Review Article

Diagnostic procedures in pediatric dermatology

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Abstract

Diagnostic procedures in pediatric dermatology are different and significantly more challenging than those in adult patients, especially on how to approach the patients. We need to acknowledge that pediatric patients have unique anatomical, physiological, and psychological aspects. Compared to adults, children have smaller procedure area, are less cooperative, and more difficult to understand. For these reasons, we should perform diagnostic procedures on children cautiously. Having extensive knowledge in this field can facilitate us to carry out an ethical, efficient, targeted procedure with less risk. This article reviewed the most appropriate, most comfortable, and least invasive diagnostic procedures for children. Some of the most commonly performed pediatric dermatology procedures highlighted in this article are potassium hydroxide examination, Gram staining examination, acid fast bacilli examination, skin test for allergies, and skin biopsy for children. We also discuss the process of obtaining a written informed consent from the parents who were involved in decision making process and play a crucial role in assisting physicians to calm their children during the diagnostic procedures.

Keywords: children, dermatology, diagnostic procedures

Background

In the field of dermatology and venereology, in addition to the clinical signs and symptoms, diagnosis is also established based on results of diagnostic procedures. Performing various diagnostic procedure is more difficult in children. This is caused by small procedure area, difficulty to cooperate, and inadequate comprehension, leading to bigger role played by the parents. The parents' psychology status, such as anxiety, will greatly influence the child's psychology and the decision made.

In 2015, there were 69 biopsy procedures, 6 skin tests for allergies (5 skin prick tests, 1 patch test), 85 slit skin smear procedures, and 766 skin scraping procedures performed on children at Dermatology and Venereology Clinic, dr. Cipto Mangunkusumo General Hospital.

It is wise to look for less invasive procedures, especially for younger children. Children are more prone to drug toxicity, thus post-procedure instruction should be strict and given in detail to avoid complications. This article reviewed the implementation of pediatric diagnostic procedures, especially the most common procedures conducted at Dermatology and Venereology Clinic.

Approach on pediatric patients

Physician should develop rapport with patients before performing the procedures, especially if the procedures will induce pain or fear on the children. Being friendly is an important characteristic to create comfort when approaching a child. Physician should be honest and try to assure the children.

Babies

Babies will usually cry when being laid down on bed. Gentle touch on a baby's belly will reduce the fear and give a chance to examine the baby quietly. Baby can usually be quiet and relaxed after the local anesthesia starts acting. This is important so
the baby will not move during the procedure, especially skin biopsy procedure. Parents’ cooperation and trust are very important when performing a procedure.3

Children
In general, school aged children are the most difficult to be approached when performing medical procedure. The patient’s trust is very important, thus the trust should have been built since the first consultation.3 Diagnostic procedures which will induce pain should be explain first to the child, although the child might not understand why the procedure should be performed.3,5 Explanation should use a proper language suitable for the child’s age and the child should be able to ask questions. In certain procedures and conditions, children can be provided with opportunity to choose, such as which position is more comfortable or location for the procedure to be performed.5 Physician should encourage and praise them if they are cooperative. Toys, candies, or simple joke can help to calm them. Sometimes, children cannot stay calm due to fear. In that case, sedation can be used as an alternative.3

Adolescents
Performing medical procedures and physical examinations in adolescents can be difficult because at this age, they are usually reluctant to show their body. In that case, physician should show their sympathy, listen for anxiety, ensure confidentiality, and treat them like adults.3 Adolescents tend to be shy to admit pain, especially in front of other people. On the other hand, adolescents may act like children when facing pain. Adolescents can be provided with an option to choose whether they want to be attended by their parents during procedure or not. This autonomy might make them accept the conditions they are facing easier.5 Another thing that should be worried about is whether this procedure can cause cosmetic problem which will affect their social interaction.3

Parents
Parents are usually very worried with their children’s conditions. Their worries can induce fear and worries in their children.3,5 Parents should be informed regarding the importance of the procedure and the potential risks. Furthermore, parents should be assured and asked to sign the informed consent form.5

Informed consent for children
Informed consent is a process of showing effective communication between physician and patient. This process bridges the idea regarding what will or will not be performed on the patient. This informed consent is a statement from patient (or their authorized guardian) containing consent on the medical procedure planned by the physician, after receiving adequate explanation to be able to make decision whether they consent or do not consent to this procedure.7 Principle of autonomy is the basis of this process.7,8

All procedures that will be performed should get consented beforehand. The consent is provided after the patient is provided with the necessary explanation regarding why the medical procedure needs to be performed. There are 2 types of consent, which are written consent and verbal consent.9,10 High risk procedures should be provided with written consent.9,10 The decision to perform this medical procedure should be documented in medical record.9,11

There are two types of informed consent, which are general and specific informed consent. General informed consent is an informed consent taken before history taking, physical examination, and standard prescription (during administration, before entering the clinic). Specific informed consent is a consent taken for certain diagnostic procedures, especially large scale and high risk procedures.12

Some government and professional organizations’ documents, such as the World Health Organization (WHO), Good Clinical Practice, and Declaration of Helsinki, suggest that informed consent for pediatric patient needs “consent dyad” which is parents’ permission and informed assent which is the child’s permission.11 Patient’s autonomy consists of accurate and complete explanation, transparency, as well as informed consent.8 Children cannot sign informed consent; thus, they should be represented by their parents or guardians.8,12 Currently, United Nations (UN) has provided children with the rights to make decision for their own good, although these rights are limited.11 Some of these following terms should be recognized in the concept of informed consent for pediatric patients, which are8,12

a. Proxy consent: adult who receives information and represents the child to sign the informed
b. Informed assent: child’s consent on medical procedure, although the child is neither legally authorized nor competent in providing consent.8

c. Implied consent: if parents bring their child to a physician to be treated or to undergo a procedure, it possibly means that the parents give consent for medical procedures performed on their child.12

Many ethics and legal experts do not approve proxy consent. Informed consent cannot be provided for other people; therefore, currently, “informed permission” and “assent” are more preferred. These processes are started with written informed permission from parents as the child’s guardians.11

Legally, children and adolescents are not considered to be able to make decision because they are not mature and have limited comprehension regarding the medical procedures.7 In Indonesia, based on the laws (constitutional law no. 39 year 1999) about human rights, a child is everyone who is under the age of 18 years old.13 Children are considered as legally incompetent population based on the laws in Indonesia, according to the Article 7 of the Regulation of the Minister of Health of the Republic of Indonesia Number 290/MENKES/PER/III/2008, it is stated that this explanation should be provided to the family or the guardian.9 On the other hand, children also need to be involved in decision making and explained regarding the medical procedure. Legally, children have the rights to receive that information.7,13 The parents’ authorities to provide consent should be used for the best interest of their children.7

Physician explains protocols, facilitates discussion, and provides information suitable with the age, maturity, and psychological status of the children in a supportive environment.5,11 This relates to the law of children’s rights, which states that every child has a right to receive information in accordance with their intellectuality and age.13 Attention from the physician will form closer bond with the child, leading to higher compliance and accurate report regarding the adverse effects of the procedure. The decision-making process is affected mainly by how the physician provides information, condition and the time of information provided. Explanation should be provided right before the procedure is performed.5 Location for providing the information should be conditioned as comfortable as possible and free of noise. Children have limited ability in focusing their attention; therefore, the physician should be patient and must be able to find the right time when the child can focus their attention. For example, the physician should not provide information and perform informed assent when the child is hungry.11

Various methods can be performed to optimize informed consent on children, such as the use of media, honest communication, and simpler form. The availability of third party as a witness or education by a nurse prior to the education by physician also eases this process. Sometimes, parents also have difficulty in decision making. In this case, parents have a choice to give the full authority to the physician to make the decision.11,12 All of these processes should be documented in the medical record by the physician. This document should be ensured to be in accordance with patient’s age.11

There is no specific standard regarding the age of children when they are considered to be able to provide informed assent. Children are considered able to provide informed assent if they are competent to understand the mechanism, risks and benefits of the procedure. The age limit is different in several literatures.5,11,12 Some literatures state that children age 7 years old or older are competent enough; while others state that children under 9 years old are not competent enough to provide assent.11,12

Diagnostic procedures

1. Skin tests
There are various techniques for skin tests and the choice of the test depends on the diagnosis.

a. Skin prick test
There is no age limit for children for skin prick test.14-16 This test is safe and can be performed on babies and children.5,16 Standards of Care Committee of the British Society for Allergy and Clinical Immunology have standard operational procedures for performing skin prick test on children.17 The child can sit on the parent’s lap across the examiner. A pillow is placed between the physician and the patient so the patient can be more relaxed and the arm can be more stable when the skin prick test is performed. Arm is preferred to the back because with this method, eye contact can be maintained and the child can witness the whole process.17 The
space between two skin pricks should not be too close to prevent cross contamination. Skin test can be performed on both lower arms on the volar side if the child’s arms are too small.\(^2\) However, the choice of skin test’s location should be suited with the child’s age, preference, and skin condition. Various distractions can be performed to decrease the anxiety and to increase compliance.\(^1\) The method of reading skin prick test result for pediatric patients is not different from adults.\(^15,16\)

Physician should interpret skin prick test result carefully in pediatric patients, especially in terms of clinical relevance. Positive result does not always mean that the child is allergic to the material. Many children with positive result against certain type of food, have negative result on provocation test. History taking and knowledge regarding the disease are necessary in order to choose a rational test and how to interpret it.\(^19,20\) The cause of this false positive result should also be evaluated, including the presence of dermographism, deeper prick, or irritant reaction.\(^18,21\) Tests against various food allergens without clear history of allergy are not recommended because sensitization often happens without being clinically allergic.\(^19\)

b. Patch test
Patch test is a diagnostic test to determine delayed type hypersensitivity in patients with allergic contact dermatitis. Most authors agree that patch test is safe to be performed on children, but there is no guideline on how early the procedure can be introduced to the children. The key problem is the technical problem due to smaller location for patch test, lots of motion and parents’ reluctance.\(^22,23\)

Mallory et al.\(^24\) suggested several things as follows:

- If the test area is too small, patch test should be performed in several sessions.
- If the test material is detached, the parents should be educated to report it and not to attach it themselves.
- Stronger adhesive can be used but we should be careful of irritation.
- Patch test process should be performed as quick as possible when the child is vulnerable.
- Draw a map of allergen location which will be tested. This process is the same with adult.

- Inform the parents about the procedure and its assessment to optimize the condition of patch test.

Method of the test used for adults is considered safe for children.\(^25\) The tested allergens are placed on Finn chamber\(^®\) fixated by special bandage, then patched on the upper back.\(^3\) The test area is smaller in children, thus in some literatures it was advised to use Finn chamber\(^®\) in children; compared to other types of chamber, Finn chamber\(^®\) is the smallest kit that can be used for patch test.\(^22,23\) Finn chamber\(^®\) has aluminum edge that provides better occlusion and is relatively small size, with surface area of 50 mm\(^2\) for a chamber with diameter of 8 mm.\(^22\) Currently, special unit for pediatric patch test is available, which is IQ Ultimate\(^®\) from Chemotechnique Diagnostics. This unit has some advantages which are elastic, transparent, anti-leak, and water-resistant. This unit is considered ideal for active children and can be used during bathing. Different from Finn chamber\(^®\), this unit does not use aluminum, so it is more comfortable and can reduce the risk of chemical reaction between allergen and aluminum.\(^22,25\) Children and parents should be instructed to keep the material patched dry, stayed on place and away from sunlight.\(^3\)

The criteria and indications for pediatric patch test are the same with adults.\(^25\) Thin-layer rapid use epicutaneous (TRUE) patch test is easier to be performed on smaller children due to shorter preparation time.\(^3,26\) Generally, the standard substances tested are in accordance with European standard series, which can be added with additional allergens depending on the history taking.\(^3,27\) Study by Machovcova\(^28\) used European baseline series patch test with 25 allergens on 218 children and reported that this series of patch test was safe for children and adolescents. Many authors suggest that classic standard series of allergens can be used on children, moreover other series of tests can be added as necessary.\(^22,23,25\) However, several authors limit the types of allergen tested on children.\(^22,27\) This is due to the risk of new sensitization.\(^3,27\) On the other hand, determination of the allergen is also important to prevent skin disorder in children.\(^25\)

Based on the consideration that allergen exposures on children are uncommon compared to adults, and children have narrower
area for patch test, Brasch and Geier\textsuperscript{29} suggested a standard patch test using 16 allergens. This series is less than the simplified international standard series which uses 20 allergens or European standard series by European Society of Contact Dermatitis (ESCD) and European Environment and Contact Dermatitis Research Group (EECDRG) that uses 28 allergens.\textsuperscript{30} Retrospective study by Groupe d’Etudes et de Recherches en Dermato-Allergie (GERDA) in France observed patch tests on 959 children under the age of 15 years old in 1995-1997. Allergens used in this study can be seen in Table 1.\textsuperscript{29} The study proposed to include P-phenylenediamine (PPD), cobalt, chloride, mercapto mix, mercaptobenzo-thiazole, para-tertiary butylphenol (PTBP) resin, and methylchloroisothiazolin as standard allergens because there were reactions in more than 1% tested patients. Other allergens suitable with the patient’s history and environmental exposure should also be tested.\textsuperscript{23,29}

There are many contradictions regarding concentration of allergen for patch test in children. Several authors recommend lower concentration in children, especially for certain allergens, such as nickel, formaldehyde, mercury, potassium dichromate, mercapto-benzothiazole, and thiuram mix.\textsuperscript{3,22,23,27,31} However, current consensus agrees to use the same concentration as adults.\textsuperscript{27} Follicular reaction and/or eczematous reaction are often considered as positive reaction. In fact, this reaction is irritant reaction. This reaction often happens in children aged under 5 years old.\textsuperscript{3,22} Marcussen\textsuperscript{31} reported that epithelial barrier factor was varied between the age of 0-8 years old and the percentage of irritant reaction decreased linear with the children’s age and started to stop at the age of 7-8 years old.

Currently, there is no special standard operational procedure (SOP) for children regarding prick test and patch test at Pediatric Dermatology Clinic in dr. Cipto Mangunkusumo General Hospital as SOP for adults is applied for children as well. If considered necessary, different SOP should be established in order to adjust the procedure for children’s safety and comfort.

<table>
<thead>
<tr>
<th>No.</th>
<th>Agents</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Potassium dichromate</td>
<td>0.5% pet.</td>
</tr>
<tr>
<td>2.</td>
<td>Neomycin</td>
<td>20% pet.</td>
</tr>
<tr>
<td>3.</td>
<td>Thiuram mix</td>
<td>1% pet.</td>
</tr>
<tr>
<td>4.</td>
<td>PPD-free base</td>
<td>1% pet.</td>
</tr>
<tr>
<td>5.</td>
<td>Cobalt chloride</td>
<td>1% pet.</td>
</tr>
<tr>
<td>6.</td>
<td>Formaldehyde</td>
<td>1% aq.</td>
</tr>
<tr>
<td>7.</td>
<td>Colophony (colophonium)</td>
<td>20% pet.</td>
</tr>
<tr>
<td>8.</td>
<td>Balsam of peru (Myroxylon Pereirae)</td>
<td>25% pet.</td>
</tr>
<tr>
<td>9.</td>
<td>Alcohol lanolin</td>
<td>30% pet.</td>
</tr>
<tr>
<td>10.</td>
<td>Mercapto mix</td>
<td>2% pet.</td>
</tr>
<tr>
<td>11.</td>
<td>Paraben mix</td>
<td>16% pet.</td>
</tr>
<tr>
<td>12.</td>
<td>PTBP-FR</td>
<td>1% pet.</td>
</tr>
<tr>
<td>13.</td>
<td>Fragrances mix</td>
<td>8% pet.</td>
</tr>
<tr>
<td>15.</td>
<td>Methyl(chloro)isothiazolinon</td>
<td>0.67% aq.</td>
</tr>
<tr>
<td>16.</td>
<td>Mercaptobenzothiazol</td>
<td>2% pet.</td>
</tr>
</tbody>
</table>

*Adapted from Machovcova\textsuperscript{29}
2. Specimen collection taking in various pediatric skin infections

Specimen collection taking for Gram staining and Tzanck examination is less invasive. The method of specimen collection taking for those examinations in children is the same as adults. Meanwhile, specimen collection taking for superficial mycosis and acid-fast bacilli often causes pain and fear due to the use of scalpel, hence the method of collection and method of pain management will be discussed further. Generally, diagnostic test for skin infection in pediatric patients is not different from adults.¹

a. Specimen collection taking for superficial mycosis

Scalpel
Skin specimen to support diagnosis of superficial mycosis can be used for both direct microscopic examination and fungal culture. Skin specimen collection taking in superficial mycosis on face, neck, armpit, groin, or genital can harm the patients, especially pediatric patients because they seldom stay still.³² Skin scrapping is usually performed using scalpel no. 15, object glass, or Foman knife.¹³³ Foman knife is spatula-like instrument with two edges. This knife is the safest equipment to prevent trauma on skin if the baby moves during scrapping.¹ Specimen collection taking technique using scalpel is considered uncomfortable by some authors and takes relatively more time than other techniques.³⁴ To reduce the possibility of wound, the sharp edge of the scalpel should be placed in the opposite direction of the scrapping direction. Blunt scalpel can also be used to take nail specimen from children suspected to be infected by fungi. The location for scrapping is not different from adult, however, the specimen collection taking should be performed gently and carefully. In addition to the scrapping using scalpel, specimen can also be collected from nail clipping.²⁷

Another device often used for skin scrapping in our hospital is object glass because children are often frightened when they see a scalpel. Ironically, object glasses are sometimes sharper than a blunt scalpel; moreover it has sharp edges and can break easily. Therefore, object glass should be used with caution as skin scraper even though it is considered effective to take adequate amount of sample.

Adhesive band
Specimen collection taking using adhesive band can be an option.³² Adhesive band is usually from vinyl and transparent material.³²,³⁵ Various brands of adhesive band available in Indonesia are 3M®, Daimaru®, Tulip®, Scotch®, etc. The method of use is by pressing the adhesive band over the lesion, remove it, and then the adhesive side is pressed on the microscope object glass. This band can be used later for culture if the specimen is taken with sterile technique.³³ This method can be used for patients with both dermatophytes infection and candida infection.³²,³⁵

The advantages of this technique in diagnosing superficial mycosis are: (1) painless especially in children (2) shorter time and easier (3) reliable result (4) cheaper, no need of disposable scalpel or cover glass (5) the possibility of storing the specimen to be examined in the future (6) no knife is used which usually scare the children.³²,³³,³⁴,³⁵ This method is considered superior for specimen collection taking in patients with tinea capitis if the scales are few.³³ Other experts suggested that use of adhesive band would make the physician try to take more specimen. The surface area to be taken is generally wider than by scrapping, so the specimen can be abundant and the result is more reliable.³⁵ The use of adhesive is considered to increase patient’s compliance. This technique is suitable to be used for daily clinical practice.³²

The disadvantage of this technique is that the adhesive band is often insufficient to take specimen from wet lesion and lesions on hands or feet. This technique is also less suitable for specimen collection taking from lesions on head and nail.³²

Brush and comb
Hubbard et al.³⁴ studied specimen collection taking from 70 pediatric patients with tinea capitis using brush and compared it to scrapping method. Specimen collection taking was performed by brushing in circular motion slowly on the area with scales and the edge of alopecia plaques using sterile brush. This brush was later pressed on the culture media and the brush was thrown away. This study showed that specimen collection taking using brush resulted in culture with faster growth compared to the
scraping method. Brush was considered effective and provided shorter time to diagnosis tinea capitis. Comb could also be used with the same technique.\textsuperscript{33}

**Cotton swab**

Another study by Friedlander et al.\textsuperscript{36} proved that the use of cotton swab is similarly effective compared to brush in the case of tinea capitis. Both brush and cotton swab resulted in 100% positive cultures.\textsuperscript{36} Specimen collection taking for candidiasis case in children, both oral candidiasis or lesion at external urethra orifice or vulvar, usually uses cotton swab technique.\textsuperscript{1}

b. **Acid-fast bacilli**

Borderline tuberculoid (BT) is a type of leprosy, commonly found in children which accounts for 55-78.8% of leprosy cases. Borderline lepromatous (BL) type is found in approximately 7.8% of pediatric patients and polar lepromatous (LL) type is found in 1.6-4.9% of pediatric patients.\textsuperscript{37} Acid fast bacilli (AFB) and histopathology examination are advised to be performed in children suspected with leprosy. Histopathology examination is often advised for pediatric patients, especially in non-endemic areas, to exclude the possibility of other diseases mimicking leprosy.\textsuperscript{37}

Slit skin smear with Ziehl Nielsen staining to find AFB is the standard technique used to estimate the amount of Mycobacterium leprae in the skin lesions. However, slit skin smear has limitation in establishing the diagnosis of leprosy. This is because most of the leprosy in children is the tuberculoid type.\textsuperscript{37}

In the guideline of slit skin smear procedure by leprosy national program in The United States, there are some methods to manage pain during the procedure.\textsuperscript{37} The methods are by pinching skin slowly or if it is not possible, compressing using gloves. Local anesthesia is usually not necessary, however, if the lesion is not anesthetic or hypoesthetic, 1% xylocaine spray or chloride spray can be used.\textsuperscript{37}

The number of location for AFB examination was different in each literature. This usually depends on hospital’s policy. Based on the SOP in the Dermatology and Venereology Department of dr. Cipto Mangunkusumo General Hospital, the minimum number of locations for AFB examination are three. The location and number of specimen collection taking are not different from adults.\textsuperscript{38}

On daily practice in dr. Cipto Mangunkusumo General Hospital, at least one lesion (which is the most suspicious lesion) is taken for biopsy to make it less invasive for children. Furthermore, if a lesion most likely will require biopsy, the child may not undergo the slit skin smear test and only undergo the biopsy instead.

3. **Skin biopsy in children**

Before performing procedure, the physician should ask whether the child is allergic to topical antibiotics, antiseptic, local anesthesia, and wound dressings. It should also be asked if the child suffers from bleeding disorder or is on medication affecting hemostasis. The determination of biopsy location is similar to adult. It should be taken into account the possibility of hypertrophic scar on deltoid and chest area as well as slower healing time on bony area.\textsuperscript{39}

Parents or caregivers can attend their child during procedure and help distracting the child’s attention.\textsuperscript{39} The child’s position should be as comfortable as possible. Smaller children or babies can lie down or sleep on their parent's lap.\textsuperscript{39}

Baby’s skin is different from adult’s skin. Skin disorder, healing process, the possibility of scar tissue, and allergy in children can be different from adult. Many differences in baby’s skin can increase the risk of systemic toxicity due to use of topical medications.\textsuperscript{40} Although skin biopsy is a minor surgical procedure, it should be remembered that this would feel like a major procedure for children and their parents. Physician should provide information and explanation in detail about sampling location, the technique used, possible complications, and optimal method in collecting the specimen.\textsuperscript{39}

The process of informing the patient about biopsy procedure must be comprehensive. However, in practice, biopsy in children are easier said than done and more challenging in practice. Not all children will have good understanding after they hear long explanations and sometimes they are still not cooperative. Depending on the circumstances, usually on non-emergency cases, biopsy may be delayed until the child is ready.
a. Local anesthesia in pediatric dermatology procedure

Before starting the procedure, local anesthesia is usually used. In several cases, general anesthesia may be used. Consideration for general anesthesia technique depends on many things, such as the need for absolute immobilization, duration of the procedure, patient’s general condition, etc.

Topical anesthesia

Topical anesthesia can be applied on the biopsy location before the procedure. A study found that patch anesthesia was more effective than placebo in managing pain on the site of injection. Special attention needs to be given for children with history of atopy when using this material. Topical anesthesia or patch anesthesia should be cleaned, washed and dried after we are assured that the child’s skin is anesthetized.

The choice of local anesthetic agent depends on location, desired onset, and duration of the anesthesia needed. Before using the topical anesthesia, there are several steps to be performed, which are:
- History taking, including history of previous local anesthesia and the adverse effects
- Documenting drug dosage, drug delivery time and allergic reaction
- Taking informed consent from the parents
- Explaining to the child regarding the topical anesthesia which will be used

Mixed topical anesthesia

Mixed topical anesthesia which are usually used are 2.5% lidocaine and 2.5% prilocaine with oil in water emulsion. These materials are often used in babies and considered to be quite safe if used carefully. This anesthesia is very useful to reduce pain during infiltration of local anesthesia and pain caused by the superficial dermatology procedure. The cream induces anesthesia until maximum depth of 5 mm, so it cannot be used for excision or punch biopsy. The degree, depth, and onset of anesthesia correlate to the duration of use. The recommended dose is different based on age, presented in Table 2.

The use of this mixed anesthesia in babies aged under 6-9 months old should be careful due to risk of prilocaine-induced met-hemoglobinemia. In general, the use of this mixed anesthesia is usually well tolerated. In smaller babies, it is advised to use it in a short time and in less amount, which is less than two grams. Comorbidities that can increase the risk of methemoglobinemia are hemoglobinopathy, glucose 6-phosphate dehydrogenase deficiency (G6PD), exposure against aniline dyes, and oxidant. Drugs which can induce and increase the risk of methemoglobinemia are sulfonamide, acetaminophen, benzocaine, dapsone, phenobarbital, antimalaria, and phenytoin. The use of this anesthesia in children aged under 3 months old is not recommended if they are using those drugs. The local side effects of this drug are transient blanching, erythema, eye irritation, edema, and dermatitis. Considering the possible local side effects, this drug should be used carefully before biopsy because it can disrupt histologic interpretation for certain diagnoses. Petechial or purpuric eruption had also been reported after the use of this material in neonates, children, and adults. The eruption did not correlate with the dose nor the duration of use. This eruption happened during or immediately after the drug was applied. The purpura would resolve in few days.

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Table 2. Recommended maximum dose of mixed topical anesthesia for neonates, infants, and children

<table>
<thead>
<tr>
<th>Age</th>
<th>Maximum Dose (g)</th>
<th>Maximum Skin Area (cm²)</th>
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</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>3-12 months</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>1-5 years</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>6-11 years</td>
<td>20</td>
<td>200</td>
</tr>
</tbody>
</table>

*Adapted from Chang

J Gen Proced Dermatol Venereol Indones. 2018;3(1):34-45. 41
**Topical lidocaine**

Lidocaine is available in the form of topical preparation, i.e. 4% liposomal lidocaine. Like other topical anesthesia, this material is recommended to be used in a short time and limited amount in children to avoid toxicity. The anesthetic is free from risk of methemoglobinemia because it does not contain prilocaine. Topical anesthesia can be used before local infiltration anesthesia.

**Infiltration anesthesia**

The most common infiltration anesthesia used is lidocaine. In many skin surgeries, the recommended anesthesia is 1% lidocaine with epinephrine. The advantages of this combination are lower risk of allergy, faster onset, and minimal bleeding. The preparation available on the market usually contains 1% lidocaine (10 mg/mL) and 1:100,000 epinephrine.

The operator preparation steps in performing local infiltration in children are:
- History taking, including history of previous local anesthesia and the adverse effects
- Measuring body weight to determine the dose
- Taking informed consent from the parents
- Explaining the infiltration technique and the possible uncomfortable sensation
- Documenting the technique in detail in medical record
- Documenting the adverse effects due to the technique being used
- Operator should be competent in performing cardiopulmonary resuscitation (CPR)

Subcutaneous infiltration will give stinging or burning sensation. This can be reduced by mixing 1 mL NaHCO₃ with 9 mL lidocaine (buffering) and injecting perpendicular to the skin. Furthermore, subcutaneous infiltration is performed using spider-web technique and lifting the skin fold to ensure that the subcutaneous injection enters the subcutaneous tissue. The smallest needle should be used in children. In general, 0.5 inches 30 G needle is used for children. Several other methods to manage the pain caused by injection are by warming the lidocaine and storing the needle at 27°C.

The half time of lidocaine in neonates is longer than adults. The volume distribution of lidocaine in neonates is twice than adults. In neonates, lidocaine binding to protein is only 20% compared to 60-70% in adults. The higher bioavailability of lidocaine in neonates makes them more susceptible to toxicities compared to adults.

In general, lidocaine has lower systemic toxicity. Some possible toxic reactions are cardiovascular symptoms, central nervous system symptoms, and even death. The central nervous system toxicity might start with agitation, leading to seizure, unconsciousness, and breathing depression. Lidocaine toxicity rarely happens if the dose is calculated correctly. The maximum recommended dose for 1% lidocaine without epinephrine is 4.5 mg/kg and the maximum dose for baby weighed 5 kg is 2.3 mL. The drug dose and volume should be confirmed. In our hospital, local anesthesia is routinely used in surgery and skin biopsy. Currently, there has been no adverse effect reported with the use of local anesthesia in children in the dermatology outpatient clinic. General anesthesia was used if necessary, in collaboration with the Anesthesiology Department.

**b. Skin biopsy technique**

There are various techniques of skin biopsy and these depend on the lesion, location and the physician’s skill. Various techniques that can be chosen are shave biopsy, saucerization, incision, excision, or wedge biopsy. Basically, the least invasive procedure should be chosen, however, it should be suited with the diagnosis.

Shave biopsy is a fast and easy technique without the need of suture. The elevated lesion on the surface or having limited pathology in epidermis are suitable for shave biopsy technique. Saucerization biopsy is ideal for vesiculobullous disease and epidermal neoplasm. If all of the skin layers are needed for analysis, punch biopsy is the ideal procedure for diagnosis. This technique can also be used for removing small lesion. This biopsy provides better result cosmetically compared to shave biopsy. Punch biopsy can heal with secondary intention but a section wider than 3 mm is better to be closed with 1 or 2 sutures. Incisional and excisional biopsy can be the technique of choice if more specimens are needed, i.e. for
culture, histopathology, immunofluorescence, electron microscope, in cases of inflammatory disorder affecting panniculus, and larger tumor.39

The wound dressing should not be too sticky. Immunocompromised children should be given topical antibiotic applied after hemostasis and 48 hours after the suture is removed. The biopsy location should be let dry and should not be touched for 48 hours. Written instruction regarding wound care after biopsy should be provided and explained to the parents.39

Even though they are rare, complications can happen during skin biopsy such as bleeding, injection reaction, allergy, and irritation (towards topical antibiotic, wound dressing, and bandage). Dermatologic procedures performed in premature babies can result in scar tissue. Scar tissue can occur from peeled off skin due to adhesive. Atrophic scar tissue called "anetoderma of prematurity" might happen in premature babies.43

Conclusion

Diagnostic procedures in pediatric dermatology are different and significantly more challenging than adult patients, especially in how to approach them. We need to acknowledge that pediatric patients have unique anatomical, physiological and psychological aspects. Compared to adults, children have smaller procedure area, are less cooperative and are more difficult to understand. For these reasons, we should be more cautious in performing diagnostic procedures in children.

The process of written informed consent before the diagnostic procedure performed in children is different from adult. Consent can be represented by the guardians or parents, nevertheless children also need to be explained about the procedure in accordance with their understanding. Daily dermatology procedures performed in dermatology and venereology clinic are microscopic examination with potassium hydroxide smear, Gram staining examination, slit skin smear test, allergy skin test (patch test and prick test), and skin biopsy for children. All dermatologic procedures in children are better performed under the supervision of pediatric dermatology division to optimize the approach and documentation. Procedures in children should be dynamic. Considering most of the procedures do not have specific standard operating procedures for children, physician should adjust the procedures for children to give optimal result with the highest level of comfort for them. The choice of procedure technique should be the least invasive, with minimal pain, and comfortable for children. Baby’s and child’s skin is usually thinner, leading to the increased risk of toxicity caused by topical/infiltration anesthetic agents. Parents’ cooperation and trust are very important in performing the procedure.

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