

Rectal Routes as an Alternative for Drugs Administration in Children

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Abstract: Giving drugs to children has their own difficulties due to several conditions that make children unwilling to take medicine. Although oral administration of the drug is the most convenient route of choice, there are some conditions that require other drug delivery. The rectal route of drug administration is often used in children for several conditions, such as fever and seizures. In addition, rectal drug administration can be an alternative route of drug administration when the child's condition makes it impossible to get the drug orally or intravenously. The rectal environment is relatively stable and constant that gave benefit to drug absorption. There are some conditions that will be more favorable with rectal administration, but there are some conditions that do not allow rectal administration of the drug. In short, rectal administration route of drugs may be the right choice depending on the type of drug and the patient's clinical condition.

Keywords: rectal drugs, rectal paracetamol, rectal diazepam, children

1. Introduction

The most convenient route for drug administration is the oral route. However, there are several conditions that cause difficulty in administering drugs via oral access. This can be due to several things that are not possible, either due to clinical reasons or pharmacology of the drugs[1]. Administration of drugs through the rectum can be considered as an access option, especially in children. Rectal routes administration of drugs can be used for both local and systemic drugs[2].

2. Physiological and Pharmacological

Rectum is the final part of the colon, start from the sigmoid colon to the anal canal. Rectum has a function as a transport system or temporary storage site in the defecation process. Rectum involved minimally in water absorption and electrolyte[3]. This is related to fewer villi and micro villi in the rectum so that the absorbing surface area of the rectum is smaller[4]. The main anatomy difference of the rectum between adults and children is its size, where the length of the rectum in adults is 15-20 cm with a surface area of 200-400cm², whereas in children it is smaller depending on the child's age. In children aged 1 month, the length of the rectum is about 3cm with a surface area of 18 cm². Children aged 10 years have a rectum with a length of 12 cm and a surface area of 230 cm². The rectum will start functioning after the baby first feed orally[5]. The environment in the rectum is relatively constant and static in comparison to other parts of the gastrointestinal tract.[5]

There are several factors that influence the rectal route drugs absorption which are drugs form, drug concentration, length of the rectal catheter, presence of feces in the rectum, pH of the rectum, retention of drugs in the rectum, and differences in blood flow based on the rectosigmoid region[1].

Rectal region drain by rectal veins or hemorrhoidal veins and lymphatic vessels[6]. Veins in the distal rectum consist of superior hemorrhoid veins that flowing to the inferior

mesenteric. There is also a portal system in the middle and inferior hemorrhoid veins which enters systemic venous circulation through the internal iliac veins. This anatomy affects the rate of drug absorption when it is absorbed in the distal rectum because it does not need to be metabolized in the liver first before reach systemic circulation. Meanwhile, if drug absorption occurs in the proximal rectum, the drug will be absorbed through the superior rectal vein and will pass through the portal vein, so that the drug will be metabolized first in the liver. Therefore, the location where the drug is absorbed in the rectum is very important, especially for drugs that have a high hepatic extraction ratio[1],[4]. This rectal route can be useful for drugs that undergo high hepatic first-pass metabolism, drugs that absorb in limited amount in the upper gastrointestinal tract, or unstable in the gastrointestinal tract. Besides, drugs that can cause stomach irritation may be considered[2].

Apart from the veins, there is also a lymphatic system that drains the rectum. Although its function is not completely known with certainty in drug absorption, several studies state that this lymphatic system contributes to the absorption of highly lipophilic drugs[5],[6]. Based on this, administering drugs in the distal rectum area will help the absorption of the drugs, although there are things that need to be considered if the drug administration is too distal because it's expulsion will be occur easily so that it will reduce the absorption level of the drug and cause difficulty in estimating the amount of drugs that needs to be given back to achieve the desired effect [1].

The environment in the rectum is relatively stable and constant compare to the other parts of the gastrointestinal tract[5]. There are around 1-3 ml fluid in the rectum and have a neutral pH of 7-8, with a minimal buffering capacity[6]. Rectum pH in children still needs further investigation, but based on the research the mean rectal pH was reported 9,6 with a range in rectal pH 7,2-12,1. The mean rectal pH of well neonates is 6.47 which significantly lower than older infants (>28 days)[2]. Rectal pH determines drug absorption by its effect on drug ionization. The higher

the lipid solubility of the drug in the non-ionic form, the more it passes through the biological membrane. Drugs with pKa close to the physiological range are well absorbed through the rectal mucosa of the child [1].

3. Advantages

Rectal route drug administration can be used in various conditions, such as for pain, fever, nausea and vomiting, migraines, allergies, and sedation. Rectal route drugs tend to have cheaper production costs so it can help people in rural area and developing countries. Moreover, no special technique is needed to administer the drugs so it can be done by any people, even though they are not well-trained [2]. It is also less invasive and less painful compared to the intravenous route administration. Rectal drugs can be the drug of choice for children when they can't take any oral drug, due to nausea, vomiting, or pre- or post-operation. Rectal drug administration is very helpful in an emergency condition for children, such as when they have seizures or are unconscious [5].

Sometimes, oral drugs can deliver an unpleasant taste for the children that makes it hard to take. Besides that, orally drug administration can cause gastric irritation and the drug can go through high first pass drug elimination processes in intestine and/or liver. Furthermore, there are factors that influence the environment in gastrointestinal tract that can also affect the stability, solubility, and permeability of drugs, such as gastric pH, gastrointestinal transit time, gastrointestinal mucus, and metabolism through enzymatic or microbial degradation[2,7]. Therefore, the rectal route for drug delivery can be an alternative choice for drugs with poor stability, solubility, or permeability following oral administration[2]. The latest researches reported trial for vaccination through rectal route, for example are tuberculosis vaccine and herpes vaccination that showed good results. But, there is still no further evidence-based on how if the vaccine administered to humans [8].

4. Disadvantages

There are several considerations in administering drugs through rectal access, one of which is cultural issues and/or potential for discomfort or leakage[2]. When compared to oral drugs administration, rectal drugs administration is more uncomfortable due to pain, especially when the child is fighting back during the process. In addition, not all drugs are available in rectal dosage form and there are still few clinical conditions that can be treated with rectal drugs[2]. In some children, rectal mucosal irritation may occur. Use of the drug rectally in premature infants must be very careful because it can cause torn of the rectal lining which can lead to infection. Based on that reason, then rectal route drugs should not be given to immunosuppressed patients because it can cause abscesses with only minimal trauma [1]. In addition, the right position to obtain maximum drug absorption cannot be ascertained if it is given by poorly trained health personnel. We also cannot confirm that there is no stool in the rectal at the time of administration, as the presence of feces can make the drug easier to expulsion [5].

5. Common drugs administered rectally in children

1) Diazepam

Intravenous diazepam is a drug of choice in the treatment for acute seizures in both children and adults. The difficulties to find vein access in a convulsive patient is one of the most faced obstacles that can delay the drug administration. Oral administration of diazepam is also impossible to be given when a patient, especially children, is convulsive. In this condition, the rectal route drug administration can be very useful and the best choice to treat acute seizure.

Rectal diazepam was effective to treat 80% of cases of seizure. In one prospective study in children, rectal diazepam was shown to be effective in up to 96% of seizures when given within 15 minutes of onset. After 15 minutes of onset, the effectiveness reduces to 57%[1],[9]. Peak serum levels will be reached within 5-45 minutes with a bioavailability of 80-100%, comparable to intravenous diazepam administration. Diazepam levels in the blood will vary [10]. Rectal administration of diazepam solution leads to rapid absorption with peak plasma levels within 10 minutes[11].

The best distance for drug administration so as to have the best absorption rate is at a distance of 4-6 cm from the anus to prevent metabolism in the liver before reaching the systemic circulation[1]. The dosage of rectal diazepam for children with a seizure is 5 mg for children with body weight below 12 kg and 10 mg for children with bodyweight more than 12 kg[12]. Rectal diazepam has almost the same side effects as intravenous diazepam[13].

2) Paracetamol

Paracetamol is a drug that is very often used in the management of fever and pain. In some patients, especially children, many healthcare providers give paracetamol rectally if the fever does not tend to reduce after oral paracetamol administration. Some research concluded that there is no significant effect between oral and rectal administration of paracetamol [2],[13],[14],[15],[16]

The low effectiveness of rectal paracetamol is because paracetamol can be absorbed quickly in the intestine that makes oral administration is a very good choice of drug route administration, both in syrup or tablet preparation, and can provide a good outcome. Other than that, rectal paracetamol tends to be absorbed more slowly or not completely absorb, resulting in significant variations in peak levels for each patient and not achieving the serum therapeutic levels required (10-20mg/dl) for antipyretic or analgesic effects[1].

6. Conclusion

Rectal drug administration is a very useful alternative of drug administration route whenever oral drug administration

can not be given due to certain conditions. A good selection of drugs is also important. It is necessary to consider what kind of drug is better given rectally which can provide better benefits to the patient.

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Author Profile



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