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OUTCOME OF CARPAL TUNNEL SYNDROME OPEN SURGICAL DECOMPRESSION IN MISRATA CENTRAL HOSPITAL DURING THE YEAR OF 2015

By

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ABSTRACT

Carpal tunnel syndrome, the most common peripheral entrapment neuropathy, is caused by compression of median nerve at the wrist. Treatment options include the use of NSAIDs, local steroid injections, night splints, as well as physical therapy and surgical release. The aim of this study was to assess the outcome of surgical decompression via mini-palm incision. A Prospective case series evaluating the outcome of mini-palm incision surgical decompression of carpal tunnel syndrome in Misrata Central Hospital during the year 2015. 51 cases (out of 55 cases operated during the study period) were included in the study, as they committed to follow-up or respond to our calls at two weeks and at three months. The other four cases were excluded, as they neither attended nor responded to our calls at three months. The outcome of treatment was evaluated in terms of wound healing problems, in addition to other possible complications. Patient satisfaction at three months was noted. Complications occurred in three cases; one case showed a minimal improvement of symptoms at two weeks and at six weeks, and was re-operated and incomplete decompression was found. Two cases had developed superficial wound infection that was treated with oral antibiotics and healed with no consequences. 48 cases (94.12%) had no clinically evident complications.

At three months postoperatively, 49 patients (96.08%) indicated that they were happy and satisfied with their surgery results. The patients (3.92%) said that they are fairly satisfied. Open surgical decompression through mini-palm incision is an easy, effective and safe method of treatment as evidenced by the obtained excellent outcomes.

KEY WORDS: Carpal tunnel Syndrome, Outcome, Surgical Decompression.

INTRODUCTION

Carpal Tunnel Syndrome (CTS) is a clinical disorder resulting from compression of median nerve in the carpal tunnel at the wrist. It was first described by Sir James Paget in 1854, but the term was coined later by Moerisch (1,2). It is the most common peripheral entrapment neuropathy (3,4). It affects most often those aged 30-60 years old, it is much more common in women than in men. Aged, overweight, and physically inactive individuals are more likely to develop carpal tunnel syndrome.

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Female gender, obesity, cigarette smoking, and vibrations associated with job tasks have been identified as risk factors to develop carpal tunnel syndrome in industrial workers. Most patients complain of numbness or parasthesia (or both) in the lateral three and half fingers. Pain rarely prevents patient from sleep but it may awaken the patient from sleep after few hours. Many patients complain of finger stiffness upon arising in the morning. Discomfort or numbness, or both, may be incited by activities requiring sustained wrist flexion for long periods. Discomfort and pain may radiate from the hand up the arm to the shoulder or

neck (1-5). Atrophy and weakness of muscles innervated by median nerve indicates severe long-standing disease and is rare in most cases of recent onset. Diagnosis is basically clinical utilizing provocative tests and supported with electrodiagnostic studies.

Provocative tests

Tinel's sign: Percussing the median nerve at the wrist reproduces electric or tingling sensation radiating to median nerve supplied fingers.

Phalen's test: Elbow is maintained in extension, wrist is passively flexed for a while, reproduction of electric or tingling sensation radiating to median nerve supplied fingers within 60 seconds of wrist flexion indicates positive test.

Durkan's test: Direct compression is applied to the median nerve for 30 seconds, in positive test, symptoms are reproduced.

Phalen's test is most sensitive and Tinel's sign is most specific and least sensitive among the three tests. Durkan's test is more sensitive and more specific than the other tests[1].

ELECTRODIAGNOSTIC STUDIES

These techniques are reliable confirmatory tests, which include nerve conduction velocity study and electromyography. A distal motor latency of more than 4.5 ms and a sensory latency of more than 3.5 ms are considered abnormal. Asymmetry of sensory conduction velocity > 0.5 m/s vs. opposite side, and asymmetry of motor conduction velocity > 1 m/s vs. opposite side are abnormal results suggesting the diagnosis. EMG may show signs of nerve damage, including increased insertional activity, positive sharp waves, fibrillations at rest, decreased motor recruitment and complex repetitive discharges. These studies are of 90% sensitivity and 60% specificity for CTS. False negative results are reported to be 10% in several studies.

Treatment options include NSAIDs, night splints, physical therapy, local steroid injections and surgical release. Patients with intermediate or advanced CTS are probably better treated with early surgical release (1).

The Mini-palm incision open decompression uses an incision that begins just distal to the distal wrist flexion crease and slightly ulnar to the midline of the wrist, and extends distally three cms in line with third web space. Transverse carpal ligament is exposed, the parallel palmar fascia fibers and hypothenar fat are retracted. TCL and then the distal two cms of antebrachial fascia are divided with Metzenbaum scissors. If median nerve is adherent to the divided radial TCL leaf, external neurolysis may be needed. Incision is then closed and compressive dressing is applied (1).

MATERIALS AND METHODS

A Prospective case series evaluating the outcomes of mini-palm incision surgical decompression of carpal tunnel syndrome. During the period from 01 January 2015 to 31 December 2015, 55 cases of carpal tunnel syndrome were treated in Misrata Central Hospital by surgical decompression via mini-palm incision, 51 cases were included in the study as they committed to follow-up or responded to our calls at two weeks and at three months. The other four cases were excluded as they neither attended nor responded to our calls at three months.

Results of provocative tests (Tinel's, Phalen's & Durkan's) and electrodiagnostic studies (EMG/NCV) were documented. Operative findings were compared to results obtained from both clinical tests and electrodiagnostic studies.

The outcome of treatment was evaluated in terms of wound healing problems and other possible complications. Patient satisfaction at three months was also noted.

RESULTS

The youngest patient was 24-year-old, while the oldest was 73-year-old, both were females. The only male patient was 37-year-old. The mean age was 47.96 years. About 64% of patients were between 41 and 60 years old. (Table 1).

Table 1: Age distribution.

age	≥30	31-40	41-50	51-60	61-70	≤71
%	2.4%	11.22%	18.35%	15.29%	4.8%	1.2%

Fifty patients were females (98.04%), while only one was male (1.96%), forty patients were married (78.43%), 10 were single (19.61%), and one patient was a widow (1.96%).

Four female patients described themselves as non-working women (7.84%), while 25 were housewives (49.02%), and 21 were working women (41.18%). The male patient worked in construction (1.96%).

Regarding symptoms, 48 patients (94.12%) suffered from pain, while three patients (5.88%) had no pain symptoms. Forty patients (78.43%) suffered nocturnal pain. Fifty patients (98.04%) experienced tingling. 17 patients (33.33%) suffered from sleep disturbance. (Figure 1).

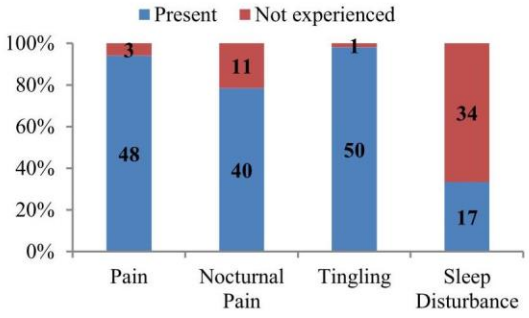

Figure 1: Patient symptoms.

The involved side was the right in 21 patients (41.18%), the left in nine patients (17.64%) and bilateral in 21 patients (41.18%). The operated side was the right in 33 patients (64.71%), and the left in 18 patients (35.29%). (Figure 2). Among 21 cases with bilateral disorder, 12 chose right side (57.14%), and nine chose left side (42.86%). (Figure 2) .

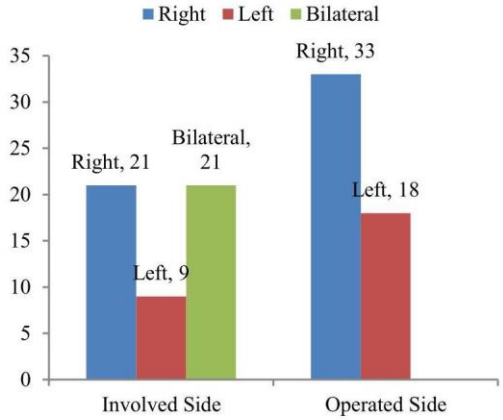

Figure 2: Involved side and operated side.

Forty-seven patients (92.16%) had no history of previous carpal tunnel decompression surgery, whereas one patient (1.96%) had the same operation done on the same side (revision surgery because of incomplete release), and three patients (5.88%) had history of carpal tunnel decompression surgery for the contralateral side. Furthermore, 10 patients (19.61%) were diabetic, but only two of these patients were also hypertensive. One patient (1.96%) had Nephrotic Syndrome.

Regarding conservative management prior to deciding surgical decompression, 46 patients (20.20%) used NSAIDs. Forty-fore patients (86.27%) used vitamin B-Complex. Thirty-six patients (70.59%) used night splint. Eleven patients (21.57%) tried physiotherapy.

Provocative tests in the study population showed approximately similar results. Phalen's test was positive in 44 patients (86.27%).

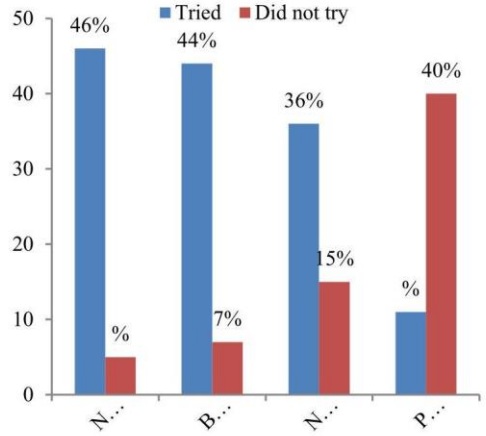

Figure 3: Conservative management.

Tinel's sign was found positive in 46 cases (90.20%). Durkan's test was found to be the most sensitive with 47 cases (92.16%) having a positive test and 4 cases (7.84%) having negative test. (Figure 4).

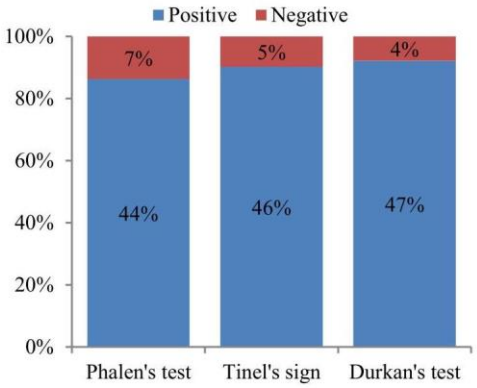

Figure 4: Provocative tests for carpal tunnel syndrome patients.

In all the cases the electro diagnostic studies were positive for carpal tunnel syndrome; 27 cases (52.94%) had severe CTS on EMG/NCV study report. Operative findings showed that 31 cases (60.78%) had severe "severely tight TCL", and 3 cases (5.88%) had mild CTS. (Figure 5).

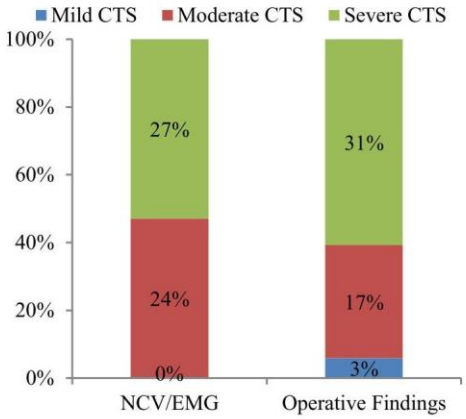

Figure 5: Electro diagnostic studies for carpal tunnel syndrome patients.

Comparison of NCV/EMG findings and operative findings showed 38 cases (74.51%) with matched NCV/EMG and operative findings. Three cases (5.88%) had moderate CTS NCV/EMG and mild operative findings. Seven cases (13.73%) had moderate CTS NCV/EMG and severe operative findings report. while three cases (5.88%) had severe CTS NCV/EMG and moderate operative findings. (Figure 6).

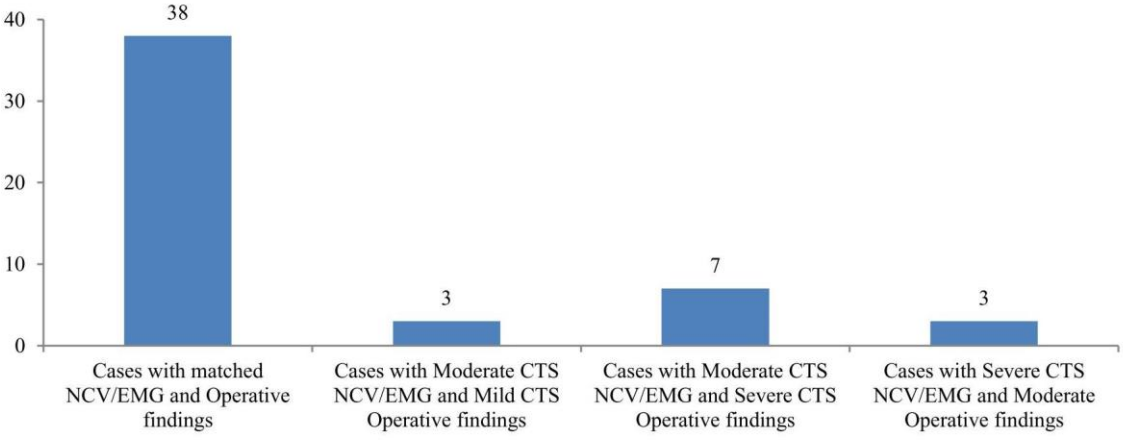

Figure 6: Correlation between NCV/EMG report and operative finding report.

Correlation of Negative Provocative test to other tests, NCV/EMG and Operative findings is shown in (table 2): Eleven cases (21.57%) showed a minimum of one negative provocative test, of them, three cases had two negative provocative tests, while one case was presented with three negative tests. At surgery, the transverse carpal ligament was found to be mildly tight in two cases, which showed a minimum of two negative provocative tests, one of these cases had all provocative tests negative.

Table 2: Correlation of Negative Provocative test to Other tests.

Case	Phalen's test	Tinel's sign	Durkan's test	NCV/EMG	Op. Finding
I	Negative	Positive	Negative	Moderate CTS	Mild CTS
II	Positive	Negative	Positive	Moderate CTS	Moderate CTS
III	Negative	Negative	Negative	Moderate CTS	Mild CTS
IV	Negative	Positive	Positive	Severe CTS	Severe CTS
V	Negative	Positive	Positive	Severe CTS	Severe CTS
VI	Negative	Positive	Positive	Severe CTS	Severe CTS
VII	Positive	Negative	Positive	Severe CTS	Severe CTS
IIX	Positive	Negative	Negative	Moderate CTS	Moderate CTS
IX	Negative	Positive	Positive	Moderate CTS	Severe CTS
X	Positive	Negative	Positive	Moderate CTS	Moderate CTS
XI	Negative	Positive	Negative	Moderate CTS	Moderate CTS

The type of anesthesia used in the operation was regional "Bier Block" anesthesia in 47 cases (92.16%), local anesthesia in one case (1.96%), and general anesthesia (after failed regional anesthesia) in three cases (5.88%).

Some complications occurred in three cases; the first patient showed incomplete decompression, in addition to minimal improvement of symptoms at two and six weeks postoperatively. The other two cases developed superficial wound infection at six and eight postoperative days respectively. These two patients were diabetic females, who were treated with oral antibiotics and healed without notable side effects. Forty-eighth cases (94.12%) had no clinically evident complications (Figure 7). At three months postoperative, 49 patients (96.08%) reported that they were happy and satisfied with their surgery results. Two patients (3.92%) reported being fairly satisfied. Scar discomfort, deep wound infection, wound dehiscence, nerve and vascular injuries, as well as stiffness, and complex regional pain syndrome were not reported.

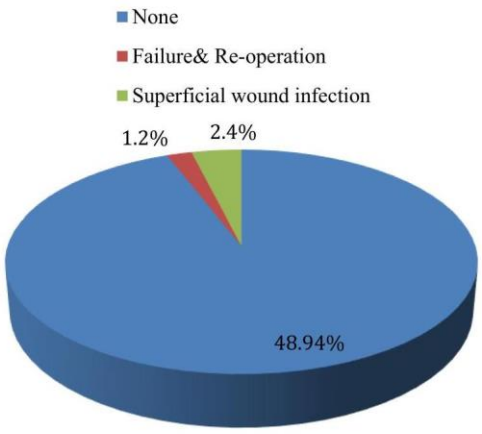

Figure 7: Complications.

DISCUSSION

In the current study, the majority of patients were middle-aged, and most of them were females. Similar studies used

populations with only slightly different properties. For instance, in the study by Rahman et al (2014), 91.1% of patients were females with a mean age of 41.8 years (6). Furthermore, in a study conducted by Khan et al (2015), females represented 81% of the recruited patients (2). In another similar investigation females represented 87.5% of the study population with a mean age of 39 years (3), while Zyluk and Strychar (2006) included slightly smaller proportion of females (77%) in their study population, with a mean age of 48 years (7).

For females, occupation did not emerge as a significant risk factor among the current study population, as the obtained findings were almost similar for housewives and working ladies. Furthermore, pain and tingling were the major symptoms, night pain was frequent, while sleep disturbance was less frequently observed.

Bilateral involvement was as common as the sole involvement of right side. Severity of symptoms among bilateral disease cases suggests no or little effect of hand dominance, as patients almost equally chose the side on which to operate.

Diabetes represents the most common comorbidity. Diabetic patients require special attention for wound care, as they are known to be more susceptible to infection. Conservative management including (NSAIDs, vitamin B-complex supplements, night splint and physical therapy) appeared to have little or no assistance to patients with moderate/severe CTS.

Our study findings show that provocative tests are of good sensitivity to moderate/severe CTS with Durkan's test being the most sensitive. The combination of the two tests lowers the false negative rates to the minimum.

This study also shows that electrodiagnostic studies are very helpful to confirm diagnosis and determine severity of carpal tunnel syndrome, and that when used in combination with the three-provocative test, they form a very accurate diagnostic tool in most of the cases as correlated to operative findings.

Complications of mini-palm incision open carpal tunnel decompression are minimal, diabetic patients seem to be more susceptible to these complications, especially wound infection. Short-term outcome is excellent with very high patient satisfaction rate. International studies also indicate that mini-palm open surgical decompression is a safe technique for treatment of carpal tunnel syndrome, with lower complication rates. Khan et al (2015), found that only 6% of their patients had residual pain at three months after surgery and 94% were satisfied with their treatments (2). Maliyappa et al (2014) found that only one hand out of 27 hands developed superficial wound infection that was treated conservatively (4). In addition, Rahman et al (2014) found that superficial wound infection occurred in two out of 382 cases (6).

CONCLUSION

Diagnosis of CTS is more accurate especially when combined with provocative clinical tests and EMG/NCV studies. Open surgical decompression through mini-palm incision is an easy, effective and safe method of treatment with excellent outcome.

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PROSECTED PLASTINATED CADAVERS IN ANATOMY PRACTICAL TEACHING: COMPARATIVE ASSESSMENT STUDY IN RELATION TO OTHER METHODS

BY

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ABSTRACT

Considerable attention must be paid to the anatomy course as an important fundamental base for medical undergraduate students. Continuous evaluation of the teaching outcomes can positively affect the education process. Comparative study has been proposed to achieve the continues assessment for recognizing the superior method in anatomy information retention and recall during the anatomy practical classes. Prosected plastinated method was used in relation to other modern and classical anatomy teaching methods, in the same time recording the level of satisfaction and efficiency of the superior method by the student's opinions. 240 students were distributed as two equal groups according to the topic to be taught (A & B): (muscles of the upper limb for group A, posterior abdominal wall for group B), Each topic was explained by the same teacher for both groups. Further, both groups were sub divided into six subgroups (A1, A2, A3) & (B1, B2, B3), 40 students for each, according to the method using plastinated cadavers, plastic models, atlas images, respectively. This was followed by ten minutes arrowed unlabelled diagram quiz, and questionnaire covering the satisfaction and efficiency for the superior method according to the scores. Quantitative data from the questionnaires and the quizzes scores were analyzed using descriptive statistics for comparisons of answers and results between groups and One Way ANOVA test to evaluate the difference and variability of the methods used. In a good rate of satisfaction response, the higher scores for the subgroups (A1 & B1) who were subjected to plastinated cadavers. The students gained the excellent marks, were 42.5% for group A1, 27.5% A2, 15% A3. while B1, B2 and B3 were 62.5%, 32.5% and 27% respectively. The present study considers the prosected plastinated cadavers to be a superior teaching method. While cadaveric as a classical method, achieves a considerable amount of satisfaction and efficiency, other tools such as plastic models and images on data show, can be considered as a supportive rather than a replacement teaching method.

KEYWORDS: Anatomy, Practical Class, Plasinated Cadavers, Medical Students, Questionnaire.

INTRODUCTION

Studying the validity and effectiveness of the methods used in undergraduate anatomy teaching will be very helpful to improve the anatomy curriculums. Comparative evaluation can overcome the limitations and gives a clear idea to the educator and coordinators about the designing of anatomy programs in future (1-5). Although different methods are used to evaluate the teaching levels and student's outcome still the valid standardized questionnaire assessment has the superiority. Since it reflects the evaluation according to the opinions of students themselves, who are the core-subject of the information receiving methods. An interesting experience in Aga khan university in Pakistan, since more than thirty three years, they have regular annual and semi-annual evaluation for the medical education level (6). The

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assessment of the anatomy teaching tools was recognized through the descriptive type. Research projects using comparative studies have been limited. Thus, few studies are available to compare and contrast different approaches for teaching and learning anatomy (7) as reported by Prince and others (2003), the medical imaging approach may not be equally conventional for preclinical students (8), since it was shown to be more effective among students exposed to regional anatomy sessions for diagnostic knowledge (9). While strong relationship was found between the human body basic and clinical knowledge and the cadavers use in anatomy learning (10), questionnaire filling, focuses on collecting information about the student's interest in anatomy. Continuous assessment is essential for improving student's performance and development. It also enables educators to explore more closely students' abilities to benefit from academic lesson. (11). In order to assess student' attitudes towards learning, a set of questions are created for the purpose of gathering information about the adequacy of anatomy mastering when applying a new learning process (8). Various scientific approaches have been developed to reliably evaluate student' performance and motivation, including the use of standardized questionnaires such as Likert test analysis. The higher scores, will reflect the superior preparation level, while the total student's GPA can assist in the judgment, which is considered a valid assessment tool (12,13).

MATERIALS AND METHODS

A total of 240 undergraduate students, at the faculty of medicine, Tripoli University were included in this study. 106 (44%) of the targeted population were males and 134 (55,8%) were females. The students were subjected for the first time to an anatomy topic as a practical class, followed by ten minutes arrowed unlabelled diagram quiz aimed to assess student' ability to identify structures mentioned during the class. Some questionnaires were used to monitor the effectiveness of some factors in anatomical teaching tools (14).

During the second part of the study, the students were asked to fill in a questionnaire regarding satisfaction and efficiency.

Questionnaire form:

The assessment questions included the following questions:

1- Is this class decrease my self-study hours in this topic

2- By this I have adequate rate of information retention after this class

3- I fully understanding of the basic outlines

4- Now I can confidently discuss the topic.

5 - This method made me more interactive during the class.

6 - I think my information recall have been improved.

7 - I kept attention during the class without my written notes.

8- This method increases my orientation and interest.

The expected answers were: Strongly disagree, Disagree, Neutral, Agree, Strongly agree.

The questionnaire was specified to the subgroups learned with prosected plastinated cadavers, for the purpose of evaluation and assessment of the relatively more appropriate method used in teaching anatomy practical sessions. As the participant students are distributed into two equal groups according to the topic to be learned (A & B) (muscles of the upper limb for group A, posterior abdominal wall for group B). Each topic was explained by the same teacher for

each group. The methods to be comparatively assessed were plastinated cadavers, plastic models, and atlas slides. Each group was subdivided into 3 subgroups (A1, A2, A3) & (B1, B2, B3) forty students in each, followed by ten minutes arrowed unlabelled diagram quiz. No pre-exposure test was obtained because the students were selected to be first exposed to the explained topic. The post exposure test was homogenous (exposed for the same time with the same teacher), for both groups of students. The students subjected to plastinated bodies were asked to participate in satisfaction and efficiency evaluation of this method. The efficiency reflected in form of information retention and recall. all students responded to the questionnaire, so, a 100% response rate were achieved.

Statistical analysis: Statistical analysis was carried out using SPSS 19.0 software (SPPS Inc). Quantitative data from the questionnaires and the quizzes scores were analyzed using descriptive statistics for comparisons of answers and results between groups. Describe the study tool as constant, and with great validity according to Cronbach's Alpha analysis, while the simple Regression test recognizing the statistical relation of the satisfaction and efficiency for the students learned with cadavers. The variability and correlation of the different groups together were evaluated using (One Way ANOVA test) according to the methods to be used (plastinated, plastic, atlas).

RESULTS

The quiz results, (table 1), recorded a higher score for the subgroups (A1 & B1), were subjected to plastinated cadavers, with excellent marks as following 42.5% of group A1, 27.5% A2, 15% A3 while B1, B2, B3 were 62.5%, 32.5%, and 27% respectively.

Table 1: Variability in Quiz Scores according to teaching method.

Teaching Methods	Group A Quiz Results			Group B Quiz Results		
Degree	E (n) %	V. G (n) %	G & B (n) %	E (n) %	V. G (n) %	G & B (n) %
Prosected Plastnate	(17) 42,5%	(11) 27.5%	(12) 30%	(25) 62.5%	(5) 12.5%	(10) 25%
Plastic Models	(11) 27,5%	(8) 20%	(21) 52.5%	(13) 32.5%	(9) 22.5%	(18) 45%
Atlas (Slides Show)	(6) 15%	(9) 22.5%	(25) 62.5%	(11) 27%	(7) 17%	(22) 55%

E: Excellent, V.G: Very Good, G & B: Good & Below.

The very good degrees in Group A were 27.5%, 20%,22.5%. While group B are 12.5%,22.5%,17%, respectively. Lower marks were related to atlas slides method in both groups 62,5% for A3 and 55% B3. Which documents the plastinated cadaver as great. The results obtained from the survey explained into two blocks of questions in (table 2), those related to the satisfaction during practical class (questions from 1 to 4) and those related to the Efficiency of the method (questions from 5 to 8). resulted in high satisfaction and efficiency rate. Details of assessment of internal evaluation system by students are shown in (table 2). Which described by each question as the following: Eighty eight percent of the students, agreed and strongly agreed that the class decrease their self-study hours in this topic. Valid method in anatomy practical class teaching. While 83.02% of students, were satisfied with adequate rate of information retention after this class. And 92.2% of

the respondent's thinks, they strongly agreed and agreed that Full understanding of the basic outlines. Now the respondents can confidently discuss the topic reaches in 73.3%. On the other hand, the efficiency part of questions,

was of high level in the same manner as the following; Students said the evaluated method made them more interactive during the class were (93%), While whom their information recall has been improved (100%).

They kept attention during the class without using written notes approximate (93%). The method increases the orientation and interest is about (91%) of the examined sample, Cronbach's Alpha analysis was (0.853) for the study tool validity.

Table 2: Survey results of the Subgroups Subjected to prosected cadavers method (A1 & B1).

Answers	Satisfaction n(%)				Efficiency n(%)			
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Strongly disagree	1(1,2%)	3(3.7%)	0	1(1,2%)	0	0	1(1,2%)	1(1,2%)
Disagree	1(1,2%)	3(3.7%)	1(1,2%)	6 (7,5%)	2(2.5%)	0	1(1,2%)	1(1,2%)
Neutral	7(8,7%)	8(10%)	5(6,2%)	13 (16.2%)	3(3.7%)	0	3(3.7%)	4(5%)
Agree	43(53,7%)	41(51,2%)	45(56,2%)	49(61.2%)	51(63.7%)	58(73%)	51(63,7%)	51(63,7%)
Strongly agree	28(35%)	25(31,2%)	29(36,2%)	11(13,7%)	24(30%)	22(27%)	24(30%)	23(28.7%)

The simple Regression test recognizing the statistical relation of the satisfaction and efficiency, which appeared as strength as (R=0.815). While the determination factor was (R square=0.86) that explain the efficiency, according to the student's satisfaction with (F=154,411) at value of significances (sig=0.000).

The variability and correlation of the two groups together, that learned with plastinated cadavers, were evaluated using (One Way ANOVA test) according to the methods to be used, which summarized as (table 3). That (F) value is (3.965) at (sig=0,054) For the first group. While (F) value is (4.701) at (sig=0.036) for the second group. From here we can say the statistical differences are at value of (P≤0,05).

Table 3: One Way ANOVA test to evaluate the difference and variability of the methods to be used.

		Sum of Squares	df	Mean Square	F	Sig.
Group1	Between Groups	1.736	1	1.736	3.965	.054
	Within Groups	16.639	38	.438		
	Total	18.375	39			
Group2	Between Groups	1.344	1	1.344	4.701	.036
	Within Groups	10.867	38	.286		
	Total	12.211	39			

DISCUSSION

Several studies have appeared in recent years reporting the prosected cadaver, as a basic influential method for anatomy learning, in medical schools. Seeking expert advice and consultation, though old, is still a successful and effective approach despite incessant incorporation of new teaching methods and technologies, (9,15,16). Cadaveric dissection has long been used as an effective teaching method of anatomy in medical schools.

Students exposed to this traditional teaching approach have been shown to achieve significantly higher scores compared to their counterparts in other groups. (10,11). The cadaveric teaching based on small groups of students, under the supervision of a qualified anatomist, remains the gold standard teaching process for anatomy teaching, with a strong suggestion about the newly incorporated tools, to be used as supporting materials rather than being a total replacement for the cadaveric teaching (16-19). However, most of the mentioned studies do not take into account some disadvantages which can limit the effectiveness of this method.

Exposure to cadaveric dissection has been linked to some undesirable impacts in various academic, social, or behavioural aspects. Indeed, cadaveric dissection has been appraised to be a source of anxiety for anatomy students. Therefore, a remarkable proportion of students exhibited a propensity to avoid practical anatomy classes (6). These findings were attributed to a number of potential factors including, low encouragement (75%), sluggishness and low activity (27%), in addition to other contributors such as poisoning, sensitivity and nightmares (7). In our faculty during undergraduate anatomy course designing, some anatomy courses are devoid from cadavers use, because of very large number of students, opposing to less anatomy teaching stuff. In similar research targeted a new medical college in the United Kingdom, cadaveric tools were the also excluded owing to high costs and students' safety requirements. This, of course, does not include the surgical anatomy and pathological autopsy classes (6,7,8). Another important limitation of the cadaveric dissection the curriculum designer could encounter is the cultural and religious acceptance of the concept of body donation and dissection. (12,20). Evaluation based on survey and only post exposure test scores were considered for our study and the variability was relying on the method, but not the topic. unlike the study which based on pre and post class exam scores. Academic performance among students may vary significantly across different anatomical topics. In this regard, the abdomen as well as head and neck were associated with higher student scores as compared to neuroanatomy section (21).

CONCLUSION

the aim of this study was to evaluate the effectiveness of various anatomy teaching tools among undergraduate medical students using post exposure tests combined with simple standard questionnaire. It can be concluded that the use of prosected plastinated cadaver is remarkably helpful approach for teaching of anatomy practical classes, as indicated by the students post exposure test score analysis, and the survey according to statistical Likert test, which reflect the same basic lines and interests for most of the samples. These findings highlight the necessity of periodic evaluation of the anatomy program curriculum and tools of teaching in order to ensure better learning outcomes among undergraduate medical students. Incorporation of other supporting methods and teaching tools, such as plastic models as well as atlas slide show can undoubtedly improve the efficiency of teaching and the quality of learning.

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Response to Recombinant Human Growth Hormone Therapy in Libyan Children with Growth Hormone Deficiency in Misurata

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ABSTRACT

Recombinant growth hormone (rhGH) is used for the treatment of growth hormone deficiency (GHD). Children with growth hormone deficiency characterized by short stature. The aim of this study was to assess the efficacy of rhGH as a therapeutic intervention for treatment of children with GHD in Misurata following a year of therapy. Medical records of 174 GHD children attended the department of pediatric endocrinology in the Misrata Specialized Center for Diabetes and Endocrine. From June 2012 to January 2022 were retrospectively evaluated. Among them 50 patients met the inclusion criteria of receiving the rhGH treatment for a year. The relevant anthropometric data at baseline and follow-up were recorded. A retrospective study that included 50 GHD children treated with rhGH was performed. Patients were divided into two groups according to treatment response: poor responders with average mean increase of height by < 3 cm/year and good responders with increase of height by ≥ 3 cm/year. Patients with idiopathic GHD constitute almost two-thirds of the pathogenesis of GHD (70 %). Forty-six patients (92%) showed good response (Δ height >3 cm after one year of therapy). The response to treatment were; 93% in the age group 3-5 years old, and 83% in the age group 10-12 years. The mean difference in the growth rate was ΔHV = 5.163 cm/year after one year of rhGH therapy. Our study demonstrated that the use of rhGH for one year has an promising effect on increasing the height of patients diagnosed with GHD. We highly recommend the early use of rhGH in with GHD.

Keywords: Growth hormone, Growth hormone deficiency, Recombinant growth hormone.

INTRODUCTION

Human GH is a 191 amino acid single-chain polypeptide which is synthesized and secreted by the somatotroph cells of the anterior lobe of the pituitary gland (1). As its name implies the GH has a crucial role in growth regulation during the childhood (2). The synthesis and release of GH are under the control of various hormones, including GH releasing hormone (GHRH). Concentrations of GH are higher in the fetal, neonatal and pubertal periods than in adulthood, and increase with chronic malnutrition, exercise, physical trauma and sepsis (3).

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In children and adolescents, GH has a role in increasing bone length and density; however, GH is also important throughout life in increasing muscle mass, regulating lipid, carbohydrate metabolism and body water levels (4). Normal pulsatile GH secretion is crucial for postnatal growth and development, but not for intrauterine growth (5). As GH is secreted in a pulsatile manner (usually six pulses during 24 h, mainly during the night with low levels between pulses), random measurements of serum GH are of little value for the diagnosis of GHD (6,7). GH exerts its biological effects by binding to the extracellular domain of the GH receptor, a

single pass protein that also contains transmembrane and intracellular regions (8), this GH induced GH receptor dimerization is thought to be the first step in the signal pathway that ultimately results in the various biological effects associated with GH (9). GH is acting both directly and via its stimulation of insulin-like growth factor I (IGF I) production to promote linear growth (2). Growth hormone deficiency (GHD) results when the pituitary gland does not produce enough growth hormone to stimulate the body to grow and manifest as a slow or flat rate of growth in both early and later childhood (2). Children with GHD usually have typical body proportions, but are often chubbier, shorter, and may be perceived to be younger than their age when compared with peers of the same age and gender (10,11). The prevalence of childhood GHD is within the range of one in 3000 to one in 4000 (12,13). Although this is an probably overestimated in view of the reversibility of the deficiency in 25-75% of patients (14). However; according to different studies, the incidence of the deficiency is thought to vary substantially between countries, for example in the UK, estimates that GHD occurs in about one in every 3800 births (15). Another study in Belgium indicates an overall prevalence of GHD of 1 in 5600 (16). A recent study reported the incidence of childhood onset GHD to be 2.58 for males and 1.70 for females per 100,000 (17). Limited studies were performed in Libya to assess the efficacy of rhGH in improving height outcome in GHD pediatrics patients. Performing a study to investigate the use of rhGH for one year to treat GHD patients will contribute to the effectiveness of rhGH in treatment of GHD patients. The aim of this study was to assess the use of rhGH for one year in treatment of children with GHD in Misurata.

Patients and Methods

This is a cross-sectional retrospective study of GHD children treated with rhGH for one year in the Misrata Specialized Center for Diabetes and Endocrine. The Department of Pediatric Endocrinology at this center is the only department that treats GHD children. These children were under follow-up at the Department of Endocrine. The study was approved by the ethical committee .

Medical records of 174 GHD children (101 were males and 73 were females) attended the department of pediatric endocrinology in the Misrata Specialized Center for Diabetes and Endocrine. From June 2012 to January 2022 were retrospectively evaluated. Among them 50 patients met the inclusion criteria of receiving the rhGH treatment for a year. The relevant anthropometric data at baseline and follow-up were recorded. The height of these children at the study time > 2SD below the mean of comparable age and gender, aged (3-15) year. The medical records of identified patients were reviewed and data were extracted using data extraction form. The data included: a child age, age at the initiation of treatment, gender, average GH dose (mg/kg/day), cause of GHD, chronic disease data at baseline, height at start GH treatment, height after one year of rhGH treatment, final height expressed as standard deviation determined by the World Health Organization. First-year height velocity (HV) (cm/year), were calculated as the increment in height between start of treatment and a measurement made after 12 months of rhGH treatment. The observed first-year HV (cm/ year) was expressed as mean (SD). Data were also extracted on pubertal status of each patient which was documented according to the Tanner stage. Pre-pubertal status was defined as Tanner stag1. Response

to treatment was defined by acceleration of head growth in cm/year from the pre-treatment growth rate. Patients were divided into two groups according to treatment response: poor responders ($\Delta HV < 3$ cm/year) and good responders ($\Delta HV \geq 3$ cm/year).

Statistical analysis:

IBM SPSS statistics 21® software was used for all statistical analyses. Descriptive statistics were performed to describe Baseline auxological characteristics of children.

RESULTS AND DISCUSSION

rhGH is used for the treatment of GHD. Many studies suggested that administration of rhGH at an early age can maximize the growth potential and support the overall well-being during childhood (18,19). The aim of this study was to evaluate the use of rhGH as a therapeutic agent for treatment of GHD children in Misurata following a year of therapy. One hundred seventy-four children with GHD were identified in our retrospective study. However, not every child identified in the study was included. There were only 50 child met the inclusion criteria of administrating rhGH therapy for a year. Challenges such as refusal to follow-up, parental ignorance of social and psychological impact of GHD disease, the availability and the expenses of the treatment may play a role in reducing the number of patients attending for follow up.

Gender distribution:

Among the 50 participants, 52% were males while (48%) were females. Although not statically different (P value >0.05) this is in agreement with a previous study in which the percentage of males were (64%) outnumbered the percentage of females (36%)(20). Lé ger, J., stated that boys have lower serum levels of growth hormone binding protein (GHBP) than girls before puberty (21), also some diseases can occur in males than females which could explain outnumbering of boys (22). Furthermore, Parents may perceive that short girls are more socially accepted than short boys although this may vary across different cultures and communities (23). Gender was not significantly related to the response to rhGH in this study. This finding is consistent with other larger studies investigating the response to rhGH therapy such as the Kolej international graduate studies index (KIGS) database (24).

Causes of growth hormone deficiency:

Table 1, shows the causes of GHD among the fifty participants. 70% of children had idiopathic GHD, 26% had genetic causes, and 4% had pituitary hypoplasia.

Table 1: Causes of GHD

Cause	No.	%
pituitary hypoplasia	2	4%
Genetic	13	26%
Idiopathic	35	70%

In consistent with a previous study in which patients with idiopathic GHD constitute almost two-thirds of the pathogenesis of GHD (70 %) (25) and 83 % of 208 patients were diagnosed with idiopathic GHD in a sample selected from the National Registry of GH Treatment of Children by the Dutch Growth Foundation (26). Also, out of 54,996 patients in the National Cooperative Growth Study (NCGS) registry between 1985 to 2006; idiopathic GHD represented the largest treated group (42%) (27).

Response to rhGH after one year of treatment:

In this study, the children age was between 4 and 12 years old (Table 2). The mean age before starting rhGH therapy was 6.74 years and the mean of initial height was 104.72 (Table 2). In addition, the mean difference in the growth rate for the patient was $\Delta HV = 5.163$ cm/year after one year of rhGH therapy.

Forty-six patients (92%) met the criterion (Δ height >3 cm after one year of therapy).

Table 2: The age of children at initiation of therapy

	Age	No.	%
The age at initiation therapy (years)	4	5	10%
	5	8	16%
	6	2	4%
	7	14	28%
	8	6	12%
	9	9	18
	10	2	4%
	11	3	6%
	12	1	2%
	Total	50	100%

Growth response after one year of rhGH therapy administration is one of the best indicators of long-term height gain (28). In this study, most patients showed improvement in their growth rate (92%). These results were comparable to those of Alzahrani et al. (29) who studied the effect of use of rhGH on increasing the height of patients diagnosed with both idiopathic short stature (ISS) and idiopathic GH deficiency (IGHD). Alzahrani et al. found an increase in the height of participants after use of rhGH for one year regardless of the cause of the GHD; (the height gain in IGHD and ISS patients were 134.231±12.88, 134.04±10.90, respectively (29).

Age of diagnosis and response to treatment:

Unsatisfactory response to treatment was defined by the criteria: ΔHV acceleration of less than 3 cm/year from the pre-treatment growth rate. In the current study, patients were divided into groups according to treatment response: poor responders (ΔHV < 3 cm/year) and good responders (ΔHV ≥ 3 cm/year). The total number of children meeting the criteria as a good responder after a year of treatment was 92% (46/50). The percentage according to their ages, 93% (14/15) were 4-6 years old, 93.1% (27/29) were 7-9 years and 83% (5/6) were 10-12 years (figure 3). .

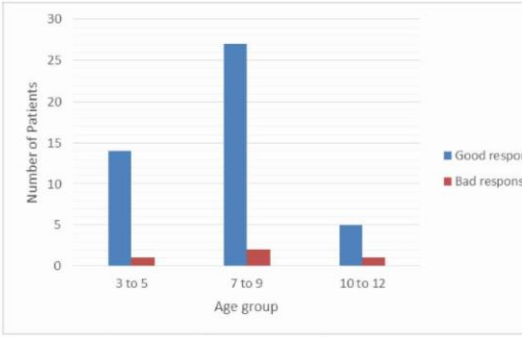

Figure 3: Age of diagnosis and response to treatment

It has been shown that total gain in height correlates significantly with younger age at the start of treatment in GHD (3,16,30). Therefore, the Growth Hormone Research Society advises that treatment should be initiated as soon as the diagnosis is made although no specific optimal time was specified for children diagnosed with GHD (1, 8, 31). In the current study, patients who began therapy at a younger age responded better to the treatment overall across all indications. Early age at start of therapy was identified as a predictor of adult height in children with ISS as well in other studies (16, 30, 32).

rhGH Dose (mg/kg/day)

The dose of rhGH treatment for 44 patients was 0.035 mg/kg/day, and for 6 patients was 0.045 mg/kg/day. The mean initial dose of rhGH was 0.0362 mg/kg/day and remained at same level throughout the observation period. A dose of 0.036 mg/kg/day (0.25 mg/kg/week) is recommended as the optimal initial dose (33). In order to achieve the optimum height velocity response, the dose of rhGH should be tailored according to GH responsiveness (34). In another study, the mean rhGH dose of GH treatment to treat IGHD

was (0.040 mg/kg/day) (35). The discrepancy in doses between studies may be due to differences in patient age, compliance, and the specific growth response being targeted (36-38).

Chronic disease:

Three children (6%) had confirmed type 2 diabetes after administration of rhGH. A review of the Kabi/Pfizer revealed that11 patients with type 1 diabetes, 18 patients with type 2 diabetes and 14 with impaired glucose tolerance (39). The National Cooperative Growth Study NCGS reported 22 children from a total of over 20.000 had developed diabetes while receiving GH therapy (40). After cessation of GH therapy 13 children still had diabetes, and 10 of these had existing risk factors for developing diabetes. It was concluded that in the absence of known risk factors, GH therapy during childhood and adolescence was unlikely to induce diabetes (39, 40).

In our study, chronic renal disease was detected in only one child (2%). The growth rate for the patient was 2.87 ($\Delta HV < 3$ cm/year) after one year of rhGH therapy. Growth failure is a common problem in children with chronic renal disease. Important factor which modifies GH responsiveness is the predominant chronic renal failure treatment that the patient is receiving (41). In addition, dialysis has a negative effect on GH efficacy because it can alter drug metabolism, protein binding and clearance rates (42).

Puberty state:

In 44 patients at the beginning of the therapy, puberty had not started yet (Tanner stage 1); one patient was classified as Tanner stage 2, four patients as stage 3 and one patient as stage 4 (table 3). The majority of cases (88%) in our study were prepubertal (Tanner stage 1), which is similar to the study of Miller et al (43). Strategies that combine rhGH treatment with suppression of puberty using GnRH analogs may result in improved height outcomes (44). Due to frequent delay in diagnosis of patients with short stature, rhGH treatment is often initiated close to, or even after, the start of the pubertal growth spurt. Studies have generally indicated that the growth response is greater if rhGH is started at a younger age, and particularly at the pre-pubertal stage, irrespective of the cause of short stature (45). While an increase in rhGH dose during puberty has been suggested, there are no clinical studies that have shown a convincing beneficial effect on adult height. Therefore, delaying puberty to allow exogenously administered rhGH to act for a longer period has been suggested as a strategy to improve overall linear growth. Oxandrolone administration has been examined in boys with constitutional delay of growth and idiopathic short stature, but had no significant effect on adult height (46). However, addition of oxandrolone to rhGH therapy has been studied in girls with Turner syndrome and provided approximately 3 cm of extra adult height gain (47).

Table 3: Frequency and percentages of patients at each pubertal stage

Frequency	Percent	
Tanner stage 1	44	88%
Tanner stage 2	1	2%
Tanner stage 3	4	8%
Tanner stage 4	1	2%
Total	50	100%

Conclusion

The aim of this study was to assess the efficacy of recombinant human growth hormone (rhGH) as a therapeutic intervention for one year treatment of children with GHD in Misurata. Data presented here suggested that the most common cause of GHD in our study

was idiopathic. In addition, the prevalence of GHD in males was more than that in females. Furthermore, it has been shown that the total gain in height was higher in children with younger age at start of the rhGH treatment; suggesting the importance of early intervention in treatment of GHD. Finally, the use of rhGH for one year has an effect on increasing the height of pediatric patients diagnosed with GHD. While our results were based on a small sample size and short period of follow-up, the findings reported here have provided insight into the GHD in Libyan children and the effectiveness of rhGH in increasing the height of children diagnosed with GHD.

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CYCLOPENTOLATE VERSUS TROPICAMIDE AND CYCLOPENTOLATE IN LIBYAN CHILDREN

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ABSTRACT

The young children have very strong ciliary muscle tone, that need cycloplegic agents to paralyze it, which done by instilling of cycloplegic eye drop. As eye drop usage in young is challenge. The frequent use cycloplegic drugs and the duration needed for cycloplegia to tack place, both bring the child to get bored. The aim of this study is to make cycloplegic refraction procedure shorter with less apply of eye drop. The study conducted as cross-sectional study on 40 Libyan children, between 3- 4 years old with dark iris, where two regimens (cyclopentolate 1% as a regimen 1 and cyclopentolate 1% with tropicamide 1% as regimen 2) was applied on each eye of same person at same time (to minimize bases due to change in machine or surrounding factors). The refraction is measured after application of those regiment three time, with 10 minutes interval. The refraction was measured by autorefractometer ± retinoscope when needed, the changes in spherical equivalent was used to determine maximum cycloplegia of each regimen at certain point of time. The result showed that there is mild difference between 30 and 40 minutes in regimen 1 (42.5%: 40% subsequently), in compare to regimen 2, maximum cycloplegia occurred at 30 minutes (50% of cases). The frequency of maximum dilatation at 50 minutes was 17.5% in regimen 1 and 12.5 % in regimen 2. This indicate that maximum cycloplegia occurred at 30 minutes in regimen 2. We concluded the effectiveness of regimen 2 in fasting onset of maximum cycloplegia only after twice eye drop, which saving time and effort without effect on cycloplegic outcome.

KEY WORDS: Tropicamide, Cyclopentolate, Cycloplegic refraction in children

INTRODUCTION

The refraction of the eye:

Normally, when the lights reflect from any object to the eye, its rays undergo a refraction mechanism to focus on the retina to create a clear retinal image, this done by the cornea (main refractive structure of the eye) and the lens. When this process is done in a perfect way, the state of the eye called emmetropia (figure 1). However, when the reflected rays from an object don't focus on the retina, they will create a blurred retinal image, the state called ametropia (1).

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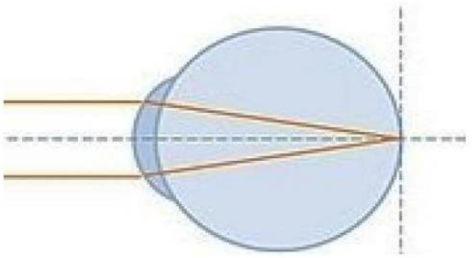

Figure 1: Illustrates the position of reflected rays on the retina in emmetropia.

Classification of the refractive error:

As emmetropia occur when the image of the object falls on the retina, the ametropia occur when the image focus in front or behind the retina, which divided into:

1-Nearsightedness or myopia: occur when the image of the object created in front of the retina, result in blurred image for far, with relatively clear image for the near (figure 2). Myopia usually more common in the adult, less common in the children (1% of rural Nepalese, 4% of south Africans, 12% of US population), myopia corrected either by concave glasses, contact lens or refractive surgery (2).

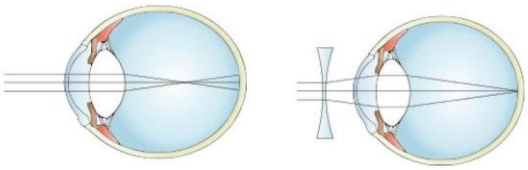

Figure 2: Shows the position of image that creating in myopic eye (first image) & how its position change by corrected glasses (second image) to make clear image.

2-Far-sightedness or hyperopia or hypermetropia: where the image falls behind the retina, person with this type of refractive error usually able to see relatively clear far object with blurred near object, which need more accommodation to overcome this near blurred vision (Figure 3) (3). It could be mild hyperopia (< +2.00Ds), moderate (between +2.25 to +5.00Ds) and high hyperopia (> 5.25Ds) (4). It affected primary the young children with 8% at six years and 1% at fifteen years. This type of error can be correct by either convex lenses, contact lens or refractive surgery (3).

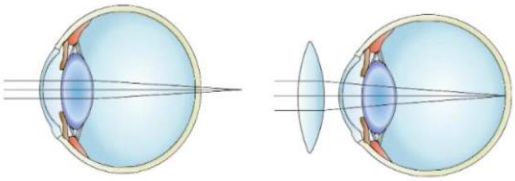

Figure 3: Shows the position of image in hyperopia and its correction by convex lens.

3-Astigmatism: secondary to imperfect spherical shape of either cornea (corneal astigmatism), lens (lenticular astigmatism) or both, where the image is always burred at all distances (figure 4). It can be corrected by cylinder and Toric lenses as well as contact lens.

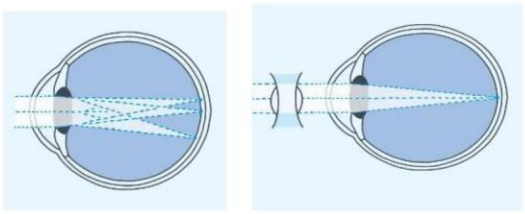

Figure 4: Astigmatism (upper image, where image can't focus on one point, and its correction by cylinder lens.

The accommodation and its function:

Accommodation is the ability of the eye to change its power to focus the image of seeing near objects. This occurs due to increase the power of the crystalline lens of the eye. Relaxation of the zonules allows the lens to becomes more spherical by change its capsule shape, increase its curvature and its anteroposterior diameter leading to the increase of its dioptric power (passive accommodation). The active component of accommodation is caused contraction of circular part of the ciliary muscle leading too relaxation of the zonulas, (figure 5). Cycloplegic drugs are used to abolish the ciliary muscle function reaching a state of cycloplegia.

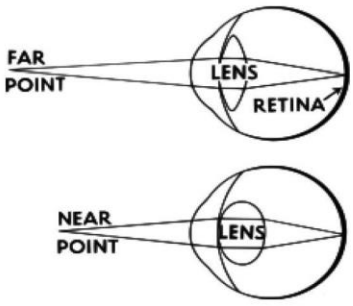

Figure 5: Illustrates the change in the shape of the crystalline lens for far (upper image) to near (lower image).

The distance between the near point and far point is called the accommodation range, which is very large in children, and decrease with age. The near reflex, is induced when the eye changes its focus from far to near, it is composed of three processes (accommodation of the lens by increase its convexity, constriction of the pupil to increase the depth of focus, and converging of the eyes to have similar parity of both eyes (5).

Cycloplegic refraction and its benefit:

Cycloplegic refraction is the procedure to measure the total refractive error by temporary paralysis of ciliary muscle, eliminating any effort of accommodation. This is achieved by cycloplegic eye medication, which could be in the form of drops or ointment.

In children the accommodation is very strong giving them ability to change their refractive power, so they are unable to control their focusing leading to false estimation of their refractive error, over myopia (6).

The measurement of cycloplegic refraction is done by retinoscope or autorefractometer.

The cycloplegic agents:

Cycloplegic agent is a drug which temporarily paralyze the ciliary muscle (loss of accommodation of lens). A mydriatic drug paralyze the sphincter muscle of the iris (induce mydriasis). Both groups are parasympatholytic having both functions to a variant degree and also in onset of action and duration of cycloplegia (Table 1). Parasympatholytic agents includes atropine, homatropine, scopolamine, cyclopentolate and tropicamide (7). Regarding to atropine which is one of most powerful cycloplegic and mydriatic agent, which present as 0.5% and 1% solution and ointment, with disadvantage of prolonged onset of action (six to twenty-four hours) and very long duration of action (ten to fifteen days) which interrupt daily activities of patient. The maximum cycloplegic effect occurs after 3 days of application. Side effects secondary to systemic absorption include, rapid pulse, fever, flushing, dry mouth and agitation with possibility of allergic reaction in the form of eczematous rash around the eye combined with conjunctival injection.

Table 1: Shows a comparison between some cycloplegic agents.

Drug	Onset	Duration
Atropine	6-24 hours	10-15 days
Homoatropine	1 hour	1-2 days
Scopolamine	30-60 minutes	3-4 days
Cyclopentolate	30-45 minutes	12-24 hours
Tropicamide	20-30 minutes	4-10 hours

On the other hand, cyclopentolate (cyclogyl, cylate, AK-pentolate) is a cycloplegic agent with less cycloplegic action but much more rapid onset (just thirty to forty-five minutes), shorter duration (six to twenty-four hours) and maximum cyclopregic effect at one hour. In compere to atropine those advantages make it a good option to replace atropine in some situation. Also, cyclopentolate has much less adverse effect in compere to atropine, where just occasionally the child could show sign of systemic toxicity secondary to systemic absorption. It is applied as a one drop, which can be repeated after five to ten minutes for two to three times. Its side effect includes burning sensation with irritation of the eye, temporary blurred vision, the serious side effect include irritation with dizziness and fainting, hallucination or even seizure, however, they are rare. It is available in form of 0.5%, 1% and 2%.

Moreover, tropicamide (mydiacyl, tropicacyl) which present as 0.5% and 1%, is another cycloplegic agent, weak but with more rapid onset (only twenty minute) with shorter duration (four to six hours) this advantage makes it the best choice

for fundus examination. Additionally, its weak cycloplegic effect can be used to relive ciliary spasm in anterior uveitis (so relive the pain) and induce mydriasis, so prevent posterior synechia or break it if it is present. In addition to the previous uses, tropicamide can be use in some objective refraction for those patients whose have weak accommodation, and they don't need strong cycloplegic refraction (7).

Measuring of maximum cycloplegia:

As the maximum cycloplegia is needed in young children to avoid underestimation of hypermetropia or overestimation of the myopia secondary to strong ciliary muscle. For cyclopentolate, the maximum cycloplegic effect starts between 10 to 60 minutes from fist drop application according to the age and color of the iris (8).

Literature review:

By looking to "Comparison of cyclopentolate versus tropicamide cycloplegia: A systematic review and meta-analysis" study, which aimed to compere cycloplegic efficacy of cyclopentolate and tropicamide. Where it presented meta-analysis of six study, the conclusion suggested that tropicamide could be another valid option to cyclopentolate with exception of some cases like infant, young children, high hyperopia and those whose examination result not match with manifested visual problem (9, 10). This conclusion can support our idea to use tropicamide with cyclopentolate to increase its onset and shorting the maximum cycloplegic effect (shorting examination process) and whole cycloplegic duration (rapid recovery of the patient).

Also, as mentioned by "Cycloplegic effect of atropine compared with cyclopentolate-tropicamide combination in children with hypermetropia" study, that compare cycloplegic effect of atropine 1% in one hand, with cyclopentolate 1% with tropicamide 1%, on sixty-three subject with hyperopia, aging between five to twelve years old, and spherical equivalent was the main parameter of comparison, the conclusion was that the combination of 1% cyclopentolate with 1% tropicamide could be an effected alternative regimen in compare to atropine for hyperopic children (11). This conclusion supports our study in efficacy of cyclopentolate with tropicamide combination.

Moreover, as illustrated by "Comparison of cyclopentolate versus tropicamide cycloplegia in children" that was double masked study, on twenty non-strabismic, non-amblyopic hyperopic children aging between six to twelve years old, where compare the cycloplegic effect of 1% tropicamide a to that for 1% cyclopentolate, they used both retinoscope, distance subjective refraction and autorefractometer. The result of refraction showing no statistic difference between two regimens in both retinoscope and distance subjective refraction, with difference in autorefractometer. Additionally, no refractive difference between thirty minutes and sixty minutes after instillation of the drop, also the accommodation inhibited more strongly by cyclopentolate in compare to tropicamide by autorefractometer, those lead to conclude that the tropicamide can be useful as a cycloplegic agent for school aged children with mild to moderate hyperopia (12), which also gives some support on our study.

Regarding to "onset and duration of cycloplegic action of 1% cyclopentolate - 1% tropicamide combination" study, that involved seventy-seven student aged between fifteen to twenty-five years old, aimed to study the time course of onset, time and duration of maximum cycloplegic effect and full duration of this effect, where it compare regimen of cyclopentolate 1% with tropicamide 1% as

combination and compare to with cyclopentolate 1% alone in same person (right eye for first regimen and left for cyclopentolate alone). The comparison parameter were subjective near add and pupil diameter, the measurement done after one hour from first instillation, with five minute interval, and continue up to seven hours, the result was that, the first regimen has rapid onset (five to ten minute) with shorter time to reach the maximum cycloplegic effect (fifty-five minutes for fist regimen and ninety minutes for second one) and rapid recovery (seven hours for first versus eight for second regimen) in majority of the cases (79.2%). And the conclusion was that clinically the combination of 1% cyclopentolate with 1% tropicamide is superior to 1% cyclopentolate alone in rapidity of the onset and reaching of maximum cycloplegic effect and rapid recovery (13). however, the age group is out from our age group study, but the goal of our study is the teat those regimens in younger age group to fill this gap.

As illustrated by "Cycloplegia in African-American children" study which concerned on the selection of the cycloplegic agent depends on the desired outcome, patient character and the associated risks, where refraction of patient measured after instillation of local anesthesia, followed by one drop of tropicamide 1% with one drop of cyclopentolate in both eyes, followed by frequent autorefractometer measurement at thirty, forty-five and sixty minutes, and the conclusion was that the combination of tropicamide 1% with cyclopentolate 1% is adequate cycloplegic and mydriatic with maximum cycloplegic effect at thirty minutes after first drop in African – American race (14). This study proves our study concern.

In compare to "A randomized clinical trial using atropine, cyclopentolate, and tropicamide to compare refractive outcome in hypermetropic children with a dark iris; skin pigmentation and crying as significant factors for hypermetropic outcome" study which compared between three regimens, first was atropine 0.5% (that applied twice daily for two and half days), second was two drops of cyclopentolate 1%, and last was one drop of 1% tropicamide followed with one drop of 1% cyclopentolate, those regimens applied on sixty-seven hyperopic children with dark iris, aging between three to six years old, in outpatient clinic as a double blind randomized study, where those children received two drop of 1% cyclopentolate in one eye and one drop of tropicamide 1% followed with one drop of 1% of cyclopentolate in other eye, then after two weeks, the refraction repeated with 0.5% atropine regimen, the main comparison parameter was spherical equivalent, also the comparison of spherical equivalent was done at first according to cycloplegic regimen (compare three regimens), then done according to sex, ethnicity and skin pigmentation (which divided to light, medium and dark). The result was that atropine regimen produced more hyperopia than other two regimens in same person. However, there was no significant difference between cyclopentolate regimen and combination of cyclopentolate with tropicamide. Moreover, skin color and ethnicity had strong relation in compare to gender that showed no association, additionally, the strongest association of cycloplegic effect with type of regimen that used, was for skin color. And the conclusion of this study was that, the 0.5% atropine has the highest hyperopic refraction, children with dark pigmented skin have lower hyperopic refraction by three regimen, in compare to medium skin pigmentation which showing equal hyperopic refraction between 0.5%

atropine regimen and combination of 1% tropicamide with 1% cyclopentolate., and lower hyperopia with 1% cyclopentolate regimen (15), this study increase the value of our study, where it mentioned that the cycloplegic effect of combination of cyclopentolate with tropicamide as the effect of atropine regimen, and stronger than cyclopentolate alone in medium skin pigmentation.

Supported by the "Eye color and skin pigmentation as significant factors for refractive outcome and residual accommodation in hypermetropic children: a randomized clinical trial using cyclopentolate 1% and tropicamide 1" study, which compare between two regimen (first two drop of cyclopentolate 1%), and second regimen (one drop of tropicamide 1%, followed by one drop of cyclopentolate 1%) in two hundred and fifty-one hyperopic children, whose classified according to skin and iris color (light, medium and dark color), as a double blind randomized study, and it concluded that the skin rather than iris pigmentation is the decisive parameter in determine the cycloplegic effect. Moreover, it mentions the need for awareness of cycloplegic limitation in dark pigmented iris, however the regimen of 1% tropicamide with 1% cyclopentolate has more accurate refraction both clinically and statically in dark skin with dark iris color (16). which also increase our study value.

METHODES

The study is a prospective cross section study, involved forty Libyan children, aged between three to fourteen years old. The study was conducted in Benghazi Eye Hospital outpatient clinic in Benghazi, Libya. All cases were referred to refraction room because of strabismus, poor vision or headache. All of the patients received one drop of 1% cyclopentolate in the right eye (regimen 1) and one drop of 1% tropicamide followed by one drop of 1% cyclopentolate immediately in left eye (regimen 2), after instillation of local eye drop anesthesia. The applications where repeated two times with ten-minute interval. The refraction was measured by autorefractometer and or retinoscope when autorefractometer was not possible at thirty (immediately after instillation of last drops), forty and fifty minutes from the first drop application. If the spherical equivalent changed by more than 0.5 D; another reading was taken at sixty minutes. If the reading was stable or there is a decrease between second and third reading; we suffice by previous readings.

The spherical equivalent for each reading was recorded. The refraction was measured in all of the cases in the first reading by autorefractometer, in the second and third reading retinoscopy was done in one non-cooperative child for auto refractometer. The change in the spherical equivalent was the main parameter to determine the point at which the refraction becomes stable or start to decrease and this point was consider as the maximum cycloplegic point. Then we compare the time at which cycloplegia reach its maximum between the two regimens. The hypermetropia were classified to mild (< 2.25 D), moderate (2.5 - 4.75 D) and sever (> 5.00D).

Also, the colour of the iris and skin were evaluated.

We exclude the children whose are known to be allergic to cyclopentolate or tropicamide, along with those with CNS problem or systemic disease that may affect the cycloplegic response, addition to those with intraocular disease or anomalous. Children younger than three years were excluded because usually they need general anesthesia for examination.

RESULTS

There were 24 females and 16 males, aged between three to fourteen years old (main age was 7±2) involved in this study, one of them with myopia, seven with mild hyperopia, three with high hyperopia, and remain with moderate hyperopia with thirteen of them have strabismus, two of them are known amblyopic with history of occlusion therapy. All of the cases found to have dark iris, two with black iris and remain with brown colour, with medium to dark skin (twenty with medium pigmented skin and remain with dark skin. Then we collect the spherical equivalent for regimens 1 (R1) and regimen 2 (R2) for each patient, then we calculate at which time was the maximum cycloplegic reading for each regimen in each eye for every patient separately. The result was that, for R1 the maximum cycloplegic effect (R1 max) was in seventeen participants (42.5%) at thirty minutes, in sixteen participants (40%) at forty minutes and in seven participants at (17.5%) at fifty minutes, that make mean maximum cycloplegic effect occurred between thirty to forty minutes. In compare to R2 where the maximum cycloplegic effect (R2max) in twenty participants (50%) occurred at thirty minutes, fifteen precipitants (37.5%) at forty minutes and only in five precipitants (12.5%) at fifty minutes. make a shift to maximum cycloplegic time toward the thirty minute (as compared to R1 group:42.5% to 50 minute) which was achieved only after twice application of the eye drops (Table 2).

Table 2: R1 max and R2 max at different times.

	30 min	40 min	50 min
R1max	17 (42%)	16 (40%)	7 (17%)
R2max	20 (50)	15(37.5%)	5 (12.5%)

Decreasing the frequency of eye drops application and shorting duration of whole process without effect on maximum cycloplegia.

CONCLUSION

The combination of 1% tropicamide with 1% cyclopentolate regimen can be shorting the duration required for maximum cycloplegia in mild to moderate refractive error in children in compare to cyclopentolate alone in medium and dark pigmented skin, which is time preserving with effective clinical cycloplegic refraction.

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CELEBRATING DIVERSITY IN TWINNING: A COMPREHENSIVE NON-MEDICAL REVIEW OF TWIN TYPES AND THEIR GENETIC ORIGINS

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ABSTRACT

This review examines the complexities of twinning beyond the traditional monozygotic and dizygotic categories, encompassing a range of less conventional types. Through an examination of studies spanning the last three decades, this paper provides a comprehensive synthesis of the non-medical literature concerning the genetic and developmental diversity of twinning. It highlights the unique genetic interrelations and developmental pathways characteristic of rarer forms, such as superfecundation, superfetation, and chimerism. These insights advance the understanding of genetic individuality and offer implications for genetic counselling and the broader field of reproductive sciences. The research employs a descriptive approach to synthesize findings from a broad survey of the literature, crafting a narrative that reveals the intricate genetic and developmental intricacies of twinning. This paper, targeting both academic and wider audiences, underscores the importance of recognizing the diversity within twinning phenomena and its significance in understanding human development and genetics.

Keywords: Chimerism, Developmental Biology, Genetic Counseling, Genetic Diversity.

INTRODUCTION

Twinning, a captivating biological phenomenon, has long been a subject of both scientific inquiry and cultural fascination. While the general populace is often familiar with the basic distinctions of identical and fraternal twins, the full spectrum of twinning is far more intricate and diverse than these common classifications suggest. This paper endeavours to provide a comprehensive review of the various types of twins, delving beyond the well-known monozygotic and dizygotic categories to explore the lesser-known and more enigmatic types such as super fecundated, superfetated, and chimaera twins. By drawing upon a wealth of established research, including seminal works by experts like Segal (1), Langkamp & Girardet (2), and Fierro (3), this review aims to offer readers a thorough and enlightening overview of the multifaceted world of twinning, its genetic underpinnings, and its developmental implications.

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Zygosity

Zygosity indicates the degree of genetic similarities or dissimilarities among different types of twins, triplets, or other higher-order multiples (4). Twin zygosity is determined by DNA or blood group polymorphisms (5). The DNA test determines zygosity by comparing the blood cells of each twin (3). In other cases, the zygosity of multiple births could be determined from their perceived similarity and dissimilarity as reported by their parents (6). hair appearance (e.g., eye colour, hair colour, structure), There are, in fact, several studies in

which zygosity was determined based on answers to validated questionnaires, where the accuracy of zygosity determination was relatively high (4-12). Multiple births are routinely classified by zygosity and described based on how they form (3).

Types of Twinning

There are two primary types of twinning: identical or monozygotic twins "mono = one, zygote= egg" and fraternal or dizygotic twins "di = two, zygote = egg" (1). Both monozygotic and dizygotic twins make up closely 95% of all multiple births (2).

Monozygotic (MZ) Twins (Figure 1)**:**

MZ twins arise when a single egg and sperm meet, and a zygote is formed; that zygote can then spontaneously split into two (or more) fetuses (1), (13), (14). The timing of this splitting determines the number of placentas and the number of chorion and amniotic sacs of the pregnancy; essentially, the later the splitting occurs, the more components will be shared between the MZ twins (10). Consequently, there are three different types of MZ twins; when the zygote splits during the first three days after fertilization, the result is dichorionic–diamniotic MZ twins, each twin has his/her own placenta, chorionic sac, and amniotic sac (dichorionic–diamniotic MZ twins account for about 20-25% of all MZ twins). The second type is monochorionic–diamniotic MZ twins which occur 8 days after fertilization; they share one placenta and one chorionic sac but have their own amniotic sac (monochorionic–diamniotic MZ twins account for about 70-75% of all MZ twins). If the division happens about 15 days after fertilization, the result is monochorionic monoamniotic MZ twins; they share one placenta, one chorionic sac, and one amniotic sac (monochorionic–monoamniotic MZ twins account for only 1-5% of all MZ twins) (10) "See Figure 1". Monozygotic twin fetuses that share one placenta and one amniotic sac may be at risk for Twin-to-Twin Transfusion Syndrome (TTTS), a disease of the placenta that occurs when an unbalanced flow of blood circulates from one twin to the other (15). MZ twins have identical genetic makeup (DNA) (16), so they will always be the same sex and also share very similar physical characteristics (4), (17); their abilities may also be very closely matched (18). Nearly one-third of all twins are monozygotic (19), and the rate of this type of twinning remains relatively constant (2). However, the factors that cause monozygotic twin births remain unknown (3).

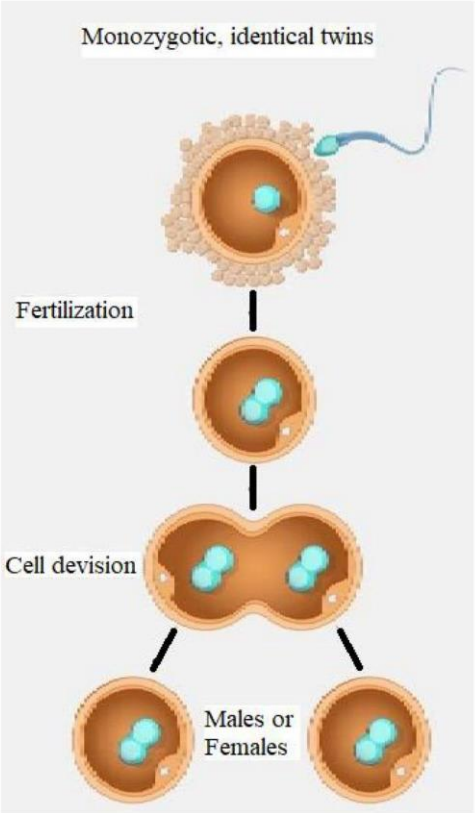

Figure 1: Courtesy National Human Genome Research Institute. (2023). Identical twins are also called monozygotic twins. Retrieved October 22, 2023, from https://www.genome.gov/genetics-glossary/identical-twins

Dizygotic (DZ) Twins (Figure 2)**:**
DZ twins, on the other hand, occur when two different eggs (or more) are fertilized by two separate sperm cells and implant in the uterus during the same menstrual cycle, resulting in two zygotes (1,13,14). Each zygote develops its own placenta, chorion, and amniotic sac; these are termed dichorionic–diamniotic DZ twins (10) "See Figure 2". DZ twins share approximately 50 percent of their DNA, similar to any two siblings born to the same parents at different times (14-16). DZ twins can be of the same gender or of different genders, and they may look alike or completely different (4), (17). They might also have distinctive abilities (18). Generally, two-thirds of all twins are dizygotic (19), and the rate of dizygotic twinning is influenced by factors such as the increased use of infertility treatments like in vitro fertilization (IVF), maternal age over 35, heredity, race, and nutrition (20) Twin studies, in general, assume that monozygotic twins are at an increased risk of stillbirth, infant death, malformations, and cerebral palsy compared with dizygotic twins (6).

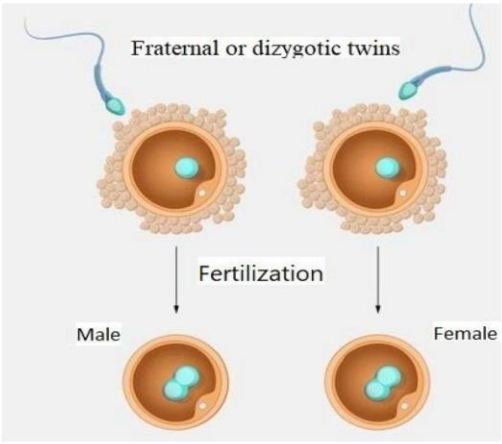

Figure 2: Courtesy National Human Genome Research Institute. (2023). Fraternal twins are also called dizygotic twins. Retrieved October 22, 2023, from https://www.genome.gov/genetics-glossary/Fraternal-Twins.

Super twins
Super twins which include triplets and other higher-order multiples (quadruplets, quintuplets), can be monozygotic, dizygotic, or even a mixture of both types (18). Triplets account for approximately 91% of all higher-order multiples (2). Twins and triplets are often delivered preterm. On average, twins are born at 36 weeks, triplets at 32 weeks, and quadruplets at 29 weeks (20). The majority of children from multiple births are born prematurely, and often, they don't reach a healthy birth weight, increasing their risk of health problems (2). As Hamilton and colleagues (20) noted, " Twins and triplets are also more likely not to survive the first year of life." The mortality rate for infants who are twins is 24%, whereas it's 5.4% for single-birth infants (21).

***Polar Body Twinning*:**
Scientists have suggested another unofficial type of twinning called polar body twinning, or semi-identical twins (19). Polar body twins occur when a single egg splits prior to fertilization. Each half then receives a different sperm, and each develops into a fetus (19). Ultimately, polar body twins share about 75 percent of their DNA. They share 100 percent of their mother's genes and 50 percent from each of their father's sperm (25). These twins can be of the same sex or opposite sex because the father's sperm determines the baby's gender (25). They would be less alike than MZ twins but more alike than DZ twins (3).

***Conjoined Twins*:**
Conjoined twins are always monozygotic twins who are physically connected in utero at certain points on their bodies (22). Conjoined twins occur when the fertilized zygote is delayed in splitting or fails to separate completely (23). The incidence of this type of twinning is very low, reported in only one out of every

50,000 to 100,000 pregnancies (24). The majority of conjoined twins are females, with a ratio of 3:1 (23), for reasons not yet fully understood by science (3).

Mirror Image Twins:

Mirror image twins are a subset of monozygotic twins (19). It's theorized that mirror image twins occur in approximately one quarter of all monozygotic twins due to delayed splitting of the zygote, after the developing fetus has slightly designated right and left sides. If this condition occurs, one twin may be right-handed and the other left-handed. Additionally, they might have many physical features (e.g., moles, hair whorls) on opposite sides of each other (3,19). These twins' risk being conjoined (25).

Superfetated Twins:

Superfetated twins are an unusual type of DZ twins. Superfetation occurs when a woman's body ovulates twice, days or weeks apart (22). In other words, a woman gets pregnant again after the first zygote has already implanted in the womb. The result is twins that are conceived at different times and may be delivered days or weeks apart (1).

Super fecundated Twins:

Super fecundated twins represent another rare type of DZ twins (22). Superfecundation refers to the conception of twins by two different fathers, resulting from multiple acts of sexual intercourse with different men within the same menstrual cycle (1).

Vanishing Twin Syndrome:

A vanishing twin occurs when a twin disappears from the uterus during pregnancy as a result of a miscarriage of one twin. The fetal tissue is absorbed by the other twin, the mother, or the placenta, which lead to the surviving twin having two sets of DNA, known as chimerism (26). According to Landy & Keith (27), vanishing twin syndrome occurs in roughly 30% of twin pregnancies.

Chimera Twins:

Chimera result from the fusion of two fraternal twin embryos and develop into one baby. This phenomenon occurs when one twin fetus dies early in the womb, and the surviving twin absorbs some cells of the vanishing fetus. As a result, the born twin contains a mixture of two types of DNA: its own original cells and the cells from its deceased twin (28).

DISCUSSION

The exploration of twinning presented in this review underscores the remarkable complexity of human reproduction and genetic variance. The phenomenon of twinning extends well beyond the traditional binary of monozygotic and dizygotic twins, encompassing a spectrum of types each with distinct genetic and developmental profiles. The occurrence of superfecundation and superfetation, for instance, challenges our understanding of human gestation and raises questions about the biological mechanisms that allow for such rare events. Similarly, the existence of chimera twins blurs the lines of individual genetic identity, presenting unique medical and ethical considerations.

One of the most striking implications of this diversity in twinning is its impact on the field of genetics and developmental biology. Monozygotic twinning offers a natural control for genetic studies, while the genetic dissimilarities in dizygotic twins can help disentangle the influences of environment and heredity. The study of superfetated and super fecundated twins could further illuminate the intricacies of fertility and embryonic development. However, the study of twinning is not without its challenges.

The rarity of certain twin types, such as polar body twins or superfetated twins, makes gathering a large and statistically significant sample size difficult. Moreover, the diagnosis of zygosity, while improved, still relies on the accuracy of DNA testing, which may not always be accessible or feasible in certain populations or regions.

The potential for future research in this area is vast. Advances in genetic testing could provide deeper insights into the zygosity of twins and the occurrence of genetic anomalies. Longitudinal studies could explore the developmental, psychological, and health trajectories of twins, particularly those with unusual twinning types. Furthermore, the increasing prevalence of assisted reproductive technologies (ART) and their role in twinning rates presents another rich avenue for investigation, especially as it pertains to the ethics and health outcomes associated with multiple births from ART.

CONCLUSION

The multifaceted world of twinning is as complex as it is captivating. Moving beyond the traditional dichotomy of identical and fraternal twins, this review has illuminated a spectrum of twin types, each with its own genetic blueprint and developmental narrative. From the shared DNA of monozygotic twins to the genetic mosaic found in chimeras, twinning provides a unique lens through which we can examine the intricacies of human genetics and embryonic development.

This comprehensive overview has bridged well-established knowledge with recent discoveries, offering a nuanced understanding of twin types such as super fecundated, superfetated, and mirror image twins, among others. These categories not only enrich our knowledge but also challenge our preconceived notions about individuality and genetic determinism.

As we continue to unravel the genetic and environmental factors that contribute to the phenomenon of twinning, our appreciation for its diversity only deepens. The implications of this diversity extend beyond academic curiosity, influencing medical practice, genetic counseling, and our understanding of human development.

In synthesizing the current state of knowledge, this review underscores the importance of continued research in the field of genetics. It is a call to action for embracing the diversity inherent in twinning and for fostering a sense of wonder at the biological processes that make each human being unique. As the field evolves, so too will our insights into the remarkable phenomenon of twinning, promising to reveal even more about the wondrous nature of human life.

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THE ROLE OF SMART PHONES IN OPHTHALMOLOGY

By

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ABSTRACT

The potential use of use Smart phones in ophthalmology is constantly evolving. This article describes the various tools available on Smart phones, for examining the ophthalmic patients. Additionally, it discusses how Smart phones can be used for ophthalmic photography and image management. The usefulness of the applications such as the Eye Handbook for the ophthalmologists, students, patients, physicians and researchers, currently available on Smart phones is also explored.

KEY WORDS: Smart phones, Eye hand books, Testing tools.

INTRODUCTION

A Smart phone, is a multifunctional electronic device that combines the features of mobile phone with advanced computing capability and connectivity. In addition to making phone calls & sending text messaging, Smart phones provides advanced functionality and ability to run multiple advanced applications, send and receive e-mails, create and display photos, videos and office documents (1,2, 3). Technological advances and increasing number of available applications, coupled with reduced costs, led to wide spread use of Smart phones. The assumed number of Smart phones users in the world in 2012 was 1 billion and is projected to increase to 1.75 billion in 2014 (4).

There has been significant increase of Smart phones users among health professionals, from estimated 30% in 2001 to 64% in 2009 (5,6). Currently, 86% of health professionals daily use Smart phones for various purposes (7), portable interface (8). Medical applications make Smart phones useful tools for the practice of evidence-based medicine, mobile clinical communication, patient education, disease self-management and remote patient monitoring (5). Aim of this article is to present many useful applications of Smart phones in ophthalmology.

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Smart phones applications in ophthalmology:

Ophthalmological applications are transforming Smart phones into medical devices & more than 342 different ophthalmological applications currently available (1). from 2009 to 2012 there was a 9-fold increase in the number of available surgical applications for Smart phones (9). Currently, there are 621 different surgical Smart phones applications available, Apple's iOS and Google's Android are two most used platforms among healthcare professionals (2,10). Some surveys indicated that the Apple iPhone to be the most popular Smart phones among the ophthalmologists worldwide (2,11). There is a wide range of Smart phones applications ranging from simple flashcards to virtual surgery applications that provide surgical exposure and familiarization with common operative procedures (9).

These applications can be divided into three groups based on their targeted user:

1. Healthcare professionals.

2. Medical or nursing students.
3. Patients (5).

Smart phones have many potential functions in the field of ophthalmology and their uses can be classified into following categories (2):

- Patient assessment tools.
- Patient education–visual aids.
- Health care profession education and reference.
- Patient records and administrative tools; and other multiple functions.

Patient assessment tools:

Ophthalmological examination requires use of various diagnostic tools. While these examinations can be easily performed in clinical settings, the use of Smart phones applications for different visual tests can be very useful in outpatient or in-patient consults & emergency room visits (2,5,8,12). Patient assessment tools include several applications. That can assess visual acuity using the Snellen visual acuity test or modern interactive visual acuity tests for preschool children and illiterate individuals. Some applications have tests for color vision, astigmatism, pupil size, Amsler grid test, oculomotor reflexes, a Worth 4 dot test and accommodation targets, red desaturation test and OKN drum simulator (2,8,13) (figure 1).

it is important to note the potential use of fluorescein light and penlight in non-ideal settings. In these conditions the examiner will need to increase the screen brightness to maximum and reduce surrounding light to minimum (3). Smart phones can be used as pediatric fixation targets that are bright & feature, motion and sound, to entertain pediatric patients (8). “Eye Handbook” is one of the most widely used applications that includes almost all of the mentioned testing tools and other popular applications are: “I Sight test”, “Vision test”, “Macula tester” and “Color blind test",

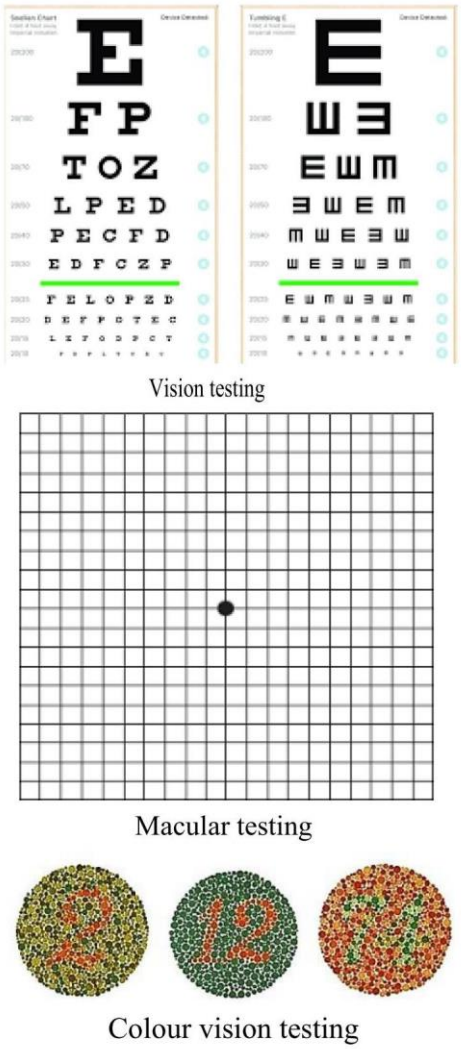

Figure 1: Eye Hand book shows: I sight test, Vision test, Macula tester & color-blind test.

Patient education–visual aids:

Patient management involves not only patient examination and treatment, but also, education to improve patients understanding of ophthalmic diseases and their processes. Clinician led patient education in disease prevention and management using of smart phones is convenient and effective (5). Educational materials such as instruction sheets, brochures and videos and can be used to help patients‟ better understanding of their condition. Smart phones are capable of reproducing high resolution images, videos and office

documents that containing information about medical conditions (8). High-resolution images of the various ocular conditions can easily explain anatomy and pathology various treatment procedures and options to the patient (3,8). Patients can download the application and the informative material to their own smartphone, review the information and show it to friends and relatives, relieving them of the burden of translating sometimes complicated explanations of their ophthalmological condition (2).

Several applications contain list of common ocular conditions that are encountered in everyday ophthalmology practice, with a short description of clinical features and treatment options (3). This information can be presented or even e-mailed to the patient and his family. In some cases, this may allow for self–diagnosis without presence of the physician (10). Currently two most popular patient education applications are "Eye Handbook" and "IKONION". With the "Eye Handbook", physician can e-mail the required educational materials directly to from patients their smartphone, which is a great feature (3). Patients with severe visual impairment can use applications such as voice–activated assistant to cope with daily activities (17). Smart phones can be also used for tracking and monitoring of disabled patients with Global Positioning System (GPS) (10).

The use of Smart phones for ophthalmic photography has become increasingly popular. New Smart phones have cameras with resolution of 5 mega pixels and higher, allowing users to capture high quality images. Several photo-adapters are available for Smart phones making them useful ophthalmic devices for taking images of both, anterior and posterior eye segments (figure 2). When using, photo-adapters the Smart phone's camera is aligned with the optical axis and placed close enough to the slit lamp eyepiece. There are also adapters designed to attach to the "Pan Optic Ophthalmoscope" for capturing fundus photos through an un-dilated pupil. It is even possible to take quality pictures of retina using only a Smart phones and indirect lens (8,14). The examiner can view the real-time images of the anterior and posterior eye segment with other practitioners, record and share their findings (15). A Smart phone using pinhole adaptor (Near Eye Tool for Refractive Assessment–NETRA) can be used to estimate the refractive error (Subjective Spherical Equivalent) without astatically significant difference from subjective refraction (16). However, when interpreting examination results, the ophthalmologist should keep in mind that testing tools are not ideally standardized and should be used the eye care professionals using their professional experience and judgment (3, 8).

Figure 2: Photo-adapters for Smart phones for anterior and posterior eye segments photography

Useful Smart phones and iPhone applications (the eye hand book EHB):

Eye Handbook (EHB) is an eye care reference book and an all-in-one application for Ophthalmologists, Optometrists as well as students and residents pursuing the field of eye care.

diagnostic and treatment reference

The Eye Handbook is a Smart phones application for Ophthalmologists and Optometrists.

Eye Handbook is the most comprehensive iPhone application available on iTunes and Android Stores, which can be downloaded for free. This application can link to meetings and various societies, and ophthalmic instruments information. Several references to ophthalmic genetics, ophthalmic acronyms and eponyms, differential diagnosis and classifications, ophthalmic dictionary and mnemonics are also available (21,25). Important journals with access to their websites and contents are available on EHB. Treatment section of EHB has ophthalmic medications, preparation of the fortified antibiotics, and laser settings for ophthalmic procedures (27). Another part in EHB which is important for training is Free download of lectures, flash cards. Patient and physician educational movies are also available. The EHB is being used worldwide, with about 50% of downloads in North America, 20% in Europe, and 10% each in Australia and Asia (34) (Figure 3).

Figure 3: Eye Hand book application.

Health care professions education and reference:

Professional development is essential for healthcare professionals. However, with limited time available for professional development can be difficult to keep up with the latest results finding (2). With the implementation of information technology, namely use of Smart phones, the latest results and findings are just a"click" away from the practitioners. All classifications and grading systems such as angle anatomy, diabetic retinopathy, macular holes, optic nerve edema and melanoma are easily accessible (3).

Several applications provide access to clinical trials database and literature searches in biomedical literature databases such as PubMed and MEDLINE. The most popular database search applications are "Pub-Search" and "PubMed on Tap". These applications also allow for sharing information with both, patients and colleagues (5). Other Smart phones applications have videos, color atlas images that are very useful in training process and surgical skills development. These applications can help in patient follow up, calculating intraocular lens (IOL) or surgically induced astigmatism (SIA) (2). Some applications include a list of diagnoses not to miss, with definition and differential diagnosis, a color– coded diagram of retinal drawings, questionnaires for commonly encountered ophthalmic diseases and a summary of benchmark randomized control trials in ophthalmology (3, 21).

Patient records and administrative tools:

The number of applications for Smart phones that can be used in medicine is constantly growing. With use of Smart phones communication between the physicians and hospitals is continuously improving (10). Dynamic interface has great functionality and potential for future growth in the field of ophthalmology (8). Applications for Hospital Information Systems (HIS) allow secure

access to patient's records from remote locations (2,5). These applications such as "OsiriX" and "MEDITECH" enable use of information's from hospitals picture archiving and communication system (PACS), as well as their secure transfer from one physician to another and from one location to another. Other useful information's including visual acuity and intraocular pressure values, eye images taken from mobile or stationary ophthalmic camera, optical coherence tomography findings, corneal topography images or even patients complete electronic health record (EHR) can also be transferred (5).

Tele-ophthalmology involves the use of electronic communication and information technologies to provide or support a diverse range of activities related to eye care (12). Smart phones applications enable true appliance of Tele-ophthalmology, covering many medical activities, including making diagnoses, treatment, prevention, education and research. Transferred information's can be later analyzed in detail or compared to previous findings. Tele-ophthalmology makes the practice of eye care independent of location or time (12). It is important to mention that there are some applications dealing with coding diseases according to The International Classification of Diseases (ICD) which can be very helpful and time saving (8,35).

Multiple functions:

There are several applications that combine many of the previously mentioned functions into one package. These features including reference search, links to journals, eye atlas, various tests, recording patient details, collaboration with other colleagues, tool kit to calculate eye related calculations such as (intraocular lens calculation, surgically induced astigmatism, vertex distance etc.) and patient information images with videos for explaining different conditions (2). On the other hand, there are several general medical Smart phones applications designed to provide information on general health conditions, including symptoms, diagnosis, differential diagnosis, pathogenesis and treatment options that can be helpful for ophthalmic patients as well as. Most popular of these are "Medscape" and "Epocrates" and "Up-to-date" which provide most recent information useful for practicing evidence-based medicine (5). There are also several applications such as Normal Lab Values and Pocket Guide to Diagnostic Test, that offer information's on common laboratory tests, including reference values and interpretation, causes for abnormal values and laboratory unit conversations. Smart phones enable the use of drug reference applications, such as Skycaps Drug's or Safe-Med Pocket, which provide information of drugs, names, indications, dosages, pharmacology, drug interactions, contraindications and costs. Other applications such as Med-Mat and Med-Calc offer options for calculating various clinical scores, individual drug dosing etc. (5). Smart phones applications with multiple functions can be very useful in limited resources settings with poor implementation of information technology such as Bosnia and Herzegovina (18).

Our mission:

As a social enterprise use are empowering all ophthalmologist as well as health workers by providing portable tools to help &to detect avoidable blindness.

Benefits but with limitations:

Smart phones are portable & come equipped with a safe light source, provide ready access to secure networks for data transmission. But, it is with caveats.

1. Learning curve:

Same as conventional method of direct & indirect ophthalmology, the Smart phones technique needs many moving parts (Doctor, camera, lens & patient). So, unless you have someone already adept at ophthalmoscopy or someone who expert in Smart phones. In general, it can be difficult to obtain high quality images that are useful for a comprehensive ophthalmologist.

2. Image Quality:

Unfortunately, you are also facing a lot of problems with image quality (Glare & improper exposure are the major culprits).

3. Field of view:

Smart phones cameras don't have the ability to access the full retina.

4. Use of Smart phones in different settings carries a risk for contamination. Special attention should be given to this (33).

CONCLUSION

Smart phones can be used as tools to facilitate the work of several professionals in improving visual assessment. They are useful in the inpatient words or travelling clinics, also

improves the understanding of patients about their clinical condition.

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