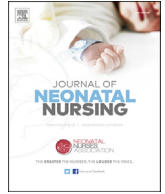




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Practice Guidelines

Variability of neonatal hyperbilirubinemia of non-immune cause in the clinical practice

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ABSTRACT

Objective: To know the variability in clinical practice related to the treatment of neonatal hyperbilirubinemia in the Neonatology Unit of the General University Hospital of Elche (Spain), where a specific clinical practice guide is not used.

Method: Retrospective audit of medical records of 130 patients ≥ 35 weeks of gestational age who presented neonatal indirect (unconjugated) hyperbilirubinemia of non-immune cause during their first weeks of life, and required treatment with phototherapy in the Neonatal Unit of the General University Hospital of Elche, during the period 2010–2014.

Result: Total serum bilirubin (TSB) levels at admission, the phototherapy time and the clinical stay vary with the type of applied phototherapy ($p < 0,01$), management of phototherapy ($p < 0,01$), and increase in TSB ($p < 0,02$).

Phototherapy time is associated with TSB levels control by blood analysis sent to the laboratory ($p < 0,05$) and capillary radiometer ($p < 0,03$), total stools ($p < 0,01$), and clinical stay ($p < 0,01$).

TSB levels at admission changes with neonatal age ($p < 0,01$), provenance ($p < 0,01$), and lactation during hospitalization ($p < 0,03$).

In addition, the clinical stay is associated with the TSB levels control by capillary radiometer ($p < 0,01$), and total stools ($p < 0,01$).

Conclusions: The results obtained show variability related to the TSB level at admission, the distribution of phototherapy time, and the clinical stay.

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Introduction

Neonatal jaundice is a very common cause of hospitalization (Ali et al., 2012; Bratlid et al., 2011; Clark, 2013; Muchowski, 2014), affects 66–84% (Bratlid et al., 2011; Muchowski, 2014) of newborns and requires specialized nursing care.

About 20% of newborns will suffer from hyperbilirubinemia, this being defined by levels of total serum bilirubin (TSB) of 12 mg/dl or higher (Gregory et al., 2012; Waldrop et al., 2013).

Bilirubin is a physiological metabolite that results from the degradation of the Hemo group of hemoglobin in the reticuloendothelial system (Aguilar Cordero and Cruz Domínguez, 2012; Amézcuca Sánchez et al., 2013; Gregory et al., 2012), and it is called

indirect, prehepatic, unconjugated, fat-soluble or toxic bilirubin (Amézcuca Sánchez et al., 2013).

The indirect bilirubina goes on to the blood and it is transported tied to the albumin to the liver, where it is transformed into direct, conjugated, water-soluble, hepatic or non-toxic bilirubin (Amézcuca Sánchez et al., 2013).

Approximately, 80% of the excreted bilirubina comes from the dissociation or degradation of the hemoglobin from the death or destruction of the red blood cells. The remaining 20% comes from the ineffective erythropoiesis and the replacement of the tissue hemo group, independently of the production of red blood cells (Aguilar Cordero and Cruz Domínguez, 2012; Sticova and Jirsa, 2013).

Frequently, the increase in bilirubin production is the predominant factor that causes the imbalance between the production and elimination processes (Kaplan et al., 2014).

Risk factors associated with severe hyperbilirubinemia that are

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related to the increase in bilirubin production include cephalohematoma or significant contusion, isoimmune hemolytic anemia, hemolytic disease, and other isoimmune pathologies, polycythemia, or infections, while those that are related to the decrease in bilirubin elimination include acidosis, sepsis, birth asphyxia, glucose-6-phosphate dehydrogenase deficiency, drugs impairing bilirubin/albumin binding or diseases that affect the liver or bile ducts, inborn errors of metabolism (galactosemia, hypothyroidism, ...). In addition, preterm newborn, the previous siblings treated with phototherapy, exclusive breastfeeding (especially breastfeeding without success and/or weight loss >10%), low birth weight, significant lethargy, respiratory failure, severe hypoglycaemia, severe hypothermia, male sex, and Asian race, are more prone to jaundice (Ali et al., 2012; Amézcuca Sánchez et al., 2013; Bhutani et al., 2013; Bratlid et al., 2011; Muchowski, 2014; Romagnoli et al., 2014; Waldrop et al., 2013; Wolff et al., 2012).

The purpose of the treatment of neonatal hyperbilirubinemia is to avoid neurotoxicity, acute neurological dysfunction that it induces kernicterus, a late and chronic neurological consequence (Aguilar Cordero and Cruz Domínguez, 2012; Ali et al., 2012; Kaplan et al., 2014). The toxic effects of bilirubin are explained by the inhibition of DNA synthesis (Kaplan et al., 2014). Therefore, it is important to systematically evaluate all newborns to detect hyperbilirubinemia (Muchowski, 2014).

Between 6 and 15% of neonates develop hyperbilirubinemia that requires treatment (Mishra et al., 2015). The main treatments are phototherapy or luminotherapy, blood exchange or exchange transfusion, and pharmacological treatment, being the most habitual first one (Aguilar Cordero and Cruz Domínguez, 2012; Ali et al., 2012; Amézcuca Sánchez et al., 2013; Dijk and Hulzebos, 2012; Houshmandi et al., 2015; Kumar et al., 2011; Muchowski, 2014; Romagnoli et al., 2014; Slusher et al., 2013; Stokowski, 2011).

Phototherapy is the most frequently used treatment when TSB levels exceed the physiological limits (Ali et al., 2012; Dijk and Hulzebos, 2012; Houshmandi et al., 2015; Kumar et al., 2011; Muchowski, 2014; Slusher et al., 2013; Stokowski, 2011), and it consists of the exhibition of the newborn's skin to the blue light that generates an electric lamp (Ali et al., 2012; Slusher et al., 2013; Stokowski, 2011), except in extreme cases when exchange transfusion is necessary (Ali et al., 2012; Slusher et al., 2013; Stokowski, 2011). The use of phototherapy has drastically reduced exchange transfusions in unconjugated hyperbilirubinemias (Dijk and Hulzebos, 2012) and its administration is a responsibility of the neonatal nurse, midwives, nursery nurses or pediatric ward, depending on the organization of the clinical context.

Absorption of light through the skin converts unconjugated bilirubin into bilirubin photoproducts that are excreted in the stool and urine (Muchowski, 2014).

The dose of phototherapy is a key factor in the speed of treatment; it is determined by the wavelength of light, the intensity of light, the distance between light source and newborn, and the body surface area exposed to light, and/or the threshold at which phototherapy starts (Bratlid et al., 2011; Muchowski, 2014; Stokowski, 2011; Woodgate and Jardine, 2015).

There are different types of phototherapy devices: conventional (halogen or fluorescent lamps), standard fiber-optic systems, and light-emitting diode (LED) devices (Amézcuca Sánchez et al., 2013; Kumar et al., 2011; Muchowski, 2014; Stokowski, 2011).

In standard or conventional phototherapy, a phototherapy device should produce at least 8 mW/cm²/nm of wavelength or with specific wavelengths of blue light (emission peak: 450 ± 20 nm) (Olusanya et al., 2015), but an effective phototherapy should produce an irradiance of 25–30 mW/cm²/nm over the waveband interval 460–490 nm, preferably in a narrow bandwidth to approximately 80% of the body surface area of the neonate

(National Institute For Health And Care Excellence, 2016; Queensland Clinical Guidelines, 2017).

Special blue fluorescent lamps or LED systems can provide a wavelength of at least 30 mW/cm²/nm with an emission peak of 460–490 nm, this being considered intensive phototherapy (Amézcuca Sánchez et al., 2013; Maisels, 2015; Muchowski, 2014; Queensland Clinical Guidelines, 2017).

LED lamps and conventional lamps are equally effective, without distinction in the phototherapy duration, rate of decrease in the TSB level, or failure of treatment (Muchowski, 2014). However, LEDs, being a light source with a high luminous intensity, a narrow wavelength bands, and to provide greater irradiation, this could make LED phototherapy more effective than conventional phototherapy in the treatment of indirect neonatal hyperbilirubinemia (Kumar et al., 2011).

Traditionally, the application of phototherapy is realized in the hospital, but it can also be provided in the newborn's home if the equipment is available and the necessary support is proportionate, it being applied exclusively in the home or it can be preceded or followed by the hospital phototherapy. To apply phototherapy in the newborn's home, the distance from the hospital must be assessed, as well as the motivation and competence of the parents (Malwade and Jardine, 2014).

TSB level that it is needed to reach to initiate the treatment with phototherapy varies widely depending on the sex, gestational age, hours of life and the etiology (Ali et al., 2012; Muchowski, 2014).

There is no evidence of toxicity in the phototherapy treatment, but the appearance of possible side effects derived from the treatment should be monitored (Amézcuca Sánchez et al., 2013; Queensland Clinical Guidelines, 2017).

On the other hand, there exists a variability observed in application of phototherapy guidelines, attributable to limited evidence on safe treatment thresholds and risk factors in preterm infants (Bratlid et al., 2011; Muchowski, 2014; Van Imhoff et al., 2011).

Multidisciplinary teams have developed their own guidelines for clinical practice mode protocols, pathways or clinical guidelines (Ali et al., 2012; Hospital for Sick Children, 2015; Malaysia Health Technology Assessment Section, 2014; National Institute For Health And Care Excellence, 2016; Ossorio Martínez et al., 2011; Queensland Clinical Guidelines, 2017; Rodríguez Miguélez and Figueras Aloy, 2011; Stokowski, 2011; Van Imhoff et al., 2011; Whitelaw, 2015; Wolff et al., 2012) for management neonatal hyperbilirubinemia in order to standardize clinical practice. The object of the present study is to analyze the possible variability of the practice and propose improvement actions.

Methods

The general objective was to know the existence of variability in clinical practice of neonatal hyperbilirubinemia due to a non-immune cause in the Neonatology Service of the General University Hospital of Elche (Spain).

The specific objectives, which define the strategies to achieve the general purpose, were to identify the variables that influence the treatment with phototherapy in newborns and the possible adverse effects that appear during the phototherapy treatment, and to know the average stay of children admitted for neonatal hyperbilirubinemia and its possible variation.

For it, a retrospective audit of medical records was carried out, during the period 2010–2014, to analyze the variables object of study that identify differences in treatment and its results during the hospitalization process, in the General University Hospital of Elche.

The target population was newborns ≥35 weeks of gestational age who presented neonatal indirect (unconjugated)

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