

## The Effect of Manna of Hedysarum Prescription on the Decrease of Bilirubin Level in Icteric Neonates

MOHAMMAD REZA SHARIF

Department of Pediatrics, Kashan University of Medical Sciences, Kashan. I.R. Iran.  
Corresponding author E-mail: dr.sharifmd@yahoo.com

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### ABSTRACT

Hyperbilirubinemia is one of the common problems that causes the most case of hospitalization of neonates. Manna of hedysarum is a plantar medicine that has been prescribed as medication in the traditional medicine. This medication has not been examined systematically through a well-controlled clinical research. The purpose of this research was to examine the effect of Manna of hedysarum on the level of bilirubin of neonates and eliminating the need to hospitalization. In this double blind clinical research, the neonates that were visited by a pediatrician and did not need hospitalization were randomly assigned into two groups of receiving extract of Manna of hedysarum or placebo prepared by Barij Essence Co. Statistical analysis was performed by using SPSS:PC version 12.0. The result of analysis using ANOVA repeated measure indicated that there was no significant difference in the level of bilirubin after 24 hours of treatment between the groups. However, there was significant difference in bilirubin level of the treatment group by Manna of hedysarum compared to the placebo group after 48 and 72 hours following the treatment ( $p=0.005$  and  $p=0.0001$ ). The bilirubin level of the group treated by Manna of hedysarum was less than the placebo group. The results of this research indicated that using Manna of hedysarum decreases the level of bilirubin in outpatient neonates that suffer from hyperbilirubinemia. Further research is necessary before firm suggestion to use this medication for inpatient or outpatient neonates that are afflicted to hyperbilirubinemia.

**Key words:** Manna of hedysarum, Hyperbilirubinemia, Neonates, Outpatients.

### INTRODUCTION

Hyperbilirubinemia is one of the common problems that cause the most case of hospitalization of neonates. Approximately 60 percent of term neonates and 80 percent of premature neonates are afflicted to jaundice in the first week of their life. The cause of this disease is the accumulation of color pigments in the skin of neonates<sup>1</sup>. In normal circumstances, the level of total bilirubin in serum of umbilical cord is 1 – 3 mg/dl and the speed of its increase is approximately less than 5 mg/dl per day. Therefore, the jaundice demonstrates itself after 2 to 3 days following birth. Following 2 days, it increases and then subsides gradually. Usually after one week it ends. However, such is not the case for some neonates. The accumulation keeps raising to the point that hospitalization and prompt treat is necessary. Kernicterus is an dangerous

complication of indirect hyper bilirubinemia that its demonstrates itself in the form of acute neurological syndrome. This syndrome is associated with high morbidity and mortality rate in neonates and the cases who survive face various disorders such as seizure, hearing disturbances, extrapyramidal signs, bilateral choreoathetosis, and muscle spasms<sup>1</sup>

Phototherapy is known as the most common way of treatment and prophylaxis for hyperbilirubinemia that in the majority of the cases results in decrease in the level of bilirubin concentration<sup>2</sup>. Applying phototherapy in hospital results in the separation of mother from her neonate. This condition not only causes emotional stress for the mother but also causes financial burden for the family as well. The use of phototherapy at home is difficult and needs special facility.

Other treatment methods include consuming non absorbable food substances that have the likelihood of attaching to bilirubin at the intestine region and through the reduction of enterohepatic cycle result in slowing of the bilirubin absorption in the intestine, thus lowering its level in the serum. Activated charcoal, agar and cholestyramine are three of the known substances that are used as the treatment to reduce bilirubin level in neonates. However, routine application of such substances needs further controlled clinical examinations.

In addition, Manna of hedysarum is another plantar substance that had been used in herbal medicine or traditional medicine to treat jaundice in neonates. However, no clinically examined research in this regard is available. Therefore, prescription of such substance as a medication needs further research including considerable number of subjects. The result of a careful literature review of PubMed data base revealed a limited number of references with one study including the human subjects<sup>2-8</sup>. Manna of hedysarum is a plant product that contains carbohydrate components<sup>5</sup>. Its scientific name is *Alhagi pseudoal hagi* and traditionally had been used as a laxative medicine in addition to using it as the medicine for coughing, infectious fevers in children. A 5 percent humid Manna of hedysarum contains 47.7 percent melizitose sugar, 26.44 percent sucrose and 11.5 percent fructose<sup>4</sup>.

Tarhani<sup>3</sup> conducted a research and used this medicine for treatment of hyperbilirubinemia in hospitalized neonates. In this research, the neonates that were afflicted to jaundice, the experimental group was treated with phototherapy treatment in addition to oral Manna of hedysarum as a complementary medication. The result of study indicated that the level of bilirubin in serum of the experimental group who received Manna of hedysarum decreased more than the phototherapy group who served as the control group. However, this difference was not statistically significant.

The effectiveness of medications for treatment of hyperbilirubinemia may be enhanced by changing the doses of Manna of hedysarum. However in that case, placing the neonate in the hospital creates the separation anxiety for the parent as well as the financial stress. Therefore, if

an effective medication is found that prevents the increase in bilirubin level of neonate, it will decrease the need to hospitalization and reduce the emotional stress of mother separation from her neonate in addition to the financial cost of treatment.

For this purpose this research was designed to determine the effectiveness of Manna of hedysarum in non-hospitalized neonates patient that were diagnosed by a pediatrician with a bilirubin level of less than 15 mg/dl.

## MATERIAL AND METHODS

In this double blind clinical research, the neonate patients diagnosed by a pediatrician as suffering from jaundice with bilirubin level between 10 to 15 mg/dl participated. These patients at the time of examination by the physician did not need to be hospitalized but were advised to follow their bilirubin level. The patients were randomly assigned into two groups of experimental and control groups. The experimental group received Manna of hedysarum extract 20 percent for three times per day. The extract was prepared by Barij Essence Company where as the control group received placebo solution that contained water only.

The neonates who were full term and weighed over 2.5 kg with bilirubin level over 10 to 15 mg/dl were included in the research. The neonates that were preterm or weighed less than 2.5 kg or suffered from direct hyperbilirubinemia or had other diseases like infectious diseases were excluded from the research. The use of this medication in the traditional medicine was explained to the parents of the neonates and if they gave their consent to use the treatment for their neonate, they were included in the study. Following a complete description of the procedure and use of this plant medicine in traditional treatment of jaundice, the mothers of the neonates signed a human consent form.

Statistical analysis of data was performed by using SPSS:PC version 12.0. Statistical test of significances including two-way analysis of variance repeated measure, and post hoc tests were employed to analyze the data. All the statistical tests were examined at the alpha level set to 0.05.

**Analysis**

In this research a total of 50 neonates were examined. Table 1 presents the frequency of the patients according to their age group. Since the age group included the neonates below one week or more than one week, chi squared test of proportion revealed that there was no significant differences between the proportion of this two age groups ( $p>0.05$ ).

The result of analysis also indicated that there was no significant differences between the proportion of boy and girl neonates in two groups ( $p>0.05$ ). These results are presented in table 2.

**Table 1: Frequency distribution of the neonates according to the age**

Age treatment	Less than one week	one week or more	Total
Manna of hedysarum extract	12	11	23
placebo	12	15	27
total	24	26	50

**Table 3: comparing the mean values of bilirubin level of experimental and placebo group in pre test state**

index treatment	Mean Deviation (mg/dl)	Standard ( mg/dl)
Placebo	13/6	2/1
Manna of hedysarum Extract	13/6	2/2

**Table 5: Frequency distribution of patients in Manna of hedysarum and placebo treatment according to the need for hospitalization**

Treatment hospitalized	Manna of hedysarum extract	placebo	Total
Have	2	10	12
Have not	21	17	38
total	23	27	50

Table 3 presents the mean value of bilirubin level of the two experiments and control group before the treatment. The result of independent t-test indicated that there was no significant differences between the bilirubin level of the experimental (Manna of hedysarum extract ) and the placebo ( $p>0.05$ ).

In table 4, the level of bilirubin in different times after the treatment is presented. Analysis of variance repeated measure was employed to examine the level of bilirubin following 24, 48 and 72 hour after the treatment by Manna of hedysarum extract and placebo. The results of analysis indicated

**Table 2: Frequency distribution of the patients according to gender**

Treatment Gender	Placebo	Manna of hedysarum extract	Total
Girl	13	13	26
Boy	14	10	24
Total	27	23	50

**Table 4: The levels of bilirubin (mg/dl) after 24, 48 and 72 hours following the treatment by Manna of hedysarum and placebo**

Time treatment	24(hr.)	48 (hr.)	72 (hr.)
placebo	15.6 ± 3.3	16.3± 3.5	16.6±3.5
Manna of hedysarum extract	14.8 ± 4.1	14.3±3.5 *	12.7±3.5*

05.0 =±significant at \*

that there was no significant difference between the two treatments after 24 hours, but the difference were significant after 48 and 72 hours of treatment by Manna of hedysarum compared to placebo ( $p=0.005$  and  $p=0.0001$ ). The level of bilirubin in the Manna of hedysarum treatment was significantly less than the treatment by the placebo.

Table 5 presents the frequency of cases that needed hospitalization despite the treatment intervention in two groups. The result of chi squared test indicated that the proportion of the cases

needing hospitalization was significantly larger in the placebo group ( $p=0.019$ ).

### DISCUSSION

Hyperbilirubinemia is one of the most common diseases of neonates and is one of the main concerns of mothers at the time of child birth. For this reason, research for findings treatment and medications that can decrease or eliminate this problem has been conducted by pediatricians. Many of the medications prescribed requires the hospitalization of the neonate that means the separation of the child from the mother. New researches are adopting interventions that eliminate or minimize the separation period. It should be noted that hyperbilirubinemia is not the disease of today but rather it has been threatening the health of neonates from very old ages; a time that no hospital or modern way of treatments existed. It is a fact that plantar medication has been prescribed for treatment of many diseases and it is very likely that plantar medicine have also been used for treatment of hyperbilirubinemia. Among the plantar medication, Manna of hedysarum is one of the most popular ones that have been used to treat different diseases.

Tarhani<sup>3</sup> was one of the researcher who examined the effectiveness of Manna of hedysarum in addition to the application of phototherapy in hospitalized neonates that their bilirubin level exceeded 14 mg/dg. The result of this research indicated that despite the fact that the level of bilirubin in the case group was less than the control group, however, there was no significant difference between

the bilirubin level of the case and control neonates after 48 hours of treatment. Even the result of this research could show significant differences in favor of Manna of hedysarum treatment, such intervention would not eliminate the separation problem that a mother is experiencing for leaving the neonate in the hospital.

In regard to using plantar medicine for treatment of hyperbilirubinemia, Farhat ( ) conducted a research to examine the effectiveness of shirkhesht in hospitalized neonates and concluded that this medication had no significant effect on reducing the bilirubin level of neonate patients whereas in another research conducted by Ghotbi and associates (2006) opposite findings were reported for the effectiveness of this plantar medicine. Plantar medicine has been examined in treating jaundice in Turkey by Kagillian and associate (1992). These researchers used edible Agar to treat hyperbilirubinemia in neonates and reported that this medication had a significant effect on reducing the bilirubin level in neonate patients. In regard to the findings of this research, no comparable results were reported in the related literature. The findings of this research showed that the plantar medication of Manna of hedysarum is effective in reducing the level of bilirubin while treating the neonates at home, eliminating the anxiety of separating the mother from her neonate in one hand and reducing the cost of hospitalization. However, further research is needed before making firm suggestion to use this planter medication for outpatient or inpatient neonates suffering from hyperbilirubinemia.

### REFERENCES

1. Nelson Textbook of pediatrics. 19ed . international Edition, Elsevier : 603-6007 (2012).
2. Gotbi, F. Nahidi. S, Zangi, M, assessing the effect of Shirkhest on reducing the bilirubin level of neonates , *Research in Medicine*, 4 , 347-52 (2012).
3. Tarhani, F. effect of oral Manna of hedysarum on reducing the billirubin level of physiologic jaundice in neonates, *Quarterly Research Journal of Lorestan University of Medical Sciences*, 23, (2004).
4. Khoshdel A, Kheiri S. Effect of shir-e-khesht (billinaster drop) consumption by the neonates or their mothers on the neonatal icter. *Journal of Shahrekord University of Medical Sciences (J Shahrekord Univ Med Sci)* 13(4): 67-73 (2011).
5. Laghari AH, Ali Memon A, Memon S, Nelofar A, Khan KM, Yasmin A. Determination of free phenolic acids and antioxidant capacity of methanolic extracts obtained from leaves and flowers of camel thorn (Alhagi maurorum). *Nat Prod Res* ; 26(2):173-6. Epub 2011 Aug 11.

- PubMed PMID: 21834635 (2012).
6. Shaker E, Mahmoud H, Mnaa S. Anti-inflammatory and anti-ulcer activity of the extract from *Alhagi maurorum* (camelthorn). *Food Chem Toxicol.* ; **48**(10):2785-90. Epub 2010 Jul 13. PubMed PMID: 20633591 (2010).
  7. Ahmad S, Riaz N, Saleem M, Jabbar A, Nisar-Ur-Rehman, Ashraf M. Antioxidant flavonoids from *Alhagi maurorum*. *J Asian Nat Prod Res.* ; **12**(2):138-43. PubMed PMID: 20390757 (2010).
  8. Atta AH, Abo EL-Sooud K. The antinociceptive effect of some Egyptian medicinal plant extracts. *J Ethnopharmacol.* ; **95**(2-3):235-8. PubMed PMID: 15507342 (2004).
  9. Atta AH, Mouneir SM. Antidiarrhoeal activity of some Egyptian medicinal plant extracts. *J Ethnopharmacol.* ; **92**(2-3):303-9. PubMed PMID: 15138016 (2004).