ROLE OF VOSORITIDE DRUG ON CHILDREN’S WITH ACHONDROPLASIA
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Abstract
Achondroplasia is a genetic condition with an autosomal dominant inheritance pattern. It is caused by detrimental heterozygous FGFR3 gene mutations. Gain-of-function mutations in the FGFR3 gene impair chondrocyte differentiation and proliferation, which has a negative impact on the formation of new bone. Vosoritide, also known as voxzogo, is the first pharmacological intervention to receive approval for the treatment of achondroplasia. This therapeutic agent has been sanctioned for administration via at-home injections, which are to be performed under the supervision of a proficient nurse.

Keywords: Achondroplasia ; Vosoritide ; Metabolism ; Dosage.

Introduction
The most commonly observed form of dwarfism is known as achondroplasia. Detrimental heterozygous mutations in the FGFR3 gene are the cause of it. This variant affects the endochondral ossification process and has long-term effects. Achondroplasia is the most often observed skeletal defect, affecting around 1 in every 20,000 infants [1]. Clinical indicators of achondroplasia include small height, abnormally short limbs, midfacial retrusion, frontal bossing in macrocephaly, small fingers, trident-shaped hands, and hypermobility in joints [2]. Frequently reported sequelae include foramen magnum stenosis, delays in motor milestones, recurrent ear infections, auditory impairments, sleep apnea, dental crowding, and spine stenosis [3]. Pain, particularly in the lower extremities, articulations, and spinal region, is a frequently observed symptom. Furthermore, it is worth noting that older children who struggle with diminished endurance and obesity may also exhibit a higher body weight. The aforementioned symptoms have a significant impact on the physical, social, and emotional development of children, hence hindering their ability to actively engage in classroom activities, maintain pace with their classmates, and engage in self-care [4–8]. As a consequence of these challenges, a considerable number of children require assistance or specialized tools to successfully accomplish mundane activities, often resulting in adverse social and emotional consequences. After receiving an achondroplasia diagnosis, a kid may feel self-conscious about their physical traits and become upset by unwanted attention, stigma, or bullying [2]. Additionally, they may perceive life to be more challenging for them in a broader sense [3]. Parents and children exhibit remarkable resilience, and a significant number demonstrate heightened levels of empathy towards individuals who receive encouragement and support from a positive peer network [5].

Developed gross motor skills
Compared to other children, infants with achondroplasia are likely to experience a delay in the development of their gross motor skills. Extra back and neck extensor strength is needed to balance a large head on a tiny, hypermobile neck, which frequently causes a delay in gaining head control. Since most achondroplasia newborns are hypotonic as well, gaining strength and control takes considerably longer. The current spinal deformity treatment significantly delays independent and upright sitting, and it also delays gross motor development. When they are young, children with achondroplasia also use unusual techniques of independent mobility, frequently as a result of their shorter limbs, and do...
not follow “normal” developmental progression. Children with achondroplasia, for instance, hardly ever play with their feet because their shorter limbs prevent them from doing so [9], regarded as being within typical ranges for these kids:

- By five months, able to lift head up when prone.
- Able to roll after seven months.
- Start to a standing position around the age of 16 months.
- Transition to sitting independently by 17 months.
- 19-month-olds can walk holding hands.
- At 20 months, be able to stand alone.

By 23 months, a child can walk alone [9].

Vosoritide represents the inaugural pharmaceutical intervention sanctioned for the management of achondroplasia, and it is amenable to daily administration by a proficient carer within the confines of the patient’s residence [10].

The method of action

Vosoritide, is known as voxzogo, in the treatment of young children with open epiphyses and achondroplasia. This medication stimulates linear growth and is categorized as an analog of the C-type natriuretic peptide [11].

![Figure 1: The mechanism of action of the Vosoritide drug.](image)

Table 1: presents the single dosage volumes in relation to body weight.

<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Voszogo 0.4 mg diluent (water for injections): 0.5 ml concentration: 0.8 mg/ml</th>
<th>Voszogo 0.56 mg diluent (water for injections): 0.7 ml concentration: 0.8 mg/ml</th>
<th>Voszogo 1.2 mg diluent (water for injections): 0.6 ml concentration: 2 mg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-11</td>
<td>0.30 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>12-16</td>
<td>0.30 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>17-21</td>
<td>0.35 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>22-32</td>
<td>0.35 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>33-43</td>
<td>0.35 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>44-59</td>
<td>0.35 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>60-89</td>
<td>0.35 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
<tr>
<td>≥ 90</td>
<td>0.35 ml</td>
<td>0.40 ml</td>
<td>0.5 mg/ml</td>
</tr>
</tbody>
</table>

Metabolism

It is expected that catabolic pathways will metabolize vosoritide and break it down into amino acids and small peptide fragments. [13].
Container nature and contents

- 0.4 mg of vosoritide powder and injectable diluent

**Powder**
Glass vial with a rubber (bromobutyl) stopper and a white flip-top, 2 mL.

**Diluent**
Glass syringe that has been pre-filled with 0.5 mL of water for injections, a bromobutyl plunger, with a tamper-evident seal and luer lock tip cap.

- For injection, powdered vosoritide 0.56 mg with diluent

**Powder**
Glass vial with a 2 mL capacity, a pink flip cap, and a bromobutyl rubber stopper.

**Diluent**
Glass syringe that has been pre-filled with 0.7 mL of water for injections, together with bromobutyl plungers with a tamper-evident seal and luer lock on the tip cap [13].

- 1.2 mg of vosoritide in powder form with injection diluents.

**Powder**
Glass vial with a rubber (bromobutyl) stopper and a gray flip cap, 2 mL.

**Diluent**
Glass syringe that is pre-filled with 0.6 mL of water for injections, has bromobutyl plungers, with a tamper-evident seal and luer lock on the tip cap.

- Only the subcutaneous (fatty) layer beneath the skin should be injected with voxzogo:
  - Avoid syringing through clothing.
  - Avoid using the same injection site more than twice in a succession.
  - Avoid injecting into painful, bruised, red, stiff, or scarred skin. It is suggested to inject in the following locations:
    - The backs of the arms
    - Legs
    - Abdomen (at the belly button, 5 centimeters)
    - Buttocks [13], as shown in (Figure 2).

**Figure 2:** Recommended locations for injection.

**Conclusion**

- The strong intra- and inter-observer agreement (ICC=0.72) of the Foramen Magnum Score for Achondroplasia is comparable to the ICC of other scoring systems used in clinical settings. It is crucial to use clinical results to prospectively validate the score.

- Each physical examination of these kids must include a check for internal tibial torsion and/or bowing, with an immediate orthopedic referral necessary if there are any issues.

- Indications for surgery in these kids are typically hard to pinpoint; however, they could include abnormal alignment, changes in gait (lateral thrust), or the onset of knee or leg pain.

- Hemiepiphysiodesis or the tibial-fibular osteotomies with or without femoral osteotomies are effective treatments for people with progressive and symptomatic leg bending.

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**Conflict of Interest**
No Conflict of Interest

**Inform Consent**
Each patients has Consent writing for study

**Ethical Statement**
Study Reflections ethical statement

**Author Contribution**
All authors participate in the work

**References**