, respectively ($p>0.05$). SLE was diagnosed in 6.0% and 92.3% of the SLE patients were female (24 females and two males). The mean age of SLE cases was 37.0 ± 13.6 (17-58) years. On the other hand, RA was diagnosed in 2.7%, so SLE was much more frequent in the society ($p<0.001$). Beside that 50.0% of the RA patients were female (six females and six males), so female predominance of the SLE was higher than RA ($p<0.001$). The mean age of RA patients was 44.5 ± 7.6 (30-57) years, so the RA patients were significantly older than the SLE patients ($p= 0.038$) (Table 1).

Table 1: Characteristic features of the study patients

Variables	Patients with SLE*	*p*-value	Patients with RA†
Prevalence	6.0% (26)	<0.001	2.7% (12)
Mean age (year)	37.0 ± 13.6 (17-58)	0.038	44.5 ± 7.6 (30-57)
Female ratio	92.3% (24)	<0.001	50.0% (6)

*Systemic lupus erythematosus †Rheumatoid arthritis

Discussion

Chronic endothelial damage may be the leading cause of early aging and premature death in human beings. Physical inactivity, excess weight, smoking, alcohol, chronic inflammation and infections, and cancers may accelerate the process (14-16). Probably, it is the most common type of vasculitis all over the world. Whole afferent vasculature including capillaries may mainly be involved in the process. Much higher BP of the afferent vasculature may be the major underlying cause by inducing recurrent injuries on endothelium. Thus the term venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the continuous endothelial inflammation, edema, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic nature that reduces blood flow and increases systolic BP further. Although early withdrawal of the causative factors may retard the final consequences, after development of HT, DM, cirrhosis, COPD, CRD, CAD, PAD, or stroke, endothelial changes cannot be reversed completely due to their fibrotic natures (17).

RA is a common and chronic syndrome, characterized by non-specific but usually symmetric inflammation and synovial hypertrophy of the peripheral joints, potentially terminating with progressive destruction of articular and periarticular tissues with or without systemic manifestations (18). It typically affects small joints of the hands and feet, but it can also affect larger joints (19). Fever, subcutaneous and visceral nodules, pleural and pericardial effusions, lymphadenopathy, splenomegaly, cytopenias, and episcleritis are just some of the samples of the extra-articular manifestations. Diagnosis is based on duration of symptoms, joint distribution, acute phase reactants, and autoantibodies including RF and anti-CCP (20). The presence of clinical or subclinical synovitis seen with ultrasonography or magnetic resonance imaging is essential for diagnosis. RA can sometimes present with a large joint monoarthritis or oligoarthritis. In cases presenting with monoarthritis, careful assessment for differential diagnosis is needed, particularly in the elderly patients where other conditions such as gout, calcium pyrophosphate deposition disease, and osteoarthritis are common (21). Early referral of patients with suspected synovitis, particularly in small joints of hands and feet, is important in long-term outcomes (22). On the other hand, RA may mimic several systemic disorders, particularly in young and middle-aged females due to the extra-articular manifestations. According to our experiences, the diagnosis of RA requires highly trained specialists who are able to differentiate early symptoms of RA from other pathologies, particularly from SLE. SLE can be distinguished by the characteristic skin lesions on light-exposed areas, oral aphthous lesions, nonerosive arthritis, positive antibodies to double-stranded DNA, renal and central nervous system (CNS) involvements, and thrombocytopenia. Although RA and SLE have similar agents in the treatment protocol, ANA and anti-double-stranded DNA antibodies should be studied in every patient suspected from RA.

SLE is an autoimmune disease characterized by skin lesions on sun-exposed areas, oral lesions, nonerosive arthritis, fever, positive antibodies to double-stranded DNA, renal and CNS involvements, and cytopenias (23). It is mostly seen in women with a younger mean age (23). Similarly, 92.3% of all SLE patients were female, and mean age of the SLE cases was 37.0 years in the present study. Additionally, the prevalence of SLE was significantly higher than RA in the society, here (6.0% versus 2.7%, p<0.001). The higher prevalence of marriage with close relatives may be an underlying cause of such high prevalences of RA and SLE in Turkey. The sera of most patients contain ANA, often including anti-double-stranded DNA antibodies (24). Articular symptoms are seen in 90% of patients, and they may exist for many years before the diagnosis (25). For instance, the average time from the onset of symptoms to diagnosis was five years in the above study (23). As a difference from RA, the majority of the polyarthritis of SLE is nondestructive in nature. Cutaneous lesions include characteristic malar butterfly erythema, discoid lesions, and erythematous, firm, and maculopapular lesions on sun-exposed areas of face, neck, upper chest, and elbows. Photosensitivity is seen in 40% of cases. Generalized lymphadenopathy is also common. CNS involvement may cause personality changes, stroke, epilepsy, and psychoses (26). Renal involvement may be silent or even fatal. The most common manifestation is proteinuria (27). There were increases in the prevalence of renal involvement and neurological symptoms throughout the disease course (23). Differential diagnosis of SLE from other pathologies may be difficult. For example, early-stage SLE can be difficult to differentiate from RA if arthritic symptoms predominate (18-20). On the other hand, clinicians in the Hematology Clinics should be aware of SLE due to the frequent thrombocytopenia in differential diagnosis, particularly with idiopathic thrombocytopenic purpura. Immunosuppressive therapy has made it possible to control the disease with improved life expectancy and quality of life (27). According to our observations, methotrexate may be the simplest, cheapest, orally used, and one of the most

effective treatment regimens for both SLE and RA. It can suppress inflammation and reduce corticosteroid dosage. But although the majority of the patients' inflammation can be controlled effectively with methotrexate alone, most of the patients need additional low dose corticosteroid for obstinate pain during the therapy with unknown reasons yet. Benefit of methotrexate initiates after a period of 3 to 4 weeks. It can be given 2.5 to 20 mg in a single dose once weekly, starting with a dosage of 7.5 mg per week.

As a conclusion, because of the similar clinical presentation types, similar treatment agents, similar prognosis, and difficulties in differential diagnosis, RA may be one step further of the SLE due to its lower prevalence in the society (2.7% versus 6.0%, $p<0.001$), similar prevalences in both genders (50.0% versus 92.3% in females, $p<0.001$), and higher mean age of onset (44.5 versus 37.0 years, $p=0.038$).

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Mass Casualty Training held in 2012 by Jordanian level 3 hospital-starbase, UN Mission in Liberia, discussion and review

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Introduction

Mass casualties are associated with a high risk of violence and injuries. The aim of this review was to assess and compare the training strategies conducted by Jordanian level 3 hospital team in Liberia to the World Health Organization guidelines in such field.

For the purposes of these guidelines, mass casualty incident is defined as an event which generates more patients at one time than locally available resources can manage using routine procedures and requires exceptional emergency arrangements and additional or extraordinary assistance.

W.H.O. Mass casualty emergency management planning

The following is adapted from WHO's Community Emergency Preparedness : a manual for managers and policy makers (WHO 1999).

An emergency plan is a set of arrangements for responding to, and recovering from, emergencies and it is about protecting life, property and environment . The development of an emergency plan should take into account existing plans at other administrative levels, plans that operate at the same level, as well as any plans developed for specific hazards.

The prerequisites for planning are: a recognition of the risks and vulnerabilty that exists and emergencies that can occur; an awareness by community, government and decision-makers of the need to plan and of the benefits of planning; implementation of a plan is guaranteed by appropriate legislation and designation of an organization responsible for coordinating both planning and emergency response and recovery in the event of an emergency.

The planning process can be applied to any community, organization or activity:

Project definition: determine the aim. objectives and scope of an emergency plan, and decision on the resources required to perform these tasks.

Planning Group formation: to gather required information and to gain commitment of key people and organizations, both of which will contribute to the successful implementation of the plan

Potential Problem Analysis: through breaking the problem into its components to examine risks, their causes, possible preventive strategies, response and recovery strategies and trigger events for these strategies

Resources Analysis: to identify the required resources for response and recovery strategies , resources available, discrepancy between requirement and availability, and responsibility roles and responsibiliites designation: to individuals and organizations.

Management Structure: concerning the command of individual organizations and control across organizations.

Developing Strategies and System: for specific response and recovery.

Documentation: : the written emergency plan will consist of outputs of each step of the process.

Training Guidelines and Standards

Along with planning, well-designed and consistently updated training is an essential component of successful emergency responses. The highest health authority must therefore set the training and education standards required for health sector staff involved in mass casualty management.

The baseline analysis should provide information about the current availability and quality of training. However this may be supplemented by additional assessment on specific training needs if important gaps are identified.

THE HIGHEST HEALTH AUTORITY will concern itself with standard-setting, planning and monitoring activities. These will include ensuring that:

Overall standards of training are identified and disseminated to all parts of health care system

Training takes into account the guiding principles such as multi-sectorality

Training is kept up to date through accreditation of courses and certification of trainees .

A significant amount of training is delivered through realistic exercise and drills, those done with cooperation with other sectors.

Adequate material and financial resources allocated for training to be widely available and of sufficient quality (training facilities, learning materials, equipment, teaching staff, etc.)

The Training Review

Twenty seven casualties were found injured in this training and they are classified by triage system to the following:

Triage Red	*Seriously injured*
Triage Yellow	*Moderately injured*
Triage Green	*Minor injuries*
Triage Black	*Deceased*

and they were managed according to priority of their condition triage.

Triage Card Attached To Casualty Case

Patient with Yellow Triage Band Received at Hospital


UN
06/10/2011


06/10/2011
UNMIL 9003

Civilian and Military Health Authorities Work Together


06/10/2011

Conclusion

Mass casualty management requires a high level of coordination and communication between the health authority and community. The preparedness for such an event is by exercises, revision and updating plans.

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Increased sexual performance of sickle cell patients with hydroxyurea

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Abstract

Background: There is a fear of infertility caused by hydroxyurea with unknown reasons in some regions of Turkey. We tried to understand effects of hydroxyurea on sexual performance in Sickle Cell Diseases (SCDs).

Methods: The study was performed between March 2007 and September 2013.

Results: The study included 337 patients (169 females). Mean number of painful crises per year was decreased with hydroxyurea (10.3 versus 1.7 crises per year, p<0.000). Mean severity of painful crises was decreased, too (7.8/10 versus 2.2/10, p<0.001). Although mean body weight, hematocrit (Hct) value, and mean corpuscular volume (MCV) increased, white blood cell (WBC) and platelet (PLT) counts and direct bilirubin, total bilirubin, and lactate dehydrogenase (LDH) values of serum decreased (p<0.000 for all). Parallel to these improvements, the mean number of sexual intercourse per month increased, significantly (2.0 versus 6.8, p<0.001). We detected hepatotoxicity in 13 acute painful crises among 1.211 episodes, totally (1.0%). All of them healed completely with withdrawal of all of the medications but not hydroxyurea alone. The solitary adverse effect of hydroxyurea was prominent anemia in higher dosages in 16 patients (4.7%), and they completely healed with transient withdrawal and decreased dosages thereafter.

Conclusion: Hydroxyurea decreases frequency and severity of painful crises, WBC and PLT counts, direct and total bilirubin, and LDH values of serum, whereas it increases mean body weight, Hct value, and MCV. Parallel to these physical and clinical improvements, mean number of sexual intercourse per month and chance of fertility increased in both genders in hydroxyurea users.

Key words: Hydroxyurea, sickle cell diseases, sexual performance, chronic endothelial damage, metabolic syndrome

Introduction

Probably aging is the major physical health problem of the human being, and systemic atherosclerosis may be the major underlying cause. Systemic atherosclerosis is an irreversible process mainly keeping afferent vasculature due to the much higher blood pressure (BP) in them. Accelerating factors of atherosclerosis are collected under the heading of metabolic syndrome in the literature including physical inactivity, smoking, alcohol, chronic inflammation and infections, cancers, excess weight, dyslipidemia, elevated BP, and insulin resistance for the development of irreversible diseases including obesity, hypertension (HT), diabetes mellitus (DM), coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), cirrhosis, chronic renal disease (CRD), peripheric artery disease, and stroke (1-6). Early aging and premature death are the terminal end points of the syndrome. Similarly, sickle cell diseases (SCDs) are accelerated atherosclerotic processes that are characterized by sickle-shaped red blood cells (RBCs) caused by homozygous inheritance of the hemoglobin S (Hb S) (7, 8). Glutamic acid is replaced with a less polar amino acid, valine, in the sixth position of the beta chain of the Hb S. Presence of valine promotes polymerisation of the Hb S. So Hb S causes RBCs to change their normal elastic and biconcave disc shaped structures to hard bodies. The decreased elasticity instead of shapes of RBCs may be the main pathology of the diseases. The normally present sickling process in whole life span is exaggerated with various stresses of the body. The RBCs can take their normal elastic shapes after normalization of these stresses, but after repeated cycles of sickling and unsickling, they become permanent hard bodies. The hard bodies induced chronic endothelial damage together with tissue ischemia and infarctions are the terminal consequences, so life expectancy of such patients is decreased by 25 to 30 years (9). We tried to understand effects of hydroxyurea on sexual performance in the SCDs.

Material and methods

The study was performed in the Medical Facuty of the Mustafa Kemal University between March 2007 and September 2013. All patients with the SCDs were included into the study. SCDs are diagnosed by the hemoglobin electrophoresis performed via high performance liquid chromatography. Their medical histories including smoking habit, regular alcohol consumption, and leg ulcers were learnt. Frequency of painful crises was detected as a mean number of crises per year, and severity of them as a mean degree between 0 to 10 according to patient's self-explanation. Mean number of sexual intercourse per month was learnt. Cases with a history of three pack-year were accepted as smokers, and cases with a history of one drink a day for three years were accepted as drinkers. A check up procedure including body weight, serum creatinine value, hepatic function tests, markers of hepatitis viruses A, B, and C and human immunodeficiency virus, an electrocardiography, a Doppler echocardiography, an abdominal ultrasonography, a computed tomography of brain, and a magnetic resonance imaging of hips was performed. Other bone areas for avascular necrosis were scanned according to the patients' complaints. Cases with acute painful crisis or any other inflammatory event were treated at first, and then the spirometric pulmonary function tests to diagnose COPD, the Doppler echocardiography to measure the systolic BP of pulmonary artery, and renal and hepatic function tests were performed on the silent phase. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in 1 second/ forced vital capacity of less than 70% (10). Systolic BP of the pulmonary artery of 40 mmHg or higher during the silent phase is accepted as pulmonary hypertension (11). CRD is diagnosed with a persistent serum creatinine level of 1.3 mg/dL or higher in males and 1.2 mg/dL or higher in females on the silent phase. Cirrhosis is diagnosed with physical examination findings, laboratory parameters, ultrasonographic evaluation, and liver biopsy in case of requirement. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter of greater than 1.0 and with the presence of Schamroth's sign (12, 13). A stress electrocardiography was performed in cases with an abnormal electrocardiography and/or angina pectoris. A coronary angiography was obtained just for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders of the cardiac walls. Then, a hydroxyurea therapy was initiated to all patients with an initial dose of 15 mg/kg/day, and then the dose was increased up to the final dose of 35 mg/kg/day according to patients' requirements and compliances. Finally, the mean number of painful crises per year, mean severity of painful crises, mean number of sexual intercourse per month, mean body weight, white blood cell (WBC) and platelet (PLT) counts, hematocrit (Hct) value, mean corpuscular volume (MCV), and the direct bilirubin, total bilirubin, and lactate dehydrogenase (LDH) values of serum were compared before and after the hydroxyurea therapy. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 337 patients with the SCDs (169 females and 168 males). Their mean ages were 28.4 ± 9.3 (8-59) versus 29.8 ± 9.3 (6-58) years in females and males, respectively ($p>0.05$). The final dose of 35 mg/kg/day hydroxyurea therapy was just achieved in 25 cases (7.4%), and the usual dose was 500 mg twice daily during the 7-year follow-up period. During the period, the mean number of painful crises per year was decreased with the treatment, significantly (10.3 versus 1.7 crises per year, $p<0.000$). The mean severity of painful crises was decreased, too (7.8/10 versus 2.2/10, $p<0.001$). Although the mean body weight, mean Hct value, and MCV increased, the WBC and PLT counts and the direct bilirubin, total bilirubin, and LDH values of serum decreased with the therapy, significantly ($p<0.000$ for all) (Table 1).

Table 1: Characteristic features of sickle cell patients before and after hydroxyurea therapy

Variables	Before hydroxyurea therapy	*p*-value	After hydroxyurea therapy
Mean number of painful crises per year	10.3 ± 10.6 (0-48)	***≤0.000***	1.7 ± 1.1 (0-6)
Mean severity of painful crises	7.8 ± 2.2 (0-10)	***≤0.000***	2.2 ± 1.7 (0-10)
Body weight (kg)	59.1 ± 11.4 (37-95)	***≤0.000***	65.2 ± 13.0 (46-107)
White blood cell (µL)	15.050 ± 6.148 (4,890-38,800)	***≤0.000***	11.349 ± 5.029 (5,010-31,850)
Hematocrit value (%)	23.2 ± 4.0 (16-35)	***≤0.000***	27.8 ± 3.4 (20-36)
Mean corpuscular volume (fL)	88.7 ± 9.6 (57-112)	***≤0.000***	105.2 ± 13.6 (66-129)
Platelet (µL)	449,840 ± 217,370 (169,000-1,.561,000)	***≤0.000***	430.840 ± 142.681 (219,000-936,000)
Total bilirubin (mg/dL)	5.3 ± 5.6 (0.6-38.2)	***≤0.000***	3.1 ± 2.2 (0.7-11.0)
Direct bilirubin (mg/dL)	2.0 ± 3.4 (0.2-15.0)	***≤0.000***	0.9 ± 0.9 (0.2-6.0)
Lactate dehydrogenase (IU/L)	647.5 ± 265.8 (196-1,552)	***≤0.000***	509.9 ± 315.4 (235-2,218)

Table 2: Sickle cell patients with associated disorders

Variables	Prevalence
Autosplenectomy	46.8%
Avascular necrosis of bones	18.9%
Leg ulcers	12.7%
Pulmonary hypertension	11.5%
Chronic renal disease	8.3%
Coronary heart disease	7.7%
Digital clubbing	6.5%
Stroke	6.5%
Exitus	5.3%
Chronic obstructive pulmonary disease	4.7%
Cirrhosis	3.2%

Parallel to these physical and clinical improvements, the mean number of sexual intercourse per month increased from 2.0 ± 1.3 (0-7) before the therapy to 6.8 ± 2.4 (0-13) after the therapy (p<0.001). During the 7-year follow-up period, we detected hepatotoxicity just in 13 acute painful crises among 1,211 episodes, totally (1.0%). Interestingly, two of the patients were females with a mean age of 38.5 years and 11 cases were males with a mean age of 32.3 years. So the hepatotoxicity during acute painful crises was significantly higher in males (6.5% versus 1.1%, p<0.001). All of the cases healed completely with withdrawal of all of the medications but not hydroxyurea alone. The solitary adverse effect of hydroxyurea therapy was bone marrow suppression with prominent anemia in higher dosages during the 7-year follow-up period. It was seen in seven females (4.1%) with a mean age of 36.5 years and nine males with a mean age of 28.0 years (5.3%, p>0.05), and they completely healed with transient withdrawal and decreased dosages of hydroxyurea thereafter. Just in a male patient with an age of 22 years, we needed to support with two units of RBCs suspensions due to the symptomatic palpitation. None of the patients needed any supportive therapy for thrombocytopenia or leukopenia. Although the presence of prominent anemia, none of the patients were on acute painful crisis during the detection. On the other hand, we detected autosplenectomy in 46.8%, avascular necrosis of bones in 18.9% (90.6% at the hip joints), leg ulcers in 12.7%, pulmonary hypertension in 11.5%, CRD in 8.3%, CHD in 7.7%, digital clubbing in 6.5%, stroke in 6.5%, exitus in 5.3%, COPD in 4.7%, and cirrhosis in 3.2% of the patients (Table 2). Although smoking was observed in 6.5% (22) of the patients, there was only one case (0.2%) of regular alcohol consumption, who was not cirrhotic at the moment. Although antiHCV was positive in two of the cirrhotics, HCV RNA was detected as negative by polymerase chain reaction in both. Prevalence of mortality was similar in both genders (4.7% versus 5.9% in females and males, respectively, p>0.05), and mean ages of such cases were 32.1 versus 29.1 years in females and males, respectively (p>0.05).

Discussion

SCDs particularly affect microvascular endothelial cells of the body (14, 15), since the capillaries are the main distributors of the hard bodies into the tissues. Because of the microvascular nature of the diseases, we can observe healing of leg ulcers with hydroxyurea therapy in early years of life, but later in life the healing process is difficult due to the excessive fibrosis around the capillaries. Eventually, the mean survival was around 42 years in males and 48 years in females in the literature (9), whereas it was 29.1 and 32.1 years, respectively, in the present study (p>0.05). The great differences between the survival may be secondary to the delayed initiation of hydroxyurea therapy by the medical doctors and a fear of infertility caused by hydroxyurea in the SCDs patients with unknown reasons in Antakya region of Turkey. On the other hand, the relatively longer survival of females with the SCDs should also be researched, effectively. As a result of such a great variety of clinical presentation, it is not surprising to see that the mean body weight and body mass index (BMI) were significantly retarded in the SCDs patients (16). Probably parallel to the lower mean body weight and BMI, mean values of the low density lipoprotein cholesterol, alanine aminotransferase, and systolic and diastolic BPs were also lower in the SCDs (16), which can be explained by definition of the metabolic syndrome (17, 18).

Painful crises are the most disabling signs of the SCDs, and infections may be the most frequent triggering factors of them. Inflammation, operations, depression, and other stressful conditions of the body may also trigger them. Although some authors reported that the painful crises themselves may not be life threatening (19), increased metabolic rate during the painful crises may terminate with an increased risk of mortality mainly due to underlying end-organ insufficiency. Probably pain is the result of a generalized inflammatory process on the vascular endothelium, and the increased WBC and PLT counts and the decreased Hct values show presence of a chronic inflammation during their whole lives in such patients (20). For example, leukocytosis even in the absence of an infection was an independent predictor of the severity (21), and it was associated with an increased risk of stroke probably by releasing cytotoxic enzymes and causing endothelial damage in another study (22). Due to the severity of pain, narcotic analgesics are usually required to control them (23), but according to our experiences, simple and repeated RBC transfusions are highly effective during the severe crises both to relieve pain and to prevent sudden deaths which may develop secondary to the end-organ insufficiencies on chronic inflammatory background of the SCDs (24).

Hydroxyurea is an effective therapeutic option for the treatment of chronic myeloproliferative disorders and SCDs. It interferes with cell division by blocking the formation of deoxyribonucleotides by means of inhibition of ribonucleotide reductase. The deoxyribonucleotides are the building blocks of DNA. Hydroxyurea mainly affects hyperproliferating cells. Although the action way of hydroxyurea is thought to be the increase in gamma-globin synthesis for fetal hemoglobin (Hb F) (25, 26), its main action may be the suppression of leukocytosis and thrombocytosis via blocking the DNA synthesis in the SCDs. By this way, the chronic inflammatory process of the SCDs that initiated at birth on the vascular endothelium is suppressed to some extent. Due to the same action, hydroxyurea is also used in moderate and severe psoriasis to suppress hyperproliferating skin cells. As in viral hepatitis cases, although presence of continuous damage of sickle cells on the capillary endothelium, the severity of destructive process is probably exaggerated by the patients' own immune systems, particularly by the actions of WBCs and PLTs. So suppression of excessive proliferation of WBCs and PLTs probably limits the endothelial damage-induced tissue ischemia and infarctions all over the body. Similarly, it was reported that the lower neutrophil counts were associated with lower crisis rates, and if a tissue infarction occurs, lower neutrophil counts may limit severity of pain

and extent of tissue damage (27). On the other hand, final Hb F levels in hydroxyurea users did not differ from their pretreatment levels, significantly (27).

Physicians at the National Institutes of Health Consensus Conference agreed that hydroxyurea is underused both in children and adults due to some reasons. Hydroxyurea is a chemotherapeutic agent, thus it is not used by women planning to become pregnant in the near future. Additionally, there is fear of potentially increased risk of cancers in people (28). However, the cancer risk has not been substantiated by more than a decade of using hydroxyurea for adults (29). Although investigational and post-marketing data show risk to fetus (30), potential benefits may outweigh potential risks in pregnancy. On the other hand, there is a fear of infertility caused by hydroxyurea with unknown reasons in Antakya region of Turkey. According to our experiences, there are several SCDs' patients with delayed menarche, early menopause, abortus, stillbirth, loss of libido, erectile dysfunctions, priapism, and an eventual infertility. Moderate anemia caused by SCDs themselves, chronic disease anemia, vitamin B12 and folic acid deficiencies, chronic vascular endothelial inflammation all over the body, end-organ insufficiencies, movement disorders due to the leg ulcers and avascular necrosis of bones, painful crises, frequent hospitalizations, invasive procedures, repeated blood transfusions and medications, anorexia, cachexia, relative immune suppression, frequent infections and major depressions may be found among several underlying causes of them in the SCDs' patients. The decreased number and severity of painful crises, increased mean body weight, decreased WBC and PLT counts, and increased Hct value with hydroxyurea therapy will probably result with resolution of most of the above problems to some extent. As a result, the mean number of sexual intercourse per month increases, significantly. So hydroxyurea does not cause infertility instead it increases chance of fertility in both genders with several pathways. It is clear that there is a need for more effective treatment regimens in the SCDs, but until they become available, hydroxyurea must be used in all cases, and its dosage has to be increased as much as possible until the normalization of all symptoms, signs, and laboratory abnormalities.

Hydroxyurea probably has a life-saving role in the SCDs. The Multicenter Study of Hydroxyurea (MSH) studied 299 severely affected adults with sickle cell anemia (Hb SS) and compared the results of patients treated with hydroxyurea or placebo (31). The study particularly researched effects of hydroxyurea on painful crises, acute chest syndrome, and requirement of blood transfusion. The outcomes were so overwhelming in the favour of hydroxyurea that the study was terminated after 22 months, and hydroxyurea was initiated for all patients. The MSH also demonstrated that patients treated with hydroxyurea had a 44% decrease in hospitalizations (31). In multivariable analyses, there was a strong and independent association of lower neutrophil counts with the lower crisis rates (31). But this study was performed just in severe Hb SS cases alone, and the rate of painful crises was decreased from 4.5 to 2.5 per year (31). Whereas in our study, we used all subtypes of the SCDs with all clinical severity, and the rate of painful crises was decreased from 10.3 to 1.7 per year ($p<0.000$) with an additional decreased severity (7.8/10 versus 2.2/10, $p<0.000$). Parallel to our results, adult patients using hydroxyurea for frequent painful crises appear to have reduced mortality rate after a 9-year follow-up period (32). The underlying disease severity remains critical to determine prognosis, but hydroxyurea may decrease severity of disease and prolong survival (32). Probably the chronic endothelial damage of the SCDs is initiated at birth, and complications may start to be seen even in infancy. For example, infants with lower hemoglobin levels were more likely to have a higher incidence of clinical events such as acute chest syndrome, painful crises, and lower neuropsychological scores, and hydroxyurea reduced the incidence of them (33). Hydroxyurea therapy in early years of life may also protect splenic function, improve growth, and prevent end-organ insufficiencies by decreasing early capillary endothelial damage. Transfusion programmes can also reduce all of the complications of the SCDs, however transfusions carry many potential risks including infection transmission, development of allo-antibodies making subsequent transfusions difficult, and iron overload.

As a conclusion, hydroxyurea decreases frequency and severity of painful crises, WBC and PLT counts, direct and total bilirubin, and LDH values of serum, whereas it increases mean body weight, Hct value, and MCV. Parallel to these physical and clinical improvements, the mean number of sexual intercourse per month and chance of fertility increases in both genders in hydroxyurea users.

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