**1st Methodological Assessment/1a Avaliação Metodológica**

**- Comments on the introduction/*Considerações sobre a introdução*:**

Adicionar parágrafo com informações sobre o manejo atual dos hemangiomas.

**- Comments on the objectives/*Considerações sobre os objetivos*:**

Acrescentar este item To describe the effects of proparanolol in a cohort of children and adolecents with hemagioma.

**- Coments on the discussion/*Considerações sobre a discussão*:**

Acrescentar parágrafo sobre segurança da intervenção analisada. Acrescentar parágrafo sobre implicações deste estudo para a prática Acrescentar parágrafo sobre implicações deste estudo para pesquisas futuras.

**- Coments on the conclusion/*Considerações sobre a conclusão*:**

Propranolol SEEMED TO BE effective in the treatment of hemangiomas in children of all ages, not only in the proliferative stage of the lesions (up to one year of age) with high response rate. Further randomized clinical trial is necessary to confirm this finding and to assess the safety of the intervention as well.

**1ª avaliação de revisor especialista da área**

**Title/Título**

**Is it clear and short enough?/*Está claro e curto o suficiente?***

Não - veja 3a. resposta

**Would you change it?/*Você o modificaria?***

Sim -veja 3a. resposta

**Does it reflect the paper's context?/*Reflete o conteúdo do artigo?***

Não - o título refere-se a pediatric hemangioma, porém forma incluídos no estudo pacientes de 0 a 19 anos, ou seja, não apenas crianças - sugestão: ou os autores excluem pacientes não pediátricos ou modificam o título para crianças e adolescentes

**Abstract/Resumo**

**Does it show the paper's objectives?/*Mostra os objetivos do trabalho?***

Sim

**Are the methods clear enough?/*Métodos estão suficientemente claros?***

Não - no texto, em método os autores citam que as lesões foram medidas e submetidas ao ultrassom e tomografia - não são referidos no resumo

**Does it describe the main results?/*Descreve os principais resultados?***

Sim

**Does it show the authors' conclusions?/*Mostra as conclusões dos autores?***

Sim

**Does it reflect what the paper says?/*Reflete o que diz o trabalho?***

Sim

**Text/Texto**

**São Paulo Medical Journal accepts papers on internal medicine, gynecology and obstetrics, mental health, surgery, pediatrics and public health. Is this Journal the right place for publishing this paper?/*São Paulo Medical Journal aceita trabalhos em clínica geral, ginecologia e obstetrícia, saúde mental, cirurgia, pediatria e saúde pública. A Revista é o lugar certo para publicação deste artigo?***

Sim

**Does the paper contribute towards the existing knowledge?/*O artigo contribui para o conhecimento já existente?***

Sim

**Does the paper read well and make sense?/*O artigo é fácil de ler e faz sentido?***

Sim, mas precisa ser modificado no título ou nos resultados, uma vez que o título fala em hemangioma pediátrico, mas foram incluídos pacientes de 0 a 19 anos - assim, o titulo deveria ser hemangiomas em crianças e adolescentes ou nos resultados deveriam ser excluídos pacientes não pediátricos, o que parece mais correto uma vez que esse tratamento é indicado para hemangioma infantil.

**Is it concise?/*É conciso?***

Sim

**Do the results matter to clinicians and patients?/*Os resultados importam para clínicos e pacientes?***

Sim

**Does this work matter for teachers and students?/*O trabalho é importante para professores e estudantes?***

Sim

**Does this work matter for health policymakers?/*O trabalho é importante para gestores de políticas de saúde?***

Não

**Has this work ever been published anywhere else?/*Este trabalho já foi publicado em algum outro lugar?***

Não

**Introduction/Introdução**

**Are the questions and objectives clear?/*As questões e os objetivos estão claros?***

Sim

**Does it show the importance of the field?/*Mostra a importância do campo de estudo?***

Sim

**Does it cite published studies to support the statements?/*Cita trabalhos publicados como subsídio das afirmações?***

Sim

**Methods/Métodos**

**Does the study design meet the proposed objective?/*O tipo de estudo responde o objetivo proposto?***

Sim

**Is the setting described and are the study conditions defined?/*O local onde foi realizado está descrito, bem como as condições do trabalho?***

Sim

**Is the sample adequately described and calculated?/*A amostra está adequadamente descrita e calculada?***

Não está de acordo com o título que fala de hemangioma pediátrico, pois inclui pacientes de 0 a 19 anos, ou seja, neonatos, crianças e adolescentes.

**Are the sample losses mentioned (and the reasons for this)?/*São referidas as perdas amostrais (e as razões para a perda)?***

Não.

**Are the procedures (interventions or diagnostic tests or exposures) adequately described?/*Os procedimentos (intervenções ou diagnósticos ou exposições) estão descritos adequadamente?***

Sim

**If it is a randomized trial: is it ethical?/*Se é um estudo randomizado: é ético?***

Não é randomizado, é aberto

**Are the main measurements adequately described?/*As principais medidas estão adequadamente descritas?***

Sim

**Is the statistical analysis adequate and well applied?/*A análise estatística é adequada e foi bem aplicada?***

Sim

**Are the methods appropriate for answering the study's question?/*Os métodos são apropriados para responder a questão da pesquisa?***

Sim, embora parte dos parâmetros de avaliação de eficácia não sejam relatados em resultados e discussão

**Results/Resultados**

**Are they presented clearly?/*Estão apresentados de maneira clara?***

Sim parcialmente. Em métodos são citados outros parâmetros de avaliação de eficácia como medidas, ultrassom e tomografia e não há nenhuma referência aos resultados, mesmo que aplicados em parte da população.

**Do the results answer the question?/*Os resultados respondem à questão?***

Sim

**Are they credible?/*São confiáveis?***

Sim

**Are there enough tables and figures?/*Tabelas e figuras aparecem em quantidade adequada?***

Não, seria interessante incluir tabela com resultados das medidas e fotografias de casos com resposta parcial e sem resposta, se houver possibilidade considerando a sessão da revista escolhida.

**Discussion and conclusions/Discussão e conclusões**

**Do the authors show the differences between their study and others already published?/*Os autores mostram as diferenças entre seu trabalho e outros já publicados?***

Não, seria interessante comparar com outras séries de casos, inclusive por faixas etárias.

**Do the authors cite bibliographic references for all the data presented (except the data originally presented here)?/*Os autores citam referências bibliográficas para todos os dados apresentados (com exceção dos dados apresentados originalmente aqui)?***

Sim

**Do they mention whether their results can be considered within clinical practice?/ *Mencionam se seus resultados podem ser considerados na prática clínica?***

Sim

**Are the conclusions based only on the results presented?/*As conclusões estão baseadas apenas nos resultados apresentados?***

Sim

**Do you think the results allow the conclusions presented to be reached? / *Acha que os resultados apresentados permitem que se chegue às conclusões expostas?***

Sim

**References/Referências**

**São Paulo Medical Journal asks authors to use the "Vancouver Style" for their references. Are the references in the right format? / *A São Paulo Medical Journal pede aos autores que utilizem o "Estilo Vancouver" para referências bibliográficas. As referências deste artigo estão no formato adequado?***

Sim

**Does the paper make use of enough references? / *O artigo traz referências suficientes?***

Sim

**Are the references up-to-date and relevant? / *As referências são atuais e relevantes?***

Sim

**Did you find any serious omissions? / *Encontrou alguma omissão importante?***

Não

**Final comments to the authors/Comentários finais aos autores**

**Here you can write anything that could help the authors to improve their paper for later submission. Please do not make any pronouncements regarding manuscript approval by the Journal / *Escreva aqui algo que possa ajudar os autores a melhorar o artigo para submissão subseqüente. Por favor, não emita nenhum juízo sobre a aceitação do manuscrito pela Revista.***

Existe uma incoerência entre título, método e resultados, uma vez que o título fala em hemangioma pediátrico, mas foram incluídos pacientes de 0 a 19 anos - assim, o titulo deveria ser hemangiomas em crianças e adolescentes ou nos resultados deveriam ser excluídos pacientes não pediátricos, o que parece mais correto uma vez que esse tratamento é indicado para hemangioma infantil. Seria interessante que fossem incluídos os resultados das medidas e dos aspectos observados no ultrassom e tomografia, citados em métodos, ainda que não realizados para todos os pacientes.

**1ª avaliação sob a ótica do leitor**

Os autores defendem a eficácia de um tratamento medicamentoso baseando-se em informações incompletas. Não se trata de um estudo controlado e randomizado. É uma série de casos que demonstraram boa resposta. No entanto, os autores não descrevem o efeito a longo prazo, após cessar a medicação; não esclarecem a evolução natural da doença e não há uma clareza quanto a descrição dos efeitos colaterais.

**RESPOSTAS A ALGUNS COMENTÁRIOS:**

**A dúvida sobre a propriedade do termo “criança” é recorrente. Legalmente, o Estatuto da Criança e do Adolescente (ECA), o dispositivo legal mais importante sobre a criança em nosso país, define:**

***Art. 2° - Considera-se criança, para os efeitos desta Lei, a pessoa até 12 (doze) anos de idade incompletos, e adolescente aquela entre doze e dezoito anos de idade.***

***Parágrafo único - Nos casos expressos em lei, aplica-se excepcionalmente este Estatuto às pessoas entre 18 (dezoito) e 21 (vinte e um) anos de idade.***

**Nota deste autor: pacientes até 21 anos em situação de risco, como aqueles em tratamento ou acompanhamento por doenças pediátricas crônicas, podem ser inseridos neste conceito. Um exemplo é a cobertura pediátrica que se estende até os 21 anos para os procedimentos hospitalares/ambulatoriais do SUS referentes a patologias crônicas e oncologia.**

**Donde depreende-se que, conjuntamente, os termos “criança e adolescente” podem referir-se a pessoas até 21 anos de idade. Na literatura técnica médica, no entanto, o termo “criança” costuma ser utilizado no sentido de toda a faixa etária pediátrica, numa metonímia muito encontrada em jornais científicos de gabarito. Um exemplo recente:**

***Prietsch, S.O.M. et al. Mortalidade por asma em crianças brasileiras de até 19 anos de idade no período entre 1980 a 2007. Jornal de Pediatria 2012;88(5):384-8.***

**Este artigo foi recentemente publicado no Jornal de Pediatria, veículo científico oficial da Sociedade Brasileira de Pediatria e um dos jornais científicos brasileiros mais lidos, com fator de impacto (2011) igual a 1,013. Também na literatura científica de língua inglesa esta generalização é frequente, e chega a ultrapassar os limites usualmente aceitos por nós. Um exemplo:**

**Numa página do National Cancer Institute sobre câncer infantil, lê-se esta passagem:**

*The Pediatric Brain Tumor Consortium (PBTC) (<http://www.pbtc.org> [xit Disclaimer](http://www.cancer.gov/global/web/policies/page8)) includes 10 leading academic institutions with extensive experience in the design and conduct of clinical trials for children with brain tumors. The group’s primary objective is to rapidly conduct [phase I](http://www.cancer.gov/dictionary?expand=p" \l "phase%20I%20trial) and II clinical evaluations of new therapeutic drugs, treatment delivery technologies, new biological therapies, and radiation treatment strategies in* ***children up to age 21*** *with primary central nervous system (CNS) tumors.*

**Mais um exemplo, na página clinicaltrials.gov:**

*Clinical Study of Vorinostat in Combination With Etoposide in Pediatric Patients < 21 Years at Diagnosis With Refractory Solid Tumors* ***(****NCT01294670).*

**Dessa forma, não causará estranheza a uma audiência de pediatras, especialistas ou não, lendo em inglês o trabalho atual, nem em relação ao título, nem em relação a outras passagens. No entanto, se os revisores acharem inadmissível para o SPMJ a atual grafia no manuscrito, os autores não terão nenhum problema em trocar as referências à “pediatric” ou “children” por “children and adolescents”. O autor correspondente apenas acha que tal não influenciará na aceitação geral do trabalho. Fiz as modificações no manuscrito.**

**Protocol: SPMJ000575/2012**

**SHORT COMMUNICATION**

**Treatment of children and adolescents with hemangioma with propranolol: preliminary results of a retrospective study**

Tratamento de crianças e adolescentes com hemangioma com propranolol: resultados preliminares de um estudo retrospectivo

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**KEY WORDS:**

Hemangioma, capillary.

Propranolol.

Retrospective studies.

Treatment outcome.

Medical oncology.

**ABSTRACT**

**CONTEXT AND OBJECTIVE:** Hemangiomas are the most common vascular tumors of children and adolescents. In 2008, it was first reported the use of propranolol to treat infantile hemangiomas. Other groups also reported similar results,showing that the treatment rapidly induced reduction of the volume of lesions. The objective was evaluating children and adolescents with hemangiomas that received treatment with propranolol.

**DESIGN AND SETTING:** A retrospective study, conducted in a children's hospital.

**METHODS:** We included patients from 0-19 years with or without prior treatment, diagnosed between January 2009 and December 2010. Response was assessed by comparing the status at start of treatment and at last appointment. We considered a partial or complete response as response to treatment.

**RESULTS:** We included 69 patients with a mean follow-up of 11 months. The average age was 31 months. Fifty-eight patients were treated for the first time, 11 had residual lesions or were refractory to prior therapy. Response (partial + complete) was seen in 60 patients (87%). The response in infantile hemangiomas was 50 of 53 (94%) and in the other hemangioma types was 10 in 16 (63%) (P = 0.3 chi-square). The response in patients less than 1 year was 37 of 38 (97%), whereas in those over 1 year was 23 of 31 (74%) (P = 0.4 chi-square). Side effects were uncommon and mild.

**CONCLUSIONS:** Propranolol was effective in the treatment of hemangiomas in children and adolescents, not only in the proliferative stage of the lesions (up to 1 year of age) with high response rate.

**PALAVRAS-CHAVE:**

Hemangioma capilar.

Propranolol.

Estudos retrospectivos.

Resultado de tratamento.

Oncologia.

**RESUMO**

**CONTEXTO E OBJETIVO:** Hemangiomas são os tumores vasculares mais comuns da infância. Em 2008, foi demonstrado o efeito do propranolol no tratamento de hemangiomas capilares. Outros relatos similares seguiram-se, demonstrando seu rápido efeito na redução do volume das lesões. O objetivo foi avaliar crianças e adolescentes com hemangioma tratadas com propranolol.

**TIPO DE ESTUDO E LOCAL:** Estudo retrospectivo, conduzido em hospital infantil.

**MÉTODOS:** Foram incluídos pacientes entre 0-19 anos, com ou sem tratamento prévio, tratados entre janeiro de 2009 e dezembro de 2010. A resposta foi avaliada comparando-se o aspecto da lesão entre o início do tratamento e a última consulta. Consideramos resposta parcial ou completa como resposta ao tratamento.

**RESULTADOS:** Sessenta e nove pacientes foram incluídos, com uma mediana de seguimento de 11 meses (idade média: 31 meses). Destes, 58 pacientes eram recém-diagnosticados e 11 tinham tratamento prévio. Resposta (parcial ou completa) foi verificada em 60 pacientes (87%). Entre os hemangiomas capilares, a resposta foi de 50 em 53 (94%) enquanto, em outros tipos de lesões, a resposta foi de 10 em 16 (63%) (P = 0,3 qui-quadrado). A resposta em pacientes com até 1 ano foi de 37 em 38 (97%), e naqueles com mais de 1 ano foi de 23 em 31 (74%) (P = 0,4 qui-quadrado). Efeitos colaterais foram incomuns e leves.

**CONCLUSÕES:** Propranolol foi eficaz no tratamento de hemangiomas em crianças e adolescentes de todas as idades, não apenas na fase proliferativa, com resposta em quase todos os pacientes.

**INTRODUCTION**

Hemangiomas are formed by the proliferation of blood vessels and are the most common vascular tumors of childhood, affecting approximately 3-10% of Caucasian children.1 They are more frequent in females (1:1.4-3.0), and in white  non-Hispanic children. Its causes are not known, with the exception of rare genetic syndromes in which hemangioma is frequent.2 Histologically, hemangiomas are a heterogeneous group,3 although the most common type is known simply as infantile or capillary hemangioma.

In 2008, a letter published in the New England Journal of Medicine first reported the use of propranolol to treat hemangiomas of infancy.4 After this first publication, other reports of cases successfully treated with propranolol were published, and the initial article has been cited about 140 times (Google Scholar survey in January 2011). Since January 2009, we have been treating pediatric patients with hemangiomas with off-label oral propranolol in our institution.

**OBJECTIVES:**

To describe the therapeutic effects of propranolol in a cohort of children and adolescents with hemangioma from a single institution. We planned to evaluate the response of children with hemangiomas to the treatment with propranolol. Side effects were not included as the main goal, once propranolol is approved by the brazillian regulatory agency for use in children. However, the adverse events reported during the treatment were recorded. A research project was approved by the Ethics Review Board of our institution in 2009. The project is still in data collection phase. This report shows partial preliminary data according to our database in June 2011.

**METHODS**

Parents or guardians received detailed explanation about the treatment and the latter was initiated after informed consent. A retrospective analysis of medical records was undertaken, using a semi-structured questionnaire. We included patients ranging from 0-19 years with a diagnosis of hemangioma with or without prior treatment, initiating treatment with propranolol between January 2009 and December 2010. Response was assessed by comparing the status at start of treatment and at last appointment, measuring the two largest diameters of the lesions. Patients with no objective measurement of response were evaluated by a qualitative assessment made by one of the attending physicians (one of the authors). The response was classified as stable disease (< 25% variation), partial response (25-95% reduction) and complete response (> 95% reduction). We considered a partial or complete response as response to treatment. Objective measurements were made by direct measure, ultrasound imaging or computed tomography, depending on the accessibility of the lesion. Deep lesions not measurable by ultrasound imaging were followed by serial computed tomography (the number of computed tomography scans was maintained at the minimum necessary for response assessment, tipically 2-3). Chi-square test was used to compare responses between different groups of patients (infantile hemangiomas versus other types and less than 1 year versus older than 1 year children).

**RESULTS**

We included 69 patients with a mean follow-up of 11 months. The average age at initiation of treatment for patients in the first treatment was 31 months, ranging from 1 month to 19 years. The median was 8 months. The average age at initiation of treatment for patients with residual lesions or those refractory to prior therapy was 3 years, ranging from 2 months to 16 years. A total of 38 patients started treatment with less than one year, while 31 commenced after completing one year. The dose used was 0.5 to 4.0 mg kg-1per day - starting with 0.5 mg kg-1 for all patients in the first week, with weekly increases up to 2.0 mg kg-1 per day. For patients with no initial response in the first 2-3 months the dose was increased to 4.0 mg kg-1 per day. The dosing interval was 8 or 12h. The treatment was contraindicated in children with asthma.

Fifty-eight patients were treated for the first time, 11 had residual lesions or were refractory to prior therapy. Response (partial + complete) was seen in 60 patients (87%). Forty six patients were female and 23 male (1:2). The lesions were classified as infantile hemangioma (53), cavernoma (03), syndromic (04), congenital and other (09). The response in infantile hemangiomas was 50 of 53 (94%) and in the other hemangioma types was 10 in 16 (63%) (P = 0.3 chi-square). The response in patients who started treatment with less than 1 year was 37 of 38 (97%), whereas in those which started after 1 year was 23 of 31 (74%) (P = 0.4 chi-square) (**Figure 1**). Side effects were uncommon and mild, no child in the series discontinued treatment because of side effects. Some reduced the dose due to side effects. **Figure 2** illustrates a typical case of infantile hemangioma with complete response to treatment.

**DISCUSSION**

In this preliminary retrospective study, treatment with propranolol was correlated with response (lesion reduction) in most children with hemangiomas. Apparently, there was a greater chance of response in children with infantile hemangiomas and less than one year of age, in contrast to patients with other types of hemangiomas or greater than one year. However, this difference was not statistically significant. The statistical power of comparing the number of responders with less or more than one year was 80% (data not shown). This indicates that the chance of type II error was small and that probably there was no real difference between the number of responders in children less or more than one year. However, this evaluation did not differentiate between a partial response (defined less strictly in this work, including what is regarded as a minor response) and complete response. One of our goals is to complete the data collection of the entire cohort analysis detailing the two different outcomes (partial or complete). However, our preliminary results already show that patients that have outgrown the so-called "proliferative phase" of the development of hemangiomas still have a potential of response that should not be underestimated.

The small number of patients with lesions other than infantile hemangiomas does not allow a conclusion about their response potential. However, the statistical power of this comparison was 83%. This heterogeneous group of patients included three patients with cavernous hemangiomas (histologically determined), four syndromic patients with apparently typical infantile hemangiomas (PHACES and Klippel-Trenaunay-Weber syndromes) and nine patients with congenital hemangiomas or late onset lesions. It is possible that patients with other forms of vascular tumors closely related to infantile hemangiomas do also have potential response. It remains to be determined whether this response potential is actually lower than that of patients with infantile hemangiomas.

The infantile hemangiomas have a typical presentation and evolution2 and express a homogeneous group of immunohistochemical markers, including GLUT1 (glucose transporter 1), a surface protein expressed by erythrocytes and the endothelium of infantile hemangiomas.5 It is possible that propranolol has a specific effect in lesions that express GLUT1, regardless of its presentation and stage of development. Indeed, infantile hemangiomas expressed GLUT1 in both the proliferative and regressive phases.6 In contrast, non evolutive congenital hemangiomas constitute a group of lesions clinically and histologically distinct, expressing not this marker.6 In our series, patients with congenital hemangiomas (clinical and radiological diagnosis) showed little or no response, unlike most other patients (data not shown). Perhaps the lesions with different presentation or evolution that respond to propranolol are actually GLUT1 positive (+) hemangiomas.

The mechanism of action of propranolol in infantile hemangiomas is still the subject of speculation. Initially, the idea was that this effect could be mediated by binding to beta-adrenergic receptors, leading to reducing of pro-angiogenic factors like VEGF (vascular endothelial growth factor) and b-FGF (fibroblast growth factor beta).7 It had already been shown that infantile hemangiomas express adrenergic receptors and are closely related to the sympathetic innervation.8 It has been speculated that in particular the inhibition of beta-2 adrenergic receptors may lead to vasoconstriction, anti-angiogenesis (via inhibition of VEGF) and induction of apoptosis in hemangiomas.9 However, no experimental evidence has corroborated these hypotheses. Other possible molecular pathways that are involved in the vascular tonus and endothelial proliferation and could directly or indirectly function as targets of propranolol include: cAMP/PKA leading to increased VEGF/b-FGF,10 inhibition of vasodilation by reducing the release of NO mediated by beta-3 receptor ligands11 and VEGF production regulated by NF-kB, which relates to the effect of steroids on hemangiomas.12 Recently, involvement of elements of the renin-angiotensin-aldosterone system has been suggested, via the inhibition of the renal renin-angiotensin-aldosterone system by propranolol, leading to inhibition of proliferation of endothelial progenitor cells that express receptors for VEGF and CD34 marker.13An anecdotal reference to the alleged direct binding of propranolol with GLUT1 has no scientific basis.14

Regardless of its mechanism of action, it is now indisputable that propranolol has an important effect on infantile hemangiomas, determining their rapid regression.15 Other groups also reported similar results,16,17 showing that the treatment rapidly induced the stabilization of lesions’ proliferation and reduction of the volume of lesions in 100% of patients. A review of several series18 showed that worldwide series of 1 to 58 patients reported effectiveness in most cases. In 205 pooled cases, 42 reported "excellent response", 69 were classified as "good" or "moderate" or "partial response", 56 had responses that were not quantified and 10 did not respond at all or "deteriorated" or showed "mild recurrence". The rest of the patients’ responses have not been described. This corresponds to a 82% response rate and 5% of refractoryness or relapse. The response in individual series ranged from 47-100%. Doses and schedules of administration varied little (1-3 mg kg-1 per day and were either increased gradually or started at full dose). The duration of treatment reported varied considerably, from 2 to 18 months, which may explain some of the variability of results. A double-blind, randomized clinical trial of propranolol reported effectiveness in 90% of 19 children (4 months to 5 years of age) treated with 2 mg kg-1 per day at 8h interval. Treatment of lesions determined softening and color change from redto purple in 24 h, stopping of growth in 2-30 days and rapid volume reduction by 4-8 weeks. Thereafter, the reduction of the residual lesions was slower. The trial showed that there was a statistically significant reduction of redness and elevation of infantile hemangiomas.19 There is no recommended length of treatment, but it has been shown that treating a minimum of six months and at least until one year of age may prevent recurrences.

Our report is as far as we are concerned the largest series published untill now in the literature and one of the few that included syndromic patients with hemangiomas or lesions different from infatile hemangiomas. We were able to reproduce the good results reported by other groups, although we have shown that a small number of patients is refractory. As for syndromic patients or other types of hemangiomas, it is still early to say for sure if patients within this heterogeneous group can also benefit from therapy with propranolol. Moreover, one can hypothesize that propranolol acts specifically on GLUT1 + lesions, regardless of their clinical presentation.

**CONCLUSIONS**

Propranolol was effective in the treatment of hemangiomas in children of all ages, not only in the proliferative stage of the lesions (up to one year of age) with high response rate. The outcome varied with the type of lesion, and age (difference not statistically significant). Infantile hemangiomas in infants under one year showed response in nearly all patients.

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**Figure 1.** Treatment response in patients with infantile hemangiomas, other types of vascular lesions, patients less than 1 year old or older than 1 year (number of patients)

**Figure 2.** Infantile ehmangioma in the feet of a 3-month old A. before treatment, and B. after 1 year of treatment. Complete remission is apparent. Residual telangiectasias remained.

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**Table 1:**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Type | First measure | |  | Last measure | |  | Follow-up | Mode | Age |
| Largest (D) | Smallest (d) | Dxd | Largest (D) | Smallest (d) | Dxd |
| HI | 6 | 4,4 | 26,4 | 9 | 5 | 45 |  | US | 2,6 |
| HI | 3,9 | 1,9 | 7,41 | 2,7 | 1,4 | 3,78 | 15 | US | 0,8 |
| HI | 5,1 | 3,9 | 19,89 | 5,6 | 3,5 | 19,6 | 7 | US | 1,6 |
| HI | 3 | 1,8 | 5,4 | 3,8 | 2 | 7,6 |  | US | 0,8 |
| HI | 3,6 | 2,7 | 9,72 | 2 | 1,6 | 3,2 | 3 | US | 0,6 |
| HI | 5,3 | 3,2 | 16,96 | 4,6 | 4,3 | 19,78 | 8 | US | 0,8 |
| HI | 1,9 | 0,9 | 1,71 | 0 | 0 | 0 | 18 | US | 0,7 |
| HI | 4,8 | 4 | 19,2 | 4,7 | 4,6 | 21,62 | 3 | TC | 0,6 |
| HI | 10 | 3 | 30 | 5 | 0,9 | 4,5 | 6 | TC | 0,9 |
| HI | 4 | 3,5 | 14 | 3,5 | 2,6 | 9,1 | 11 | TC | 11,1 |
| HI | 4 | 4 | 16 | 2,5 | 2,5 | 6,25 | 10 | OBS | 0,8 |
| HI | 7 | 7 | 49 | 2 | 2 | 4 | 8 | OBS | 0,4 |
| HI | 5 | 5 | 25 | 1 | 1 | 1 | 22 | OBS | 0,4 |
| HI | 4,5 | 4 | 18 | 4 | 4 | 16 | 3 | OBS | 0,5 |
| HI | 3,5 | 1,5 | 5,25 | 2,5 | 0,5 | 1,25 | 1 | OBS | 0,8 |
| HI | 3,5 | 2,5 | 8,75 | 3 | 2 | 6 |  | OBS | 0,4 |
| HI | 5 | 5 | 25 | 3 | 2 | 6 | 11 | OBS | 0,1 |
| HI | 6 | 6 | 36 | 4 | 2 | 8 | 6 | OBS | 0,3 |
| HI | 8 | 4 | 32 | 7 | 3,5 | 24,5 | 7 | OBS | 0,9 |
| HIGROMA | 7 | 5 | 35 | 5,1 | 4 | 20,4 | 7 | US |  |
| LT | 7,6 | 2,5 | 19 | 4 | 2,8 | 11,2 |  | US | 12,9 |
| LT | 3,3 | 2,7 | 8,91 | 3,3 | 2,8 | 9,24 | 6 | RNM | 4,9 |
| NICH | 8,7 | 6,3 | 54,81 | 11,5 | 6,5 | 74,75 | 10 | US | 3,9 |
| NICH | 4,1 | 2,3 | 9,43 | 3,6 | 3,5 | 12,6 | 6 | US | 0,3 |
| NICH | 6,4 | 3,4 | 21,76 | 6,7 | 3,6 | 24,12 |  | TC | 15,7 |
| CAV | 5,6 | 1,8 | 10,08 | 6 | 2 | 12 |  | TC | 11,4 |
| CAV | 3,2 | 3,1 | 9,92 | 2 | 2,4 | 4,8 |  | RNM |  |
| PHACES | 12 | 7 | 84 | 11,3 | 2,9 | 32,77 | 8 | RNM | 4,9 |

**Figure 3:**

**Macintosh HD:Users:Helder:SkyDrive:Trabalhos:Production:Pain:est:Rplot.pdf**