

Benefit of Clofibrate on indirect hyperbilirubinemia in newborn**Baha D. Moohy Alosy***Departments of Pediatrics- Collage of Medicine. University of Tikrit -IRAQ**Baha065@yahoo.com***Abstract:**

Background: hyperbilirubinemia develop in all newborns and resolves within the first several weeks after birth. Clofibrate is planned for management of indirect hyperbilirubinemia Aim: to evaluate Benefit of Clofibrate on indirect hyperbilirubinemia in newborn. Patients and Methods: this is a case- control study of 100 neonates on clofibrate and 100 neonates control groups, both with jaundice enrolled in fifty six months from June 2008- March 2013 in the Tikrit hospital and personal doctor's office ,Clofibrate group received clofibrate 100mg/kg.Evaluation of TSB reduction at different intervals regarding admission day,after 12-hr, 24-hr and 4-day compare with control Results:The 12-hr, 24-hr, 4-days reduction in TSB of clofibrate group were higher 19.74 ± 1.72 mg/dl , 15.49 ± 1.16 mg/dl, 10.4 ± 1.7 mg/dL than in control group 17.11 ± 2.02 mg/dL, 16.09 ± 1.96 mg/dL, 13.6 ± 1.52 mg/dL respectively with overall significant (P = .031944) The diminished need for phototherapy (P = 0.0198) and hospitalization time (P = 0.025) in clofibrate group were significantly important compare with control group Conclusion: Clofibrate (100mg) solitary dose used in neonates safely because decreasing bilirubin additionally reduce phototherapy , hospitalization time in neonates appeared within 24 hr and full action of clofibrate appeared between 24hr up to 96 hr.

Key Words: Clofibrate, phototherapy, newborn, bilirubin

الكلمات المفتاحية: كلوفبيرات، العلاج بالضوء، حديثي الولادة، اليرقان

الخلاصة:

خلفية: فرط بيليروبين الدم يتطور في جميع الأطفال حديثي الولادة و يحل في غضون الأسابيع القليلة الأولى بعد الولادة. ومن المقرر كلوفبيرات لمعالجة فرط بيليروبين الدم غير المباشرة. الهدف: لتقييم فوائد كلوفبيرات على فرط بيليروبين الدم غير المباشرة في حديثي الولادة. المرضى وطرق: هذه دراسة الحالة - التحكم ل (100) من الاطفال حديثي الولادة من مجموعة الكلوفبيرات و(100) من الاطفال حديثي الولادة من مجموعة التحكم ، كلاهما به اليرقان كان التسجيل في سنة وخمسين شهر من يونيو 2008 إلى مارس 2013 مستشفى تكريت ومكتب الطبيب الشخصي ، مجموعة كلوفبيرات تلقت من كلوفبيرات 100 ملغم/كغ. وقد أجري تقييم تخفيض البيلروبين على فترات مختلفة فيما يتعلق يوم القبول، بعد 12 ساعة، 24 ساعة و 4 أيام مقارنة مع السيطرة النتائج: لل 12 ساعة، 24 ساعة، 4 أيام كان هناك انخفاض في البيلروبين عن مجموعة كلوفبيرات أعلى 19.74 ± 1.72 ملغم/ديسيلتر ، 15.49 ± 1.16 ملغم/ديسيلتر ، 10.4 ± 1.7 ملغم/ديسيلتر، من في المجموعة الضابطة 17.11 ± 2.02 ملغم/ديسيلتر ، 16.09 ± 1.96 ملغم/ديسيلتر ، 13.6 ± 1.52 ملغم/ديسيلتر على التوالي مع إجمالية ذات أهمية معنوية (P = 0.031944) = تقلص الاحتياج للعلاج الضوئي وكذلك (P = 0.0198) = الوقت للاستشفاء (P = 0.025) = في مجموعة كلوفبيرات مهمة بشكل كبير مقارنة مع مجموعة التحكم الخلاصة: كلوفبيرات (100mg) الجرعة الانفرادي ممكن ان تستخدم في حديثي الولادة بأمان بسبب تناقص البيلروبين بالإضافة إلى تقليل العلاج بالضوء ووقت الاستشفاء في حديثي الولادة ستظهر خلال 24 ساعة وعمل كامل من كلوفبيرات ظهرت بين 24 ساعة إلى 96 ساعة

Introduction:

hyperbilirubinemia develop in all newborns and resolves in the first several weeks after birth and can go over 10 mg/dL in about 15% of newborns(1), genetic factor include 1 or extra UGT1A1 mutations with deviation at nucleotide 211 as a result emergent preventive strategies to treat and reduce the incidence of bilirubin-induced neurologic dysfunction

(2).it was alleviate by drug (clofibrate, mesoporphyrin),with or without phototherapy (3,4).Clofibrate is indicated for treatment of hyperlipidemia(5).Clofibrate is planned for management of indirect hyperbilirubinemia since it can work either as enzyme inducer or by enhance luggage compartment ability(s) (6,7).

Aim: study designed to evaluate Benefit of Clofibrate on indirect hyperbilirubinemia in newborn.

Patients and Methods: Benefit of clofibrate was assessed through both biochemical and clinical evaluation within the patients and control groups. Biochemical assessment include evaluation of serum bilirubin reduction subjected at different intervals regarding the day of admission, after 12-hr, 24-hr and at 4 day duration. Clinical evaluation was assessed through both reduced requirements for phototherapy and hospitalization time regarding on less than 5 day- duration or more than this (8).

Study design and Patients selection: A case - control study of 100 jaundice neonates on clofibrate and 100 jaundice neonates without clofibrate therapy as control group who visited private clinic and/or Tikrit teaching hospital enrolled in fifty six months from June 2008 to March 2013, the patient selection was according to American Academy of Pediatrician criteria of neonatal jaundice (8). Clofibrate group receive clofibrate single 100mg/kg (oily capsule) to assure simply given orally to neonate before any medication. Estimation of bilirubin and its frequeantation were done at admission and after receiving clofibrate dose then sequential bilirubin estimation after 12-hour ,24 hour and 4-day to compare with control group until become less than

10mg/dl , with or without need for phototherapy in both group .

Laboratory Procedures: the full test needed in jaundice is made for each group, about two-third of biochemical tests is made in two public labs {free} & other one- third of biochemical test be made in hospital.

Statistical analysis: It is completed by SPSS statistics and analysis through mean±SD and P-value for each group result on decrement total serum bilirubin. The clinical needs for phototherapy and for decrement hospitalization time in both group were compared by rate (study population percent %) and P value (9).2.

RESULTS:

The study results showed the following:- the 12-hour mean±SD total reduction in TSB of clofibrate group was (63%) (19.74 ± 1.72) mg/dL which is more than in control group (45 %) (17.11 ± 2.02) mg/dL(P= 0.13).The one-day mean±SD reduction in TSB of clofibrate group was (78.90%) (15.49 ± 1.16) mg/dL which is more than in control group (33%) (16.09± 1.96) mg/dL (P= 0.039). On the fourth-day mean±SD reduction in TSB of clofibrate group was (93%) (10.4 ± 1.7) mg/dL which is more than in control group (40%) (13.6± 1.52) mg/dL (P = 0.031944) A significantly higher in reduction TSB of clofibrate group compare to control group was shown as in Table (1) & Figure (1).

Table (1): Estimation of TSB reduction in both groups (mg/dL)

| Time of sampling(hr) | Control (n=100) /mean±SD | Patients (Clofibrate) (n=100) /mean±SD | P value |
|----------------------|--------------------------|--|-----------|
| 12 hr | 17.11 ±2.02 mg/dL | 19.74±1.72mg/dL | 0.13 |
| 24 hr | 16.09±1.96mg/dL | 15.49±1.16mg/dL | 0.039 |
| 69hr (4 days) | 13.6±1.52mg/dL | 10.4±1.7mg/dL | 0.032 |
| P value | 0.0519 | 0.0404 | 0.031944* |

Data presented as mean±SD,n=number of Patients the t-value is-2.54138, p < 0.05 is consider significant (0.031944)*

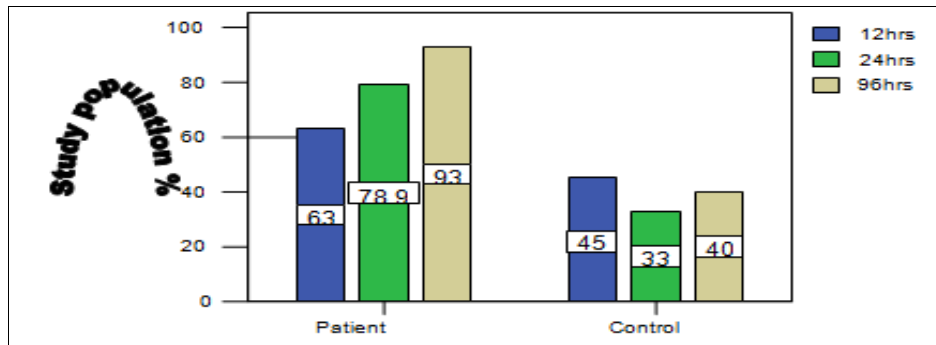


figure-1-

Figure (1) Estimation of TSB reduction in both groups (mg/dL)(study population percent %)

(P = 0.0198) compared to the patients of control group (6% vs. 76%) as presented in Table (2) & Figure (2).

Phototherapy requirements within Patients of clofibrate group was significantly low

Table (2): Comparisons in both patient and control groups need for phototherapy

| Phototherapy application | Control (n=100) Percent% | Patients Clofibrate) (n=100) Percent% | P value |
|--------------------------|--------------------------|---------------------------------------|---------|
| Yes | 76 (76%) | 6 (6%) | 0.0198* |
| No | 24 (24%) | 94 (94%) | 0.013* |

Data presented as Percentage of Patients ((%, n=number of Patients *the t-value is -1.54138. p < 0.05 is consider significant (0.0198)*

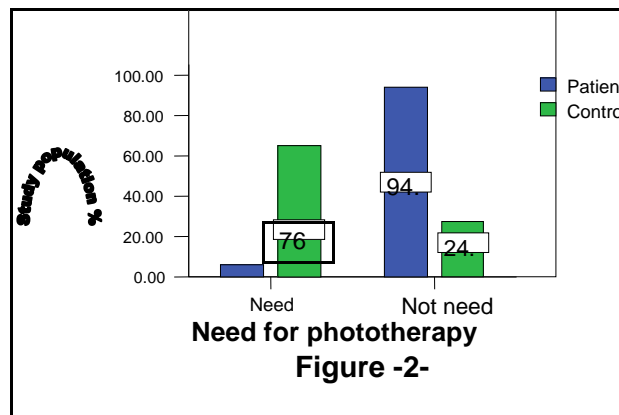


Figure -2-

Figure (2) Comparison in both patient and control cluster needed for phototherapy

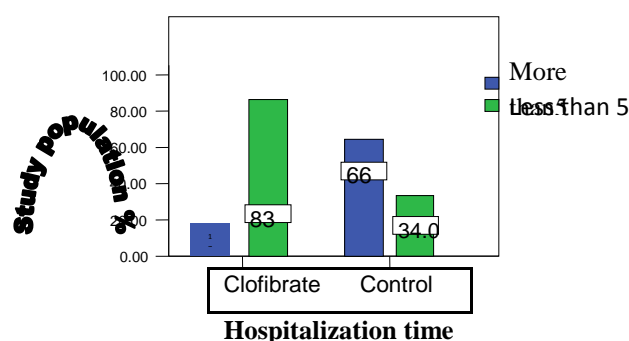
The hospitalization time of less than 5-day duration was significantly higher (P =0.025) in patients of clofibrate group (83%) than in control group (34%), Additionally , the hospitalization time of

more than 5- day duration was extensively lower (P =0.0248) on clofibrate patients cluster(17%) than control cluster (66%) as presented in Table (3)& Figure (3).

Table (3): Comparisons in both patient and control groups for decrement hospitalization time

| Time of hospitalization | Control (n=100) Percent% | Patients (n=100) Percent% | P value |
|-------------------------|-----------------------------|------------------------------|---------|
| <5days(less than 5) | 34 (34%) | 83 (83%) | 0.025* |
| >5days(more than5) | 66 (66%) | 17 (17%) | 0.0248* |

* Data presented as Percentage of Patients ((%, n=number of Patients the t-value is -1.68. $p < 0.05$ is consider significant (0.0248)*

**Figure -3-****Figure -3: Comparisons in both patient and control groups for decrement atet hospitalization time****Discussion:**

This research is the scientific trial in Iraq establishes Benefit of clofibrate on indirect hyperbilirubinemia in newborn. The proposal of this study was to decline phototherapy, exchange transfusion & hospitalization time .The 12-hr, 24-hr,4-days reduction in TSB of Clofibrate group were higher (63%)(19.74±1.72)mg/dL, (78.9%)(15.49±1.16)mg/dL,(93%)(10.4±1.7)mg/dL than in control group(45%)(17.11±2.02) mg/dL (33%) (16.09± 1.96) mg/dL, (40%) (13.6±1.52)mg/dL respectively with overall significant (P = .031944), This can be due to clofibrate effect as a tough encourage of glucuronyl transferase, so clofibrate raise hepatic bilirubin clearance in sex hours (10). owing to a tiny amount of clofibrate (100mg) do not result in sleepiness and complication (11). In the current trial, clofibrate illustrate consequence within 24- hours staring dose, There was a

demonstrate reduction of bilirubin level in clofibrate cluster with phototherapy compare to control cluster, This result are agreed with other studies of Badeli et al (12), A Ahadi et al(13)& Habibi et al (14) , but significant action of clofibrate appeared between 24hr up to 96hr from management as variation can be due to maturation of newborn and emptying of intestine and biliary system , This result are in accordance with studies of Mohammadzadeh et al 2005 (15), Caballero NB et al (16). In our study is disagreeing with results of Cuperus FJ (17).

The reduction for phototherapy requirements and hospitalization time within patients of clofibrate group were (6% vs. 76%), (17% vs. 66%) significantly lower (P = 0.0198), (P =0.0248) respectively compared with control group, this may be due to clofibrate increases bilirubin conjugation and excretion and

enhancement of glucuronyl transferase stimulation causing significant raise of bilirubin clearance, so decrease need for phototherapy & need for hospitalization & its duration. In the present study results are agreed with other studies of Caballero NB et al (16), Sakha SH et al (18), Xiong T et al (19) but disagreed with results of Cuperus FJ (17) owing to the short of blind of interference, management bias may be arise. No cases of either bilirubin encephalopathy or neonatal mortality and /or exchange transfusion happened in clofibrate group while three case exchange transfusions were needed in control group

Conclusion:

Clofibrate 100 mg/kg as a single dose can be safely used in neonates because of decreasing bilirubin and decrease need for phototherapy, hospitalization time in neonates appeared within 24 hours and full action of clofibrate appeared between 24-hr up to 96-hr.

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