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Treatment with Propranolol for Infantile Hemangioma is Less Toxic but Lasts Longer than Treatment with Corticosteroids

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Abstract

Background: The most frequent benign, self-limiting tumour in children is infantile hemangioma. Hemangiomas that impede critical structures or cause considerable deformity are treated. Corticosteroids have always been the preferred medical treatment. Propranolol, on the other hand, has been widely accepted as an effective pharmaceutical treatment for infantile hemangioma since 2008. There are presently no published data on propranolol's long-term negative effects.

Objective: The purpose of this study was to look at the long-term effects of propranolol and corticosteroids on anthropometric parameters (height, BMI) and blood pressure in children.

Methods: Between October 2007 and February 2012, the authors conducted a prospective database analysis of all infantile hemangioma patient visits to the pediatric vascular abnormalities clinic at the authors' institution. Anthropometric (height and BMI) and blood pressure measurements were examined.

Results: A total of 290 visits to the pediatric vascular abnormalities clinic (119 individuals) were examined. 18 of the patients were treated medically, and their anthropometry was measured. Patients using corticosteroids had a substantially higher BMI percentile (P=0.0039). Treatment with corticosteroids also resulted in a significant reduction in height percentile (P=0.0078). Anthropometric parameters in children treated with propranolol did not cross percentiles. The propranolol group had a substantial drop in systolic blood pressure (P=0.03), although no hypotensive values were detected. Patients who administered propranolol had a considerably longer median treatment duration (372 days *vs.* 133 days; P=0.0033).

Conclusion: Propranolol, when used to treat infantile vascular anomalies, does not have the same negative effects on patient anthropometry as corticosteroids, although it does require a longer treatment period.

Keywords: Hemangioma; Multidisciplinary clinic; Prednisolone; Prednisone; Propranolol; Surgical treatment

Introduction

Hemangioma or vascular malformation is the term used to describe the vast majority of vascular malformations that occur in children and infants [1]. The most frequent benign vascular abnormality seen in infants is Infantile Hemangiomas (IHs), which are characterized by proliferating endothelial cells. They usually have a quick proliferating phase a few weeks after birth, followed by a period of quiescence, and finally involution [2]. The majority of hemangiomas do not require treatment due to their unique natural history. For lesions that endanger critical function or are markedly deforming, pharmacological therapy with corticosteroids or interferon-alpha-2a is recommended. More recently, the creation of multidisciplinary clinics and the introduction of the beta-blocker propranolol as a treatment alternative have had a substantial impact on the management of IHs. A multidisciplinary clinic offers a number of benefits, including improved communication among care providers, more precise and protocolized patient data collection, and additional treatment options and coordination of surgical and nonsurgical techniques [3]. Our interdisciplinary vascular malformation clinic includes a nurse, a skilled photographer, two pediatricians, and a plastic surgeon. When the patient is assessed, the customary one-on-one approach is maintained. If necessary, the staff will provide therapeutic options. We started the clinic when propranolol was first given as a new therapeutic option, and we wanted to see how it worked in a multidisciplinary context.

Vascular Abnormality

The study was approved by Western University's ethics review board in London, Ontario. All patients who visited the vascular abnormality clinic at the London health sciences center's children's hospital were included in the study. Aside from clinical and descriptive epidemiological data, anthropometric measurements such as weight, height, and chronological age were gathered as part of standard clinical practise for patients attending the various clinics. The study required all staff who took height and weight measures to be trained. Measurements were taken twice, and if there were any discrepancies, they were repeated. The average was calculated. For all patients, the most recent NHANES III database (1999 to 2002) was used. The BMI was computed by dividing the weight (kg) by the square of height. Due to the unavailability of reference intervals for newborns, BMI values were not converted into age-independent z-scores for the study.

An automated oscillometric equipment (Dinamap, USA) was used to monitor blood pressure in the right arm while resting and seated, with the cuff covering two-thirds of the upper arm and the bladder enclosing 80% and 100% of the upper arm circumference. Because some patients only had two readings, the second reading was used for analysis. The 95th percentile for age, sex, and height from the fourth report was used to compute the casual BP percentile. The normative values for 17-year-old children were utilised for youngsters between the ages of 17 and 18 [4].

For these computations, the computer tool stat growth charts for iPhone (Apple, USA) (Austin Physician Productivity, USA) was employed.

At each visit, the size of the hemangioma was measured in addition to anthropometry. All parents were educated on the signs and symptoms of propranolol and prednisone side effects (hypoglycemia, hyperglycemia, limb cyanosis). At each visit, they were asked to report on these.

Anthropometric Measurements

Data was entered into a spreadsheet (Excel, Microsoft Corporation, USA) for Mac version 14.3.1 (Apple, USA), and graph pad prism for Mac version 5.0 was used to analyze it (GraphPad, USA). The digesting and Pearson omnibus test was used to check for normal distribution in continuous numerical variables. Data that were normally distributed were reported as mean SD, and the Student's t test was used to compare them. Data that were not normally distributed were expressed as median and interquartile range using the 50^{th} percentile (25^{th} percentile, 75^{th} percentile) format, with the range being stated on occasion. Because treatment duration varied, the change in height percentile per month was determined for each group (controls, propranolol, and corticosteroids). The Wilcoxon signed-rank test was used to compare the mean monthly change in height percentile to a theoretical median of zero. The calculation and analysis of change in BMI and systolic BP percentile per month were then repeated.

The current study was a retrospective examination of data from a new multidisciplinary vascular abnormality clinic in a single tertiary care centre that had been collected prospectively. A substantial percentage of patients only came to the clinic once to get a second opinion. The vast majority of patients were not treated medically or surgically. Given the nature of hemangiomas, this was to be expected [5]. The proportion of patients who got medical care versus surgical care was somewhat skewed toward medical care. Although there was a change over time as additional data for propranolol became available, a similar number of individuals received corticosteroids and propranolol. Corticosteroid therapy, not surprisingly, had a significant detrimental effect on height and a rise in BMI.

There was also a rise in blood pressure, albeit it was not statistically significant. Propranolol therapy, on the other hand, had no effect on height or BMI but did result in a small but statistically significant reduction in blood pressure. There were no hypotensive values found. The duration of propranolol medication was much longer.

Propranolol, a beta-blocker, has been found to be useful in the treatment of IH since 2008. In hemangiomas, it is thought to constrict existing blood vessels while also inhibiting future vascular growth [6-9]. It inhibits the release of vascular endothelial growth factor and fibroblast growth factor by acting on beta-adrenergic receptors [10].

Propranolol is an antihypertensive drug that has been linked to the following side effects in IH patients: Chilly extremities, irritability, lower gastrointestinal distress, emesis, hypotension, poor eating, lethargy, bronchospasm, and rash [11]. No previous researches have directly studied the effect of propranolol on height and BMI in IH patients, to our knowledge. Nonetheless, propranolol has been administered without deleterious height or BMI changes since 2008, which is consistent with our findings. The average length of propranolol treatment was 372 days, which is in line with the current literature [12,13].

It's vital to recognize the study's limitations. The data came from a single institution's new multidisciplinary clinic [14,15]. Children of various ages were referred to the clinic. Our findings may not be relevant to other contexts due to the unique characteristics of our patient population and/or institution-based treatment choices [16]. Furthermore, due to the natural history of hemangioma, only a small number of patients got medical therapy, hence these preliminary findings are based on a small group of patients.

The current study found that having one or more pediatricians at a vascular abnormality clinic is beneficial since a higher proportion of patients were treated medically rather than surgically. The findings support propranolol therapy, which is in line with current literature. The shorter treatment time cannot compensate for the deleterious effects of corticosteroids on height velocity and BMI. While the evidence is limited, the current investigation demonstrates that propranolol medication at a median dose of 2.0 mg/kg/day results in a small reduction in systolic BP with no detrimental anthropometric effects. Based on these preliminary data, the period of effective propranolol medication is anticipated to be at least one year.

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