THE PREVALENCE AND RISK FACTORS OF DERMATOLOGICAL DISORDERS AMONG NEONATES IN A TERTIARY NEONATAL INTENSIVE CARE UNIT

Ph.D. Thesis

Angéla Meszes M.D.

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Supervisor:
Zsanett Renáta Csoma M.D., Ph.D.

Department of Dermatology and Allergology
Albert Szent-Györgyi Medical Centre
Faculty of Medicine
University of Szeged
1. Introduction

Preterm birth is one of the most significant perinatal health problems worldwide. According to the WHO data for 2007, the highest rates of preterm birth are observed in Africa and North America (11.9% and 10.6%), and the lowest in Europe (6.2%), especially in the Scandinavian countries (3-4%). Unfortunately, despite extensive obstetrical and public health efforts, the preterm birth rates remain stable or are even increasing, and impose a considerable burden on both families and society throughout the world. In Hungary, the prevalence of premature birth in the past few years has been estimated as 8-10% (8.6% in 2010). Although the prevalence of preterm birth has not been reduced, there has been a marked change in the survival rates of neonates born prematurely or with low birth weight (LBW). The survival rate of infants treated in neonatal intensive care units (NICUs) in Hungary is currently over 95%.

The treatment of prematures is performed in NICUs, which are centres that combine advanced technology, diagnostic and therapeutic modalities, and well-trained health-care professionals specializing in the treatment of premature and low birth weight infants and neonates who have medical conditions requiring special medical care. The management of neonates born with LBW or extremely low birthweight (ELBW) or who are critically or severely ill is performed in level III. progressivity NICUs. In Hungary, approximately 6500-7000 infants are admitted to level III. NICUs yearly.

Prematurity involves the immaturity of all organs and organ systems. All of the anatomic elements of the skin are fully developed by weeks 22 to 24 of gestation, whereas functional and biochemical maturity requires a much longer time. The basic structural differences between the skin of a
preterm neonate, a term neonate and an adult skin are of considerable importance in clinical practice. The structure of the skin of a full-term neonate is similar to that of an adult, but it is much thinner and more vulnerable. The skin of a term neonate is structurally and functionally more ready to adapt to an air environment than the skin of a premature infant, which is in homeostasis with a fluid environment. After delivery, premature skin matures rapidly over 2 to 8 weeks, but this process takes significantly longer for the most premature neonates. In premature infants, the structural and functional maturation of the epidermis accelerates significantly, taking approximately 2 weeks after birth. Preterm neonates are obviously highly vulnerable during this 2-week window period. Septic complications mainly occur in the first few days or the first 2 weeks of life and are the most common cause of mortality in this special population.

The immaturity not only of the organs, but also of the skin can result in various clinical consequences during the intensive care of neonates. The compromised epidermal barrier function results in an enhanced susceptibility to severe, invasive infections, high rates of TEWL, thermal instability, an electrolyte imbalance, an increased percutaneous absorption of chemicals and drugs, and easily induced skin traumas; these clinical complications are relevant determinants of high morbidity and mortality rates for preterm infants in the NICU.

Premature infants are at high risk of subsequent chronic medical problems. Neurologic, cardiovascular and respiratory diseases, gastrointestinal, metabolic and haematologic problems, developmental abnormalities, the immature immune system and frequent infections demand numerous invasive diagnostic and therapeutic procedures. The treatment and prevention of organ
impairments resulting from prematurity and various neonatal diseases are enormous challenges in neonatal care. In consequence of the use of modern invasive diagnostic and therapeutic procedures, respiratory therapy techniques and technical devices ensuring the continuous monitoring of vital parameters, the incidence of iatrogenic events has also increased significantly. The various skin injuries constitute a significant proportion of iatrogenic complications.

Naturally, other severe dermatological disorders besides iatrogenic injuries can also develop in neonates. Serious viral, bacterial or fungal infections, inherited keratinization disorders or dermatologic diseases with the formation of bullae can significantly impair the first and most important protecting line of the body, and at the same time the function of all the organs. The treatment of these premature or severely ill infants must be performed in highly qualified intensive centres.

2. Aims

2.1. The aim of the current survey was to investigate the prevalence of dermatological disorders among preterm and severely ill term infants in our level III. progressivity NICU. As far as we are aware, these are the first literature data on the prevalence of skin disorders in a tertiary NICU during an exact and comparatively long-term study period.

2.2. As most of the dermatological disorders observed in our NICU in the first year of the study period proved to be skin injuries that developed as a consequence of the immaturity of the skin and iatrogenic interventions, we paid particular heed to the prevalence of these injuries in the two years of the
study period. We also made a detailed assessment of the aetiology, type and therapeutic possibilities of lesions requiring wound management.

2.3. We also reviewed factors of possible relevance as concerns the development of skin disorders resulting from the immaturity of the skin, and various iatrogenic complications in neonates requiring intensive care. The following factors that may influence (directly or indirectly) the general condition of neonates were analysed: gender, gestational age, birth weight, use of a central venous line, respiratory and circulatory support, positive microbiology culture results, the appearance of early complications (pneumothorax, pulmonary haemorrhage, intracranial haemorrhage or respiratory distress syndrome), surgical interventions and the length of NICU stay.

3. Patients and Methods

3.1. Patients and dermatological examinations

Our prospective cross-sectional cohort survey was carried out in the level III. NICU at the Department of Paediatrics at the University of Szeged between 31 January 2012 and 31 January 2014 after approval and permission had been obtained from the Institutional Review Board of Albert Szent-Györgyi Medical Centre. This NICU is a 17-bed tertiary, university-affiliated centre, which annually admits 200-270 neonates in severe perinatal conditions from the south-eastern region of Hungary (with a population of almost 1.5 million). All consecutive newborn term and preterm infants hospitalized in the NICU during the 2-year study period were included in the study. Each of
them participated in whole-body skin examinations, always carried out by the same two experienced dermatologists from the Department of Dermatology and Allergology at the University of Szeged. The dermatologists took part in the visits at the NICU twice weekly and, if needed, unscheduled visits were also made. Decisions relating to diagnoses and therapies were made in consultation with neonatologists. In view of the relatively high number of surgical procedures required among the NICU patients, paediatric surgeons also make a ward round daily in the NICU. The treatment of iatrogenic skin lesions and wound care is carried out with the collaboration of dermatologists and paediatric surgeons.

The gestational age, sex, birth weight, area of involvement, aetiology of the disorder, causative factors, diagnosis at admission and comorbidities were recorded, together with the nature of the management (dressings, ointments, medication and surgical interventions).

3.2. Investigation of the prevalence of iatrogenic dermatological lesions requiring wound management among neonates

During the first year of the study period, a great proportion of the dermatological disorders proved to be lesions associated with immaturity of the skin and consequences of iatrogenic injuries which require special wound management.

We laid special emphasis on the investigation of lesions requiring wound care, among other dermatological conditions. All wound-care objectives, management plans and wound assessment details were documented precisely (aetiology, type, localization of the wound, wound dimensions, nature of the
wound bed, status of the surrounding skin, exudate characteristics, and presence of infection). Photodocumentation was made at every, or every second examination. Follow-up visits were made 1, 3 and 6 months after wound healing.

### 3.3. Investigation of the factors of possible relevance as concerns the development of iatrogenic injuries

During the 2-year study period, we investigated the prevalence of lesions associated with skin immaturity and as a result of iatrogenic injuries, such as epidermal stripping (ES), extravasation injuries (EIs), pressure ulcers (PUs), diaper dermatitis (DD), macerations in skin folds, infection-induced cutaneous eruptions, thermal and chemical burn injuries, surgical wounds, UV light-induced exanthema and haematomas.

To analyse the data on the patients’ characteristics and case history, the official medical records were used. We investigated the potential role of the following factors in the background of iatrogenic injuries: gender, gestational age, birth weight, length of hospital stay, intensive therapeutic intervention (ventilation and circulation support, surgical interventions), complications (pulmonary haemorrhage, pneumothorax and intracranial bleeding), factors influencing attendance and prognosis (patent ductus arteriosus (PDA), bronchopulmonary dysplasia (BPD) and infections).
4. Results

4.1. Patient characteristics and demographics

During the 2-year study period, a total of 460 neonates of Caucasian origin were admitted to the NICU (mean birth weight: 2236.86 ± 965.53 (SD) g, range: 500-5470 g, mean gestational age: 33.83 ± 4.39 (SD) weeks, range: 22-41 weeks, gender distribution: 250 males and 210 females). Distribution by birth weight: 16 (3.48%) neonates with high birth weight (HBW, > 4000 g), 159 (34.56%) with appropriate weight for gestational age (i.e. normal birth weight, NBW, 2500-4000 g), 154 (33.48%) with LBW (1500-2499 g), and 131 (28.48%) weighing less than 1500 g: 81 (17.61%) with very low birth weight (VLBW, 1000-1499 g) and 50 (10.87%) with extremely low birth weight (ELBW, <1000 g), of whom 17 (3.7%) weighed < 750 g. The mean birth weight of the admitted male infants (2360.7 ± 990.87 (SD) g was significantly higher than that of the female infants (2089.4 ± 915.13 (SD) g. (p=0.003).

40.7% of the infants were born after 36 weeks of gestation, 29.5% of them between 32 and 35 weeks, 19.16% of them between 28 and 31 weeks, 9.69% of them between 24 and 27 weeks, and 2 infants before 24 weeks of gestation. There was no significant difference between the mean gestational ages of male (34.02 weeks) and female (33.59 weeks) infants.
4.2. Dermatological disorders observed in the NICU during the first year of the study period

During the first year of the study period, 211 neonates of Caucasian origin were admitted to the NICU (mean birth weight 2353.6 ± 981.6 g, mean gestational age 34.5 ± 4.3 weeks [range 23–41 weeks], 125 male, 86 female). Sixty-four neonates (30.3%; 30 male, 34 female; mean birth weight 2139.1 ± 1159.4 g, mean gestational age 33.1 ± 5.4 weeks [range 23–41 weeks] ) of the 211 infants admitted to the NICU exhibited some kind of dermatologic disorder; 15 (7.1%) had two and 5 (1.42%) had three different dermatologic conditions during their hospitalization. Overall, 89 different dermatologic cases were detected, 63 of whom needed some form of dermatologic treatment, whereas in 26 cases the conditions were merely closely followed. As regards the distribution of the diseases, significantly intercorrelated iatrogenic injuries and dermatologic conditions associated with the immaturity of the skin were observed in the great majority (67/89, 75.3%) of the dermatologic disorders. The average gestational age of these neonates was 32.6 weeks. Thirty-five (39.3%) cases of iatrogenic injuries and complications were treated, such as ES (n = 7), EIs (n = 6), PUs (n = 5), thermal burns (n = 1), surgical wound infection (n = 1), blue light–induced exanthema (n = 2), contact dermatitis (n = 2) and mechanical impact-induced suffusion (n = 1). Skin reactions presumed to be induced by infection were observed in 8 neonates, manifested as erythematous macules, papules, pustules, or in one severe case of purpura fulminans. Cutis marmorata was diagnosed in a hypoxic neonate treated by using transient hypothermia. One neonate was born in a polytraumatic
condition after an intrauterine infection, in whom disseminated intravascular coagulopathy developed and resulted in extensive purpurae and haematomas. Other common conditions that developed as a result of the immaturity of the neonatal skin (n = 32, 36.0%) were dry, scaly skin (n = 18), DD (n = 10) and maceration in the skin folds (n = 4). One neonate who had anti-human platelet antigen-la-induced neonatal alloimmune thrombocytopenia had purpura and petechiae over the entire surface of the body; it was treated effectively with intravenous (iv) immunoglobulin and a special thrombocyte infusion. One neonate had petechiae on the neck and face, caused by the umbilical cord curling around the neck. Of the common transient benign neonatal skin conditions, erythema toxicum neonatorum developed in 5 neonates. Vascular malformations were diagnosed in 4, vascular tumours in 8, and other benign congenital tumours in 3; no treatment was needed in these cases, but only observation. One neonate was born with dermal melanocytosis in the lumbosacral region.

4.3. Lesions requiring wound management during the first year of the study period

32 (17%; 17 male, 53.1%; 15 female, 46.9%) of the 211 infants admitted to the NICU required special therapy for at least 1 wound, 3 of the 32 suffering 2 wounds, i.e. a total of 35 wounds were detected and treated. The gestational age of these 32 neonates varied between 23 and 41 gestational weeks (mean: 33.02 ± 4.9 (SD) g). The mean birth weight was 2037 ± 1055 (SD) g. The 35 wounds were grouped on the basis of the causative factors. The most common wounds (10 cases, 28.6%) were erosions and excoriations that
developed in the gluteal region because of irritative contact dermatitis due to urinal or faecal irritation. Erosions due to ES were observed in 7 neonates (20.0%), in whom injuries developed after the removal of a tape used for cannula fixation. Extravasation wounds were also frequent (6 cases, 17.1%) after paravasation of parenteral feeding solutions such as amino acid, glucose and fatty acid infusions or inotropic drugs such as dobutamine and adrenaline. Another common type of wounds was PUs, which were observed in 5 (14.3%) critically ill neonates (with congenital heart disorders, after resuscitation, or with intrauterine infection); these developed mainly in the occipital region, but 1 occurred in the nose due to a nasal CPAP cannula. PUs were staged on the basis of the National Pressure Ulcer Advisory Panel (NPUAP) Staging Guidelines: 2 patients had a stage I PU ulcer, and 3 ulcers were in stage II. We observed 1 neonate with a deep surgical wound (2.8%) in the lumbo-sacral region, which developed after a closing operation for myelomeningocele, and 1 neonate with a thermal burn (2.8%) caused by a pulse oxymeter. There were 5 other iatrogenic lesions (14.3%), which could not be classified into the previous groups: 4 cases of maceration in folds (12.5%), and 1 suffusion (2.8%).

During the different steps and stages of the wound management, modern wound care methods were used, with close regard to the anatomical and physiological characteristics of the neonates. The wound management included both conventional and modern dressings. The frequency of dressing changes was always determined individually, depending on the wound type and base, the amount of wound exudate, signs of infection and the type of dressing. Swabs were always taken from wound exudates for microbiology, and parenteral antibiotics were commenced in accordance with the bacterial
sensitivity if the laboratory findings or skin signs were indicative of systemic infection.

4.4. Investigation of lesions associated with skin immaturity and iatrogenic injuries and factors of their development during the 2-year study period

Altogether 83 (18.04%; 41 male and 42 female; mean birth weight: 2055.6 ± 1045.95 (SD) g, mean gestational age: 32.85 ± 5.2 (SD) weeks, range: 23-41 weeks) neonates exhibited some kind of iatrogenic skin disorder, 66 of them suffering from 1, 15 of them from 2, 1 of them from 3, and 1 of them from 4 different dermatological conditions during the period of hospitalization.

The iatrogenic skin injuries were grouped on the basis of the aetiology and causative factors: ES in consequence of the removal of adhesive dressings, EIs, surgical wounds, infection-induced cutaneous eruptions, burns due to thermal or chemical agents, excoriation in the diaper area, macerations and erosions in the folds, PUs, petechiae, haematoma and polytrauma, irritative contact dermatitis, mechanical impact-induced suffusion, hypothermia-induced livedo reticularis and blue-light phototherapy-induced transient rashes. Only one dopamine-related extravasation injury with severe tissue necrosis and ischaemia was recorded during the 2-year study period, which resulted in deep gluteal skin necrosis as a consequence of umbilical arterial catheterization.

The mean gestational age of the neonatal infants with any of the iatrogenic skin injuries was significantly lower than that of the infants without any skin trauma. The mean birth weights in the two groups were not statistically
different, but the prevalence of iatrogenic skin injuries was significantly higher among the infants with a birth weight of <1000 g as compared with infants with a birth weight of >1000 g. The length of NICU stay was significantly longer for neonates with iatrogenic skin injuries. The mortality rate of the infants with an iatrogenic skin injury was 9.64%, while in the infants without skin injuries it was 8.22%; the difference between the two groups was not statistically significant.

The following factors, interventions and conditions proved to be associated significantly with the development of iatrogenic skin injuries: use of the INSURE (intubation, surfactant, extubation) technique, surfactant use, mechanical ventilation, insertion of an umbilical arterial catheter (UAC), circulatory/cardiac support with dopamine or dobutamine, PDA, pulmonary haemorrhage, intracranial haemorrhage, BPD and positive microbiology culture results.

5. Discussion

Preterm birth rates have increased in the past two decades in many countries, in contrast with reports of decreasing rates of preterm deliveries in Finland and The Netherlands. This tendency can be explained by many reasons, e.g. increasing multiple pregnancy rates associated with the use of in vitro fertilization, later maternal age at childbirth and an increase in maternal body mass index (BMI). While the rate of preterm births for singleton deliveries is 5-10%, the rate for preterm multiples is 40-60%. The survival rate of premature neonates has risen markedly in recent years due to medical advances in perinatal care, such as the use of antenatal corticosteroids and
surfactants. Premature infants are generally at higher risk of mortality and morbidity. This is especially true for the very preterm neonates (< 32 weeks), but moderate (32-33 weeks) and late (34-36 weeks) preterm neonates may also have worse neurodevelopmental and educational outcomes as compared with neonates born after at least 37 weeks of gestation. A notably high proportion of neonates therefore require care in NICU in their early extrauterine life.

The mortality rate of infants is one of the most important quality indicators of paediatric and public health. Premature neonates or infants who are born with severe diseases or developmental disorders and who are treated in intensive care units nowadays account for a great majority of the neonatal or infant mortality in developed countries.

5.1. Dermatological disorders among neonates requiring intensive care

Our primary aim in this study was to investigate a large population of preterm and severely ill term infants, with a view to acquiring a better understanding of the relationships between dermatological and internal diseases, and an overall picture of the frequency of these skin disorders in the NICU. A survey of comprehensive investigations of dermatologic manifestations in preterms is lacking in the literature. This is the first comprehensive study of dermatological disorders and diseases in neonates observed in a NICU during a 1-year study period. The majority of the review articles survey the aetiology of the typical iatrogenic skin injuries in NICUs (thermal burns, chemical burns, light burns, scalp injuries, EIs, PUs, ES, e.t.c.). Our own survey has revealed that dermatological conditions may be
accompanied by a wide spectrum of clinical symptoms, ranging from transient, benign manifestations such as erythema toxicum neonatorum or naevus simplex to extremely severe, rapidly progressing purpura fulminans with a lethal outcome. A considerable proportion (67%) of the disorders that were seen was the results of the immaturity of the skin and various iatrogenic complications, these factors obviously being strictly intercorrelated.

5.2. Lesions requiring wound management

Most of the skin disorders that occur in NICUs develop as a consequence of the immaturity and vulnerability of the neonatal skin. Despite the novel techniques utilized in neonatal care leading to a significant reduction in neonatal mortality, especially in premature infants, the various diagnostic and therapeutic procedures may also be conductive to iatrogenic damage, skin traumas and wounds. This is the first assessment of the aetiology and frequency of iatrogenic skin injuries and lesions that needed wound management in preterm and term neonates during a relatively long study period.

The most common acquired wound types in NICUs have been demonstrated to involve ES, as a consequence of the removal of adhesive tapes and dressings used to secure life support and monitoring devices, EIs, surgical wounds, thermal and chemical burn injuries, DD and PUs. Data on the overall prevalence of these disorders in hospitalized neonates are lacking. In a prevalence study, Noonan et al. observed that 43% of the infants and children admitted had a wound and/or surgical incision, but most of the wounds needed only nursing observations. In contrast, our study indicated 32
cases among 211 neonates (17%; 17 male, 53.1%; 15 female, 46.9%) in the NICU, i.e. a prevalence of 170 per 1000 infants hospitalized. Most skin injuries observed in our NICU proved to be erosions or superficial ulcers, and healed in a short time without any complications or sequelae following the use of local epithelizing ointments or non-adhesive silicone, foam or hydrogel dressings. Fortunately, we did not detect any worsening in wound healing, even in the more severe cases. Besides the use of modern wound dressings suitable for wound stages, the good efficacy of wound healing in neonates is also a factor contributing to a good prognosis. Naturally, the relatively small number of neonates involved is a limitation of our study.

5.3. Characteristics of wound care in neonates

With the increase in the survival rate of premature neonates in recent years, the skin care and wound management in this special patient group pose an ever greater challenge to practitioners. Skin and wound complications remain a significant source of morbidity and mortality in these vulnerable infants. The clinical practice of wound care in adults cannot be applied directly to neonates in view of the anatomical and physiological differences of their skin. The literature recommends non-adhesive and non-interactive dressing products, such as hydrogels, soft silicone wound contact layers, hydrocolloids, foams, hydrofibres and semipermeable films for routine use. In the daily routine, modern, intelligent dressing products should be used in this special population, as we preferred. Silver-sulfadiazine creams, iodine or ionic silver-containing dressings, which are widely utilized in adults, should
be avoided, especially in preterm neonates. When wounds are superinfected and odorous, extreme care must be taken regarding the systemic absorption of chemical agents used on wounds, and consequently their toxicity as concerns the increased circulation of the wound. Dressing should be gently fixed with gauze or elastic conforming bandages, avoiding adhesive dressing. The frequency of change of dressings should always be determined individually, depending on the wound type and base, the amount of wound exudates, signs of infection and the type of dressing. Swabs always have to be taken from wound exudates for microbiology, and parenteral antibiotics are commenced in accordance with the bacterial sensitivity if the laboratory findings or skin signs are indicative of systemic infection. Dressing changes should be performed under appropriate pain control.

5.4. Iatrogenic skin injuries

The impressive improvement of neonatal care during recent decades has led to a significant improvement in the survival of very low birth weight infants. Neonatal intensive care is a relevant risk factor for the development of iatrogenic cutaneous injuries. An iatrogenic event may be defined as any event that occurs during hospitalization that compromises the safety of the patient, even if the patient is not harmed. The enhanced susceptibility to iatrogenic skin lesions in infants of very low birth weight or in a critical condition is multifactorial. Overall, it may be stated that all diagnostic or therapeutic interventions and manoeuvres can potentially promote iatrogenic skin injuries. The more premature and smaller a neonate, the more immature the organs and the more severe the
developmental abnormalities, the higher the numbers of general problems, infections, essential interventions and procedures.

A wide variety of medical procedures may be utilized during the routine care of neonates in the NICU, including heel prick blood sampling, endotracheal suction, iv cannula insertion, peripheral venous blood sampling, intubation, venous long line insertion, peripheral arterial line insertion, umbilical catheter insertion, lumbar puncture and chest drain insertion.

The most common iatrogenic skin injuries include thermal, chemical and ultraviolet burns, ES, EIs, heel prick injuries, PUs, and umbilical and peripheral arterial catheter-related injuries. ES develops most frequently as a consequence of the removal of adhesive tapes and dressings used to secure life support and monitoring devices such as cannulae, tubes, probes, catheters, electrodes and pulse oxymeters. All neonates treated or nourished via iv lines may suffer extravasation injuries. Low peripheral blood flow, long-standing immobilization, artificial ventilation and an insufficient calorie intake can all lead to an increased development of PUs. Moreover, heel prick injuries, the insertion of central lines, iv catheters, thoracic drains, umbilical, central or peripheral vein catheterization or arterial blood sampling may result in scarring or anetoderma of prematurity (monitoring devices may also induce pressure resulting in hypoxaemia). Multiple heel pricks can induce iatrogenic calcinosis cutis of the heels. Other procedures, such as resuscitation, can provoke the development of haematoma, suffusion or maceration, and the use of diaper wipes may result in contact dermatitis.

A significant proportion of the iatrogenic injuries that occur in NICUs results from skin injuries. A majority of these complications are of a minor character, but in severe cases the functional impairment of the epidermal
barrier may result in important physiological consequences and induce significant pain in these fragile and vulnerable premature infants and may lead to prolonged hospitalization. Intensive, prospective surveillance methods are demanded with a heightened awareness of iatrogenesis. Every effort should be made to achieve the prevention or at least the early recognition of iatrogenesis and to devise and adhere to the skin care and wound management guidelines in the NICU with meticulous care.

6. Summary

The survival rate of premature infants has recently increased significantly as a consequence of the advances made in neonatal care. Not only does the immaturity of the lungs or other internal organs pose a significant problem during neonatal intensive care; the immaturity of the skin also results in a number of clinical consequences. These clinical complications are relevant determinants of high morbidity and mortality for preterm infants in the NICU.

The management of dermatological disorders frequently comprises a great challenge to practitioners during neonatal care. The immaturity of the neonatal skin is a significant risk factor in terms of the development of iatrogenic injuries, while impairment of the skin barrier may result in such important physiological consequences. The anatomical and functional characteristics appreciably increase the possibility of the development of skin injuries and wounds, and also significantly influence the wound healing processes in premature and severely ill term neonates. Skin injuries can induce appreciable pain; their treatment requires further interventions and
prolongs the length of hospitalization, and in serious cases, permanent aesthetic and functional complications may occur. The prevention of iatrogenic skin injuries, the careful consideration of risk factors, and the creation of protocols ensuring efficient treatment are therefore indispensable for a further increase in the standard of neonatal intensive care.

The treatment of dermatological disorders emerging during the hospital care of preterm or severely ill neonates is particularly challenging, and it is therefore important to emphasize the role of prevention and early detection. The introduction and application of modern, standardized skin care management strategies can result in significant improvements in the barrier function and in the integrity of the skin, and a decrease in the frequency of iatrogenic injuries, and can therefore increase the overall efficacy of neonatal intensive care. Well-defined, evidence-based, optimized neonatal skin care clinical guidelines for the NICU demand the constant co-operation of well-trained neonatologists, dermatologists, nurses and pharmacists.

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Original articles of the author related to the subject of the thesis


**List of publications of the author not related to the subject of the thesis**


