International Journal of Pediatric Otorhinolaryngology 75 (2011) 455–460

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Review article

A meta-analysis on the effectiveness of propranolol for the treatment of infantile airway haemangiomas

Stamatios Peridis [a,*], Gemma Pilgrim [a], Ioannis Athanasopoulos [b], Konstantinos Parpounas [b]

[a] Department of Otolaryngology Head and Neck Surgery, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom
[b] Department of Otolaryngology Head and Neck Surgery, "Aghia Sophia" Children's Hospital, Athens, Greece

ARTICLE INFO

Article history:
Received 11 October 2010
Received in revised form 23 January 2011
Accepted 25 January 2011
Available online 17 February 2011

Keywords:
Propranolol
Airway
Haemangioma
Infantile
Paediatric

ABSTRACT

Objective: To study the effectiveness of propranolol in infantile airway haemangiomas and compare the effectiveness of propranolol vs. different therapies.
Methods: A literature search of Ovid, Embase, the Cochrane database, Google™ Scholar, and Medline using PubMed as the search engine was performed to identify studies that analysed the effect of propranolol treatment in children with airway haemangiomas. Random-effect meta-analytical techniques were conducted for the outcome measures.
Results: Thirteen studies, comprising 36 patients were included in the analysis. Propranolol was found to be an effective intervention for the resolution of infantile airway haemangiomas ($P < 0.00001$). Meta-analysis of effectiveness of propranolol vs. steroids, CO_2 laser, or vincristine showed that propranolol is the most effective treatment.
Conclusions: This meta-analysis demonstrated that propranolol should be recommended as a first-line treatment in infantile airway haemangiomas. However, because of the possible side effects of propranolol, current infantile haemangioma treatment centres recommend a full cardiovascular and respiratory review be performed prior to initiation of therapy.

Contents

* Corresponding author at: Department of Otolaryngology Head and Neck Surgery, Guy's and St. Thomas' NHS Foundation Trust, Guy's Hospital, Great Maze Pond, London SE1 9RT, United Kingdom. Tel.: +44 7508250410.
E-mail address: peridis@gmail.com (S. Peridis).

0165-5876/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijporl.2011.01.028

1. Introduction

Infantile haemangiomas (IH) are the most common tumours of infancy affecting approximately 1 in 10 children [1]. IH are more common in those of Caucasian race, and are three times more common in girls [2]. IH are proliferative vascular tumours that can occur in the paediatric airway, potentially causing airway narrowing and respiratory distress. Untreated, these lesions carry a mortality of nearly 50%, especially when they involve the narrowest portion of the paediatric airway, the subglottis [3,4].

Historically, haemangiomas have been classified in a variety of ways. An important descriptive classification is related to the depth of soft tissue involvement: superficial, deep, and mixed. More recently, IH were also divided by whether they are spatially confined (localized) or whether they cover a wider territory (segmental) [1].

Airway IH with associated deep IH or diffuse cutaneous, segmental IH seems to be an extension of a more diffuse regional and/or systemic process, such as posterior fossa malformation, arterial anomalies, cardiac/aortic defects, eye anomalies, and sternal defect (PHACES) syndrome [3].

Medical and surgical interventions have been described thoroughly in the literature. They include steroids, chemotherapy agents (vincristine, alpha-interpheron), laser treatment, surgical excision, tracheostomy, or a combination of these therapies [3,5,6].

The spectacular effect of propranolol on cutaneous haemangiomas of infancy was described for the first time in 2008 by Léauté-Labrèze et al. [7]. They successfully treated 11 cases and observed a change in the colouration of the haemangioma in all the children as early as 24 h after initiation of treatment [8].

This meta-analysis aims to study the effectiveness of propranolol in infantile airway haemangiomas and to compare the effectiveness of propranolol against other therapies. It is the first published meta-analysis to look at all available treatment modalities and is important given the very small sample sizes of previous studies, the short history of propranolol as a treatment option, and the lethal nature of this rare disease.

2. Methods

2.1. Study selection

A literature search of Ovid, Embase, the Cochrane database, Google™ Scholar, and Medline using PubMed as the search engine was performed to identify studies that analysed the effect of propranolol treatment in children with airway haemangiomas. The following MeSH search headings were used: propranolol, laryngeal, haemangioma, and infantile. The following text searches and search headings and their combinations were used: propranolol, β-blocker, haemangioma, laryngeal, glottic, subglottic, supraglottic, infantile, children, and treatment. The related-articles function was used to broaden the search, and all abstracts, studies, and citations were reviewed irrespective of language. The search was most recently performed on September 1st, 2010.

2.2. Data extraction

Two reviewers (SP and GP) independently performed the search before reviewing and extracting the following: first author, year of publication, study population characteristics, study design, inclusion and exclusion criteria, number of subjects, length of follow-up and outcomes of interest. Areas of conflicts between the reviewers were subsequently discussed, and there was 100% agreement on the final interpretation of the data.

2.3. Inclusion criteria

In order to be included in the analysis, studies had to analyse the effect of propranolol in infantile airway haemangioma and report at least one of the outcomes of interest.

2.4. Exclusion criteria

Studies were excluded from the analysis if the outcomes of interest were not clearly reported or it was impossible to extract or calculate the appropriate data from the published results. When the same institution reported two studies, either the one of better quality or the one of the most recent publication was included unless the study outcomes were mutually exclusive or measured at different intervals.

2.5. Outcomes of interest

We were interested in the following outcomes:

1. Assessment of the effectiveness of propranolol in the treatment of infantile airway haemangiomas.
2. Comparison of the effectiveness of propranolol with steroids, CO_2 laser, or vincristine for the treatment of infantile airway haemangiomas.

2.6. Statistical analysis

This meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses (QUORUM) guidelines [9,10]. The odds ratio (OR) was used as the summary statistic for statistical analysis of dichotomous variables [11]. OR represents the odds of IH resolution occurring in the propranolol group compared with the different therapies group. An OR of less than 1 favoured resolution of IH with propranolol treatment. The point estimate of the OR was considered to be statistically significant if the P value was less than or equal to 0.05 and if the 95% confidence interval (95% CI) did not include the value 1. In the tabulation of the results, squares (■) indicate the point estimates of the risk factor with 95% CI indicated by horizontal bars. The diamond (◆) represents the summary estimate from the pooled studies with 95% CI. The Mantel–Haenszel method was used to combine the OR for the outcomes of interest using a "random effect" meta-analytical technique [11,12]. Yate correction was used for those studies that contained a zero in one cell for the number of events of interest in 1 of the 2 groups [13]. If there were no events for both groups the study was discarded from the meta-analysis of that outcome.

Sensitivity analysis was performed to quantitatively assess heterogeneity (HG) [12]; it was undertaken using the following

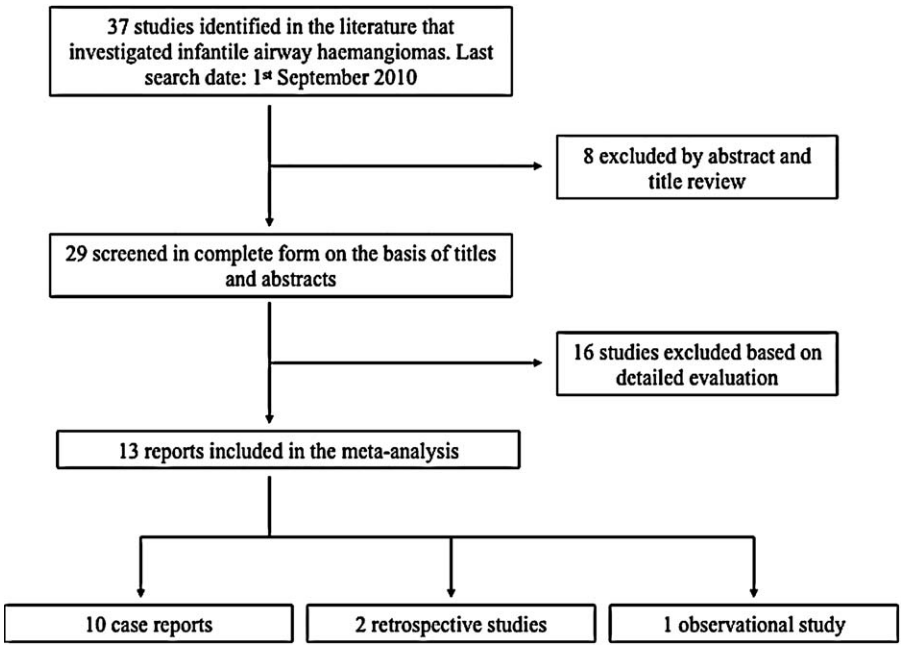

Fig. 1. Study selection flow chart.

groups: (1) papers reporting more than 3 patients, and (2) studies of higher quality with eight or more stars (as assessed by the Newcastle–Ottawa scale). Analysis was conducted by using the statistical software Review Manager Version 5.0.24 for Macintosh (Review Manager (RevMan), Version 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008).

2.7. Composite study quality

The quality of the studies was assessed using the Newcastle–Ottawa Scale [14] with some modifications to match the needs of this meta-analysis [15,16]. This was done by assessing patient selection criteria, group comparability, and the outcome in the individual studies. A star rating of 0–11 was allocated to each retrospective study based in these parameters. Two reviewers (SP and GP) assessed the quality of the studies. Where discrepancies arose, papers were re-examined and consensus was reached by discussion. Studies were considered to be of higher quality if they received eight or more stars.

3. Results

3.1. Studies selected

Using the above search strategy, 37 publications were identified in the literature that investigated infantile airway haemangiomas. Of these, 8 studies were excluded after the abstracts were reviewed and a further 16 studies were excluded after the full text was reviewed. A total of 24 were excluded because they did not meet the inclusion criteria. 13 studies published between 2009 and 2010 matched the selection criteria and were therefore included in the analysis [17–29] (Fig. 1).

The eligible studies reported outcomes on a total of 36 patients; 9.09% boys and 90.91% girls. Six studies [18,21,

Table 1
Characteristics of included studies. R, retrospective; CR, case report; OS, Observational study; pts, patients; M, male; F, female; ns, not specified.

First author	Year	Study design	No. of pts	M/F	Inclusion criteria	Exclusion criteria	Matching criteria	Follow-up (months) mean (range)	Study quality (star rating) (Max 11)
Mistry [17]	2010	CR	1	0/1	1,2,3,4,6,7,8,9,10	1	1,2,3,6,7,8,9	5	7
Buckmiller [18]	2009	CR	1	0/1	1,2,3,4,5,7,9,10,11,12	1	1,2,3,7,8,9	26	8
Maturo [19]	2010	CR	2	0/2	1,2,4,6,7,8,9,10	1	1,2,3,6,7,8,11	4.5 (3–6)	6
Truong [20]	2010	R	6	0/6	1,2,3,4,5,6,7,8,9	1	1,2,3,6,7,8,10,11	10.2 (6–14)	7
Rosbe [21]	2010	CR	3	1/2	1,2,3,4,7,8,9,10,12	1	1,2,3,4,6,7,10,11	12 (10–14)	10
Truong [22]	2010	CR	1	0/1	1,2,3,4,5,8	1	1,2,3,7,11	5	7
Denoyelle [23]	2009	CR	2	0/2	1,2,3,4,7,8,9,10,11,12	1	1,2,3,4,6,7,8,9,11	10.5 (5–16)	10
Blanchet [24]	2010	CR	1	0/1	1,2,3,4,8,9,10	1	1,2,3,7,8,9	5	8
Theletsane [25]	2009	CR	1	0/1	2,3,8,9,10	1	1,2,3,7,11	6	6
Manunza [26]	2010	CR	3	ns	2,3,7	1	8,9	ns	4
Leboulanger [27]	2010	R	12	1/11	1,2,3,4,7,8,9,10,11	1,4	1,2,3,4,7,8,9	6	8
Sans [28]	2009	OS	2	1/1	1,2,3,4,6,7,8	1,2,3	1,2,3,8,9	8	8
Jephson [29]	2009	CR	1	0/1	1,2,3,8,9	1	1,2,3,7,8,9	12	6

Inclusion criteria: 1, airway obstruction; 2, stridor; 3, propranolol; 4, steroids; 5, CO_2 laser; 6, Supraglottis; 7, Glottis; 8, Subglottis; 9, clinical history; 10, pre- and post-treatment endoscopy; 11, data of follow-up analysed; 12, vincristine. Exclusion criteria: 1, previous use of β-blocker; 2, cardiovascular disorder; 3, respiratory wheezing; 4, surgery prior to propranolol. Matching criteria: 1, age; 2, gender; 3, follow-up; 4, PHACE; 5, gastroesophageal reflux; 6, CT scan; 7, microlaryngoscopy and bronchoscopy; 8, electrocardiogram; 9, echocardiogram; 10, tracheotomy; 11, MRI.

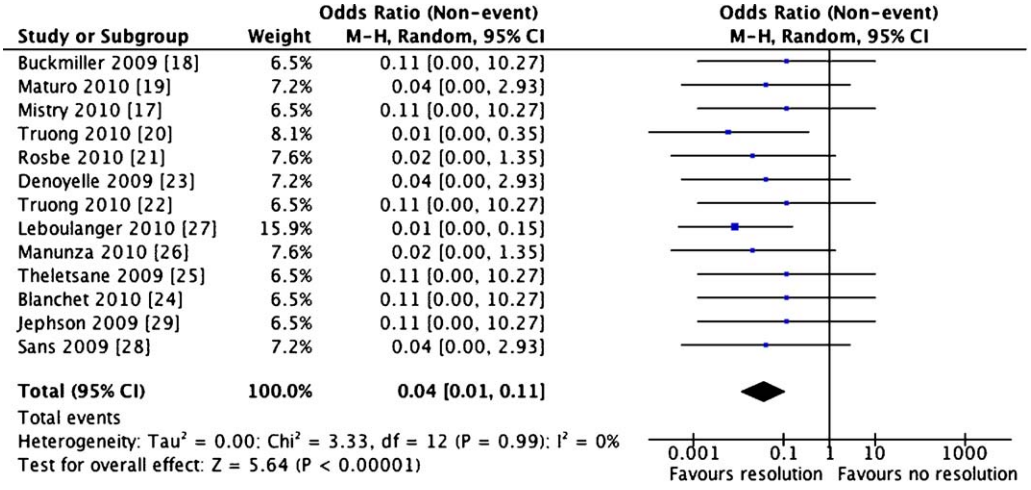

Fig. 2. Forest plot of comparison. Propranolol effectiveness.

23,24,27,28] scored 8 or more stars on the modified Newcastle–Ottawa scoring system. The study characteristics, selection criteria, matching, and quality scoring for each study are shown in Table 1.

Whether or not a treatment was judged to be effective was determined by the original authors using a combination of symptom resolution [17,18,20–22,25,26,28], direct visualization confirming a reduction in size of the haemangioma [17,19,

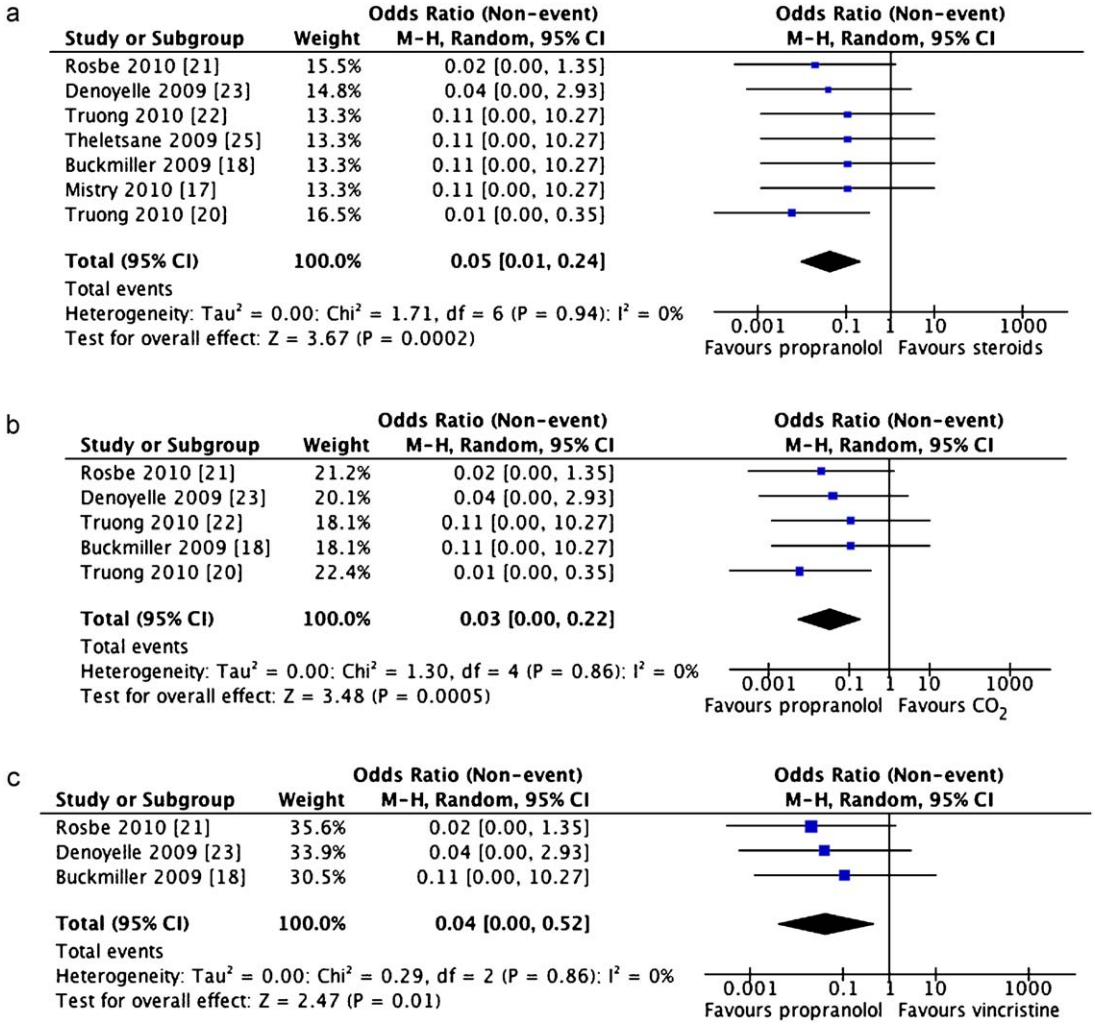

Fig. 3. Forest plot of comparison. Propranolol vs. different therapies: (a) propranolol vs. steroids, (b) propranolol vs. CO_2 and (c) propranolol vs. vincristine.

Table 2
Outcomes of interest of included studies (OR, odds ratio; CI, confidence interval; HG, heterogeneity). Statistically significant values are marked in bold.

Outcome of interest	No. of studies	No. of patients	OR	95% CI	*P* Value	HG *P* Value
Propranolol effectiveness						
Propranolol effectiveness	13	36	0.04	0.01–0.11	$P < 0.00001$	$P = 0.99$
Propranolol vs. different therapies						
Propranolol vs. steroids	7	15	0.05	0.01–0.24	$P = 0.0002$	$P = 0.94$
Propranolol vs. CO_2 laser	5	13	0.03	0.00–0.22	$P = 0.0005$	$P = 0.86$
Propranolol vs. vincristine	3	6	0.04	0.00–0.52	$P = 0.01$	$P = 0.86$

21,23,24] and MRI in one case which also involved the mediastinum [22].

3.2. Meta-analysis on the effectiveness of propranolol treatment (Fig. 2)

Propranolol for the treatment of airway IH was reported in thirteen studies [17–29] with a total of 36 patients. It is an effective intervention for the resolution of infantile airway haemangiomas ($P < 0.00001$; OR, 0.03; 95% CI, 0.01–0.12).

3.3. Meta-analysis on the effectiveness of propranolol vs. steroids, CO_2 laser, and vincristine in infantile airway haemangiomas (Fig. 3a–c)

3.3.1. Propranolol vs. steroids

Seven studies [17,18,20–23,25] with a total of 15 patients compared the effectiveness of propranolol with steroids. Propranolol is a significantly more effective treatment for IH than steroids ($P = 0.0002$; OR, 0.05; 95% CI, 0.01–0.24) (Figs. 2 and 3).

3.3.2. Propranolol vs. CO_2 laser

Five studies [18,20–23] with a total of 13 patients evaluated the effectiveness of propranolol and CO_2 laser. Propranolol is a significantly more effective treatment when compared to CO_2 laser ($P = 0.0005$; OR, 0.03; 95% CI, 0.00–0.22).

3.3.3. Propranolol vs. vincristine

Three studies [18,21,23] with a total of 6 patients analysed the effectiveness of propranolol vs. vincristine. Propranolol is significantly more effective than vincristine ($P = 0.01$; OR, 0.04; 95% CI, 0.00–0.54). All analyses are summarized in Table 2.

3.4. Sensitivity analysis (Table 3)

Similar results to the original analysis were obtained in the meta-analysis of studies reporting ≥3 patients [20,21,26,27], and those of high quality [18,21,23,24,27,28].

3.5. Other outcomes of interest

3.5.1. Infantile airway haemangiomas

The mean degree of stenosis found during microlaryngoscopy and bronchoscopy prior to propranolol treatment was 77.57% (range, 55–95%). After one week of therapy with propranolol the mean degree of stenosis was 38.3% (range, 25–50%), and after 4 weeks the mean degree of stenosis was 24.6% (range, 9.17–50%). Out of 36 children included, 32 (88.89%) had subglottic IH, 2 (5.55%) had transglottic, 1 (2.77%) glottic, and 1 (2.77%) supraglottic IH (Table 3).

3.5.2. Propranolol therapy

The mean dose of propranolol was 2 mg/kg/day (range, 0.5–3 mg/kg/day). The mean treatment duration was 6 months (range, 1.5–10 months). Clinical improvement in signs and symptoms were seen in a range of 24 h–3 weeks (mean, 3.8 days). Complications related to propranolol usage were found in one child (2.94%), who developed bronchoconstriction during the first week of treatment.

3.5.3. PHACES syndrome

PHACES syndrome was found in 4 children (11.1%).

3.5.4. Sex preponderance

Female to male ratio of infantile airway haemangiomas found in this study was 10:1.

4. Discussion

The results of this meta-analysis show that propranolol is the best treatment available for the resolution of infantile airway haemangiomas. It has many advantages over other established treatments, such as being non-invasive, of rapid onset, and avoids tracheostomy, prolonged steroid therapy, manipulation of subglottic tissues or prolonged periods of intubation. It has a low complication rate, and is inexpensive [29]. Systemic corticosteroids used alone are of limited benefit with only 25% of patients responding and long term therapy causes rebound growth upon cessation of treatment and serious side effects such as Cushing syndrome, hypertension, delayed wound healing, immunosuppresion, and growth retardation [5,17,29]. Endoscopic laser treatment for haemangiomas, mainly using the CO_2 laser, has been used for nearly 30 years. As with other therapies, its reported efficacy has varied. The main risks include high recurrence rates (with the need for multiple treatments), subglottic stenosis and subsequent need for tracheostomy [17].

Table 3
Sensitive analysis of outcomes of interest (OR, odds ratio; CI, confidence interval; HG, heterogeneity). Statistically significant values are marked in bold.

Outcome of interest	No. of studies	No. of patients	OR	95% CI	*P* Value	HG *P* value
Studies reporting ≥3 patients						
Propranolol effectiveness	4	24	0.01	0.00–0.07	$P < 0.00001$	$P = 0.96$
Propranolol vs. steroids	2	9	0.01	0.00–0.20	$P = 0.002$	$P = 0.68$
Propranolol vs. CO_2 laser	2	9	0.01	0.00–0.20	$P = 0.002$	$P = 0.68$
High-quality studies (≥8 stars)						
Propranolol effectiveness	6	21	0.03	0.01–0.14	$P < 0.0001$	$P = 0.92$
Propranolol vs. steroids	3	6	0.04	0.00–0.52	$P = 0.01$	$P = 0.86$
Propranolol vs. CO_2 laser	3	6	0.04	0.00–0.52	$P = 0.01$	$P = 0.86$
Propranolol vs. vincristine	3	6	0.04	0.00–0.52	$P = 0.01$	$P = 0.86$

Open surgical excision of airway IH was reported in only 2 patients, therefore surgery was not included as a treatment modality in the meta-analysis. Both patients developed recurrent stridor postoperatively and underwent subsequent successful propranolol therapy [20,22]. Surgery is also associated with a mean intubation or stenting period of 9 days, and carries a 10% complication rate, including subglottic stenosis, bleeding and wound infection. There is insufficient evidence to support surgical excision as a successful therapy and it should therefore be considered only for selected cases where other treatments have failed or are contraindicated [30].

The mechanism of action of propranolol is poorly understood, but it is thought vasoconstriction may be responsible for the initial colour change. Later pathways leading to IH resolution may involve the down-regulation of proangiogenic factors, such as basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF), and the triggering of apoptosis of capillary endothelial cells [7,25].

Potential side effects of propranolol include bradycardia, hypotension, hypoglycaemia, rash, gastrointestinal discomfort/reflux, fatigue, and bronchospasm, all of which tend to be quite rare and are seen at doses >2 mg/kg/day [6,18].

Prior to propranolol administration, Siegfried et al. [31] recommended baseline echocardiogram, vital sign and glucose monitoring in the first 48 h. The authors also recommended a starting dose of 0.5 mg/kg/day in three divided doses, and incrementally doubling to a final dose of 2 mg/kg/day. The Great Ormond Street Hospital guidelines [29] are more rigorous and include a full cardiovascular and respiratory review prior to initiation of therapy, blood tests (full blood count, urea and electrolytes, creatinine, liver function tests, glucose, and thyroid function tests), urine dipstick for glucose, electrocardiogram, echocardiogram, and an abdominal ultrasound scan. Monitoring includes pulse rate and blood pressure every hour for the first 4 h following initiation of propranolol therapy and after each dose change together with monthly blood glucose [29].

The use of meta-analytical techniques allowed the inclusion of 36 patients, of which 36 (100%) were treated with propranolol, 15 (41.67%) were treated with steroids, 13 (36.11%) with CO_2 laser, and 6 (16.67%) with vincristine. A sample of this size is substantial, given the small sample sizes previously reported in the literature.

Despite the strength of our study, some limitations should be discussed. Firstly, 10 out of 13 studies included are case reports [17–19,21–26,29]; 2 were retrospective studies [20,27]; 1 was an observational study [28]. Given the rarity of the condition, there is a practical consideration that limits the number of cases available for analysis. Another limitation of our study was the lack of published work that analysed the use of propranolol in IH (all of the studies were published in or after 2008). Despite these limitations, our study provides significant information concerning the impact of propranolol as a first-line therapy for infantile airway haemangiomas, which may be used in the future for designing prospective studies.

Conflict of interest

None reported.

References

[1] L.C. Chang, A.N. Haggstrom, B.A. Drolet, E. Baselga, S.L. Chamlin, M.C. Garzon, et al., Growth characteristics of infantile hemangiomas: implications for management, Pediatrics 122 (2008) 360–367.
[2] A.P. Zimmermann, S. Wiegand, J.A. Werner, B. Eivazi, Propranolol therapy for infantile haemangiomas: review of the literature, Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 338–342.
[3] J.A. Perkins, W. Duke, E. Chen, S. Manning, Emerging concepts in airway infantile hemangioma assessment and management, Otolaryngol. Head Neck Surg. 141 (2009) 207–212.
[4] J.A. Perkins, S. Oliaei, M.M. Garrison, S.C. Manning, D.A. Christakis, Airway procedures and hemangiomas: treatment patterns and outcome in U.S. pediatric hospitals, Int. J. Pediatr. Otorhinolaryngol. 73 (2009) 1302–1307.
[5] L.M. Buckmiller, Propranolol treatment for infantile hemangiomas, Curr. Opin. Otolaryngol. Head Neck Surg. 17 (2009) 458–459.
[6] L.M. Buckmiller, P.D. Munson, U. Dyamenahalli, Y. Dai, G.T. Richter, Propranolol for infantile hemangiomas: early experience at a tertiary vascular anomalies center, Laryngoscope 120 (2010) 676–681.
[7] C. Léauté-Labrèze, E. Dumas de la Roque, T. Hubiche, F. Boralevi, J.B. Thambo, A. Taïeb, Propranolol for severe hemangiomas of infancy, N. Engl. J. Med. 358 (2008) 2649–2651.
[8] F. Denoyelle, E.N. Garabédian, Propranolol may become first-line treatment in obstructive subglottic infantile hemangiomas, Otolaryngol. Head Neck Surg. 142 (2010) 463–464.
[9] M. Clarke, R. Horton, Bringing it all together: lancet–cochrane collaborate on systematic reviews, Lancet 357 (2001) 1728.
[10] D.F. Stroup, J.A. Berlin, S.C. Morton, I. Olkin, G.D. Williamson, D. Rennie, et al., Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group, JAMA 283 (2000) 2008–2012.
[11] R. DerSimonian, N. Laird, Meta-analysis in clinical trials, Control Clin. Trials 7 (1986) 177–188.
[12] M. Egger, G. Davey Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, BMJ 315 (1997) 629–634.
[13] N. Mantel, W. Haenszel, Statistical aspects of the analysis of data from retrospective studies of disease, J. Natl. Cancer Inst. 22 (1959) 719–748.
[14] G.A. Wells, B. Shea, D. O'Connell, et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.(accessed: Jan 15, 2011).
[15] T. Athanasiou, S. Al-Ruzzeh, P. Kumar, M.C. Crossman, M. Amrani, J.R. Pepper, et al., Off-pump myocardial revascularization is associated with less incidence of stroke in elderly patients, Ann. Thorac. Surg. 77 (2004) 745–753.
[16] D.P. Taggart, R. D' Amico, D.G. Altman, Effect of arterial revascularization on survival: a systemic review of studies comparing bilateral and single internal mammary arteries, Lancet 358 (2001) 870–875.
[17] N. Mistry, K. Tzifa, Use of propranolol to treat multicentric airway haemangioma, J. Laryngol. Otol. 124 (2010) 1329–1332.
[18] L. Buckmiller, U. Dyamenahalli, G.T. Richter, Propranolol for airway hemangiomas: case report of novel treatment, Laryngoscope 119 (2009) 2051–2054.
[19] S. Maturo, C. Hartnick, Initial experience using propranolol as the sole treatment for infantile airway hemangiomas, Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 323–325.
[20] M.T. Truong, J.A. Perkins, A.H. Messner, K.W. Chang, Propranolol for the treatment of airway hemangiomas: a case series and treatment algorithm, Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 1043–1048.
[21] K.W. Rosbe, K.Y. Suh, A.K. Meyer, S.M. Maguiness, I.J. Frieden, Propranolol in the management of airway infantile hemangiomas, Arch. Otolaryngol. Head Neck Surg. 136 (2010) 658–665.
[22] M.T. Truong, K.W. Chang, D.R. Berk, A. Heerema-McKenney, A.L. Bruckner, Propranolol for the treatment of a life-threatening subglottic and mediastinal infantile hemangioma, J. Pediatr. 156 (2010) 335–338.
[23] F. Denoyelle, N. Leboulanger, O. Enjolras, R. Harris, G. Roger, E.N. Garabedian, Role of propranolol in the therapeutic strategy of infantile laryngotracheal hemangioma, Int. J. Pediatr. Otorhinolaryngol. 73 (2009) 1168–1172.
[24] C. Blanchet, R. Nicholas, M. Bigorre, P. Amedro, M. Mondain, Management of infantile subglottic hemangioma: acebutolol or propranolol? Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 959–961.
[25] T. Theletsane, A. Redfern, O. Raynham, T. Harris, N.S. Prose, N.P. Khumalo, Life-threatening infantile haemangioma: a dramatic response to propranolol, J. Eur. Acad. Dermatol. Venereol. 23 (2009) 1445–1469.
[26] F. Manunza, S. Syed, B. Laguda, J. Linward, H. Kennedy, K. Gholam, et al., Propranolol for complicated infantile haemangiomas: a case series of 30 infants, Br. J. Dermatol. 162 (2010) 452–468.
[27] N. Leboulanger, P. Fayoux, N. Teissier, A. Cox, T. Van Den Abbeele, L. Carrabin, et al., Propranolol in the therapeutic strategy of infantile laryngotracheal hemangioma: a preliminary retrospective study of French experience, Int. J. Pediatr. Otorhinolaryngol. 74 (2010) 1254–1257.
[28] V. Sans, E.D. de la Roque, J. Berge, N. Grenier, F. Boralevi, J. Mazereeuw-Hautier, et al., Propranolol for severe infantile hemangiomas: follow-up report, Pediatrics 124 (2009) 423–431.
[29] C.G. Jephson, F. Manunza, S. Syed, N.A. Mills, J. Harper, B.E. Hartley, Successful treatment of isolated subglottic haemangioma with propranolol alone, Int. J. Pediatr. Otorhinolaryngol. 73 (2009) 1821–1823.
[30] R. Saetti, M. Silvestrini, C. Cutrone, S. Narne, Treatment of congenital subglottic hemangiomas, Arch. Otolaryngol. Head Neck Surg. 134 (2008) 848–851.
[31] E.C. Siegfried, W.J. Keenan, S. Al-Jureidini, More on propranolol for hemangiomas of infancy, N. Engl. J. Med. 359 (2008) 2846–2847.