

A survey on the application of oral propranolol and atenolol for the management of infantile hemangiomas in mainland China

Survey on propranolol atenolol hemangiomas

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Abstract

Since 2008, oral propranolol has evolved as the first-line therapy for infantile hemangiomas (IHs). Meanwhile, oral atenolol gradually shows comparative effectiveness versus oral propranolol with few side effects. Here, we conducted a mobile internal survey among a group of Chinese clinicians about how they choose the dosage, dose regimen, and dose escalation methods of propranolol and atenolol for the treatment of IH.

A mobile-ready internal survey on the application of oral propranolol and oral atenolol for IH in mainland China was performed and distributed to 333 potential clinicians from different levels of healthcare institutions in mainland China. Eighty-one doctors responded to the survey. All the respondents had the experience of treating IH with oral propranolol and 32 had the experience with oral atenolol.

Most of the doctors from tertiary hospitals chose 2 mg/kg/d twice daily, while most of those with the experience of propranolol from private hospitals chose 1 mg/kg/d once daily. More doctors from tertiary hospitals had the experience of atenolol than those from private hospitals.

Oral atenolol has become another medication intervention option for IH in mainland China. This survey is helpful to standardize and develop a guideline of oral atenolol therapy for IH.

Abbreviations: AHRQ = Agency for Health Research and Quality, BBB = blood-brain barrier, His = infantile hemangiomas, KMO = Kaiser-Meyer-Olkin, RCT = randomized controlled trial.

Keywords: survey, propranolol, atenolol, infantile hemangiomas

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1. Introduction

Infantile hemangiomas (IHs) are the most common vascular tumors of infancy, with a prevalence estimated at 4% of infants.^[1] The significance of drug therapy is to make the rapid proliferation of IH resolve in a short term. For many years β-blockers have been used for their anti-ischemic, anti-arrhythmic and anti-hypertensive properties. In 2008, Léauté-Labrèze et al serendipitously discovered that propranolol could effectively control the rapid proliferation of IH. Subsequently, β-blocker therapy such as oral propranolol or oral atenolol attributing to its significant effectiveness and fewer side effects plays a pivotal role in the treatment of IH.^[2,3] Propranolol often prevents or reverses IH growth before tumor reaches a pathological size or causes skin ulcers. Since then, propranolol has gradually replaced corticosteroid as the preferred drug for the treatment of IH.^[4] However, propranolol is a non-selective β -blocker, which can enter the brain across the blood-brain barrier (BBB) and may have potential side effects on the intellectual development and neuropsychiatric status of children.^[5] Recent studies have found that atenolol can also inhibit the rapid proliferation of IH and promote the regression of IH effectively.^[6] Atenolol is a watersoluble, selective B1 receptor blocker which cannot enter the brain through the BBB, and theoretically has much less potential neurological side effects. Therefore, atenolol may be an acceptable or even more appropriate alternative for IH.

Although several guidelines for the management of IH have provided expert consensus for the use of oral propranolol,^[7,8] no

prevailing guidelines have been published for the use of oral atenolol in the treatment of IH. Here, we conducted a mobile internal survey among a group of doctors in mainland China on how they chose the dosage, dose regimen, and dose escalation methods of propranolol and atenolol for the treatment of IH, and compared their responses with the newly published guidelines regarding oral β -blocker therapy.

2. Methods

2.1. Survey design and data collection

The Institutional Review Board of Shanghai Ninth People's Hospital approved this study. The mobile-ready internal survey was developed using a built-in mobile survey solution. The mobile survey was designed to protect respondent anonymity. The anonymous survey contained some detailed instructions and 22 potential questions focused on respondent demographic characteristics, treatment dose, dose regimen, and dose escalation methods of propranolol and atenolol. Branching logic was used to tailor the questions based on previous responses, and so some respondents did not see all 22 questions. The anonymous questionnaire was initially distributed to doctors from different levels of healthcare institutions in mainland China from Dec 1st, 2019 to Dec 12th, 2019. Once the survey was completed and submitted by participants, the data would be feedbacked to the investigators automatically.

2.2. Statistical analysis

Descriptive data were characterized as numbers, percentages, or means \pm standard deviations. Chi-square analysis and Fisher precise test were used to examine the correlations between characteristics and treatment choices. A *P* value less than .05 was considered statistically significant. SPSS software package (version 26.0; SPSS, Chicago, IL) was used for statistical analysis.

3. Results

3.1. Survey respondents

The survey was completed by 81 doctors. Most respondents were board-certified doctors of stomatology (25.93%), vascular surgery (17.28%) and plastic surgery (16.05%), with a mean of 13 years in practice. The mean age of the respondents was $43.99 (\pm 8.42)$ years old, ranged from 27 years old to 56 years old, and 29 (35.80%) were female. The mean response time was 186.30 (\pm 138.54) seconds, ranged from 57 seconds to 937 seconds. The Cronbach's Alpha was 0.888 in the reliability test, and the KMO value was 0.744 in the validity test. The demographic characteristics of the 81 doctors included in the survey were summarized in Table 1.

3.2. Propranolol treatment

All the 81 respondents stated that they have the experience of treating IH with oral propranolol therapy. Twenty-one (25.93%), 49 (60.49%), 4 (4.94%) of them used the dosage of 1mg/kg/d, 2 mg/kg/d, 3 mg/kg/d, respectively. The dosing frequency varied, with 15(18.52%) of respondents delivered once daily, 52 (64.20%) twice daily, and 12(14.81%) 3 times a day and 2 (2.47%) at other intervals. Fifty-five (67.90%) of the respondents titrated the dosage up to the target dose according to the patients' age, weight, and response.

Table 1

The characteristics of the respondents.

		Ν	N(%)
Gender			
	Female	29	35.80%
	Male	52	64.20%
Departme	nt		
	Invasive Technology	7	8.64%
	Stomatology	21	25.93%
	Dermatology	6	7.41%
	Surgery	10	12.35%
	Vascular Surgery	14	17.28%
	Plastic Surgery	13	16.05%
	Medical Imagery	2	2.47%
	Traditional Chinese Medicine	3	3.70%
	Others	5	6.17%
Title			
	Chief/Professor	31	38.27%
	Assistant Chief/Assistant Professor	21	25.93%
	Attending	24	29.63%
	Resident	4	4.94%
	Other	1	1.23%
Classificat	ions of Hospital		
	Primary	0	0.00%
	Secondary General Hospital	2	2.47%
	Secondary Specialized Hospital	0	0.00%
	Tertiary General Hospital	40	49.38%
	Tertiary Specialized Hospital	26	32.10%
	3AAA Hospital	0	0.00%
	Private Hospital	12	14.81%
	Others	1	1.23%

We compared the difference in the dosage among different characteristics. Doctors from different levels of healthcare institutions showed a significant difference. Most doctors from tertiary hospitals chose 2 mg/kg daily, while most of those from private hospitals chose 1 mg/kg daily (Table 2).

We also compared the difference in the regimen among different characteristics. Doctors from different levels of healthcare institutions showed a significant difference. Most doctors from tertiary hospitals chose twice daily, while most of those from private hospitals chose once daily (Table 3).

The result showed no differences between doctors who chose dose escalation or not in propranolol treatment with different characteristics (Table 4).

3.3. Atenolol treatment

Only 32 respondents had the experience of treating IH with oral atenolol. Nineteen (59.38%), 10 (31.25%), 2 (6.25%) of them used the dose of 1 mg/kg/d, 2 mg/kg/d, 3 mg/kg/d, respectively; and 12(37.50%), 14(43.75%), 5(15.63%) used the treatment regimen of once daily, twice daily, three times a day, respectively. Fifteen (46.88%) of the respondents used the incremental protocol according to the patients' age, weight, and response.

We compared the difference in the dosage among different characteristics. There was no significant difference among doctors of different characteristics (Table 5). We also analyzed the characteristics of doctors who chose atenolol and found that more doctors from tertiary hospitals had atenolol experience than those from private hospital (Table 6).

Table 2

The dose of propranolol treatment.

		1 mg/kg/d	2 mg/kg/d	3 mg/kg/d	Other	$\chi^{\rm 2}/{\rm Fisher}$	Р
Gender						2.816*	.421
	Female	5 (23.8)	21 (42.9)	1 (25.0)	2 (28.6)		
	Male	16 (76.2)	28 (57.1)	3 (75.0)	5 (71.4)		
Age (yr)		· · · · ·	· · · ·	(<i>'</i>	· · · ·	9.529 [†]	.339
	<30	2 (9.5)	1 (2.0)	0	0		
	30–39	4 (19.0)	17 (34.7)	2 (50.0)	2 (28.6)		
	40–49	11 (52.5)	16 (32.7)	1 (25.0)	1 (14.3)		
	≥50	4 (19.0)	15 (30.6)	1 (25.0)	4 (57.1)		
Title					. ,	9.956 [†]	.724
	Chief/Professor	8 (38.1)	19 (38.8)	1 (25.0)	3 (42.9)		
	Assistant Chief/Assistant Professor	4 (19.0)	15 (30.6)	1 (25.0)	1 (14.2)		
	Attending	7 (33.3)	13 (26.5)	1 (25.0)	3 (42.9)		
	Resident	1 (4.8)	2 (4.1)	1 (25.0)	0		
	Other	1 (4.8)	0	0	0		
Duration of practice (year)					7.738 [†]	0.527	
	<10	4 (19.0)	7 (14.3)	1 (25.0)	1 (14.3)		
	10–19	4 (19.0)	20 (40.8)	2 (50.0)	1 (14.3)		
	20-29	9 (43.0)	13 (26.5)	0	3 (42.8)		
	≥30	4 (19.0)	9 (18.4)	1 (25.0)	2 (28.6)		
Classification of hospital					21.916 [†]	0.002 [‡]	
Other	2 (9.5)	1 (2.0)	0	0			
Tertiary General Hospital	6 (28.6)	30 (61.3)	2 (50.0)	2 (28.6)			
Tertiary Specialized Hospital	6 (28.6)	17 (34.7)	1 (25.0)	2 (28.6)			
Private Hospital	7 (33.3)	1 (2.0)	1 (25.0)	3 (42.8)			
Total	. ,	21	49	4	7		

* Statistical significance was analyzed by chi-square test. † Statistical significance was analyzed by Fisher precise test. ‡ P<.01 was considered as significant.

Table 3

The regimen of propranolol treatment.

		Once/d	Twice/d	Three times/d	Other	χ^2 /Fisher	Р
Gender						6.762*	.058
	Female	2 (13.3)	20 (38.5)	7 (58.3)	0		
	Male	13 (86.7)	32 (61.5)	5 (41.7)	2 (100.0)		
Age (year)		()	()	· · · · ·	· · · ·	8.364*	.480
	<30	2 (13.3)	1 (1.9)	0	0		
	30-39	2 (13.3)	17 (32.7)	5 (41.7)	1 (50.0)		
	40-49	6 (40.0)	19 (36.6)	4 (33.3)	0		
	≥50	5 (33.4)	15 (28.8)	3 (25.0)	1 (50.0)		
Title		()	()	· · · · ·	· · · ·	19.126 [*]	.053
	Chief/Professor	2 (13.3)	25 (48.1)	3 (25.0)	1 (50.0)		
	Assistant Chief/Assistant Professor	3 (20.0)	12 (23.1)	6 (50.0)	0		
	Attending	8 (53.3)	13 (25.0)	2 (16.7)	1 (50.0)		
	Resident	1 (6.7)	2 (3.8)	1 (8.3)	0		
	Other	1 (6.7)	0	0	0		
Length of practice (year)						6.831*	.653
	<10	2 (13.3)	7 (13.5)	3 (25.0)	1 (50.0)		
	10–19	4 (26.7)	18 (34.6)	5 (41.6)	0		
	20-29	5 (33.3)	18 (34.6)	2 (16.7)	0		
	≥30	4 (26.7)	9 (17.3)	2 (16.7)	1 (50.0)		
Classification of hospital						27.377*	.000
	Other	2 (13.3)	1 (1.9)	0	0		
	Tertiary General Hospital	3 (20.0)	30 (57.7)	6 (50.0)	1 (50.0)		
	Tertiary Specialized Hospital	2 (13.3)	18 (34.6)	6 (50.0)	0		
	Private Hospital	8 (53.4)	3 (5.8)	0	1 (50.0)		
Total		15	52	12	2		

* Statistical significance was analyzed by Fisher precise test. $^{\dagger}P < .01$ was considered as significant.

		No Dose Escalation	Dose Escalation	χ^2 /Fisher	Р
Gender				0.958*	.328
	Female	7 (28.0)	22 (39.3)		
	Male	18 (72.0)	34 (60.7)		
Age (year)	No Dose Escalation Dose Escalation χ^2 /Fisher 0.958* 0.958* Female 7 (28.0) 22 (39.3) Male 18 (72.0) 34 (60.7) <30	.126			
	<30	0	3 (5.4)		
	30–39	4 (16.0)	21 (37.5)		
	40–49	11 (44.0)	18 (32.1)		
	≥50	10 (40.0)	14 (25.0)		
Title				1.372 [†]	.926
	Chief/Professor	11 (44.0)	20 (35.7)		
	Assistant Chief/Assistant Professor	7 (28.0)	14 (25.0)		
	Attending	6 (24.0)	18 (32.1)		
	Resident	1 (4.0)	3 (5.4)		
	Other	0	1 (1.8)		
Length of practice (year)		mose dose escalation or not in propranolol treatment with different characteristics. No Dose Escalation $\chi^2/Fisher P 0.958* .32 Female 7 (28.0) 22 (39.3) Male 18 (72.0) 34 (60.7) <30$.413		
	<10	2 (8.0)	11 (19.6)		
	10–19	8 (32.0)	19 (33.9)		
	20-29	8 (32.0)	17 (30.4)		
	≥30	7 (28.0)	9 (16.1)		
Classification of hospital				1.214 [†]	.817
	Other	1 (4.0)	2 (3.6)		
	Tertiary General Hospital	11 (44.0)	29 (51.8)		
	Tertiary Specialized Hospital	8 (32.0)	18 (32.1)		
	Private Hospital	5 (20.0)	7 (12.5)		
Total		25	56		

P<.01 was considered as significant.
* Statistical significance was analyzed by chi-square test.
† Statistical significance was analyzed by Fisher precise test.

Table 5							
The dose of atenolol	treatment.						
		1 mg/kg/d	2 mg/kg/d	3 mg/kg/d	Other	χ^2 /Fisher	Р
Gender						1.074*	1.000
	Female	5 (26.3)	3 (30.0)	0	0		
	Male	14 (73.7)	7 (70.0)	1 (100.0)	2 (100.0)		
Age (year)						7.539*	.758
	<30	2 (10.5)	0	0	0		
	30–39	7 (36.8)	2 (20.0)	1 (100.0)	0		
	40–49	6 (31.6)	4 (40.0)	0	1 (50.0)		
	≥50	4 (21.1)	4 (40.0)	0	1 (50.0)		
Title						11.355*	.957
	Chief/Professor	5 (26.2)	4 (40.0)	0	1 (50.0)		
	Assistant Chief/Assistant Professor	6 (31.6)	2 (20.0)	1 (100.0)	0		
	Attending	6 (31.6)	4 (40.0)	0	1 (50.0)		
	Resident	1 (5.3)	0	0	0		
	Other	1 (5.3)	0	0	0		
Length of practice (year)						8.092*	.525
	<10	5 (26.3)	2 (20.0)	0	0		
	10–19	6 (31.6)	2 (20.0)	1 (100.0)	0		
	20–29	5 (26.3)	2 (20.0)	0	2 (100.0)		
	≥30	3 (15.8)	4 (40.0)	0	0		
Classification of hospital						9.274 [*]	.427
	Other	1 (5.3)	2 (20.0)	0	0		
	Tertiary General Hospital	8 (42.1)	7 (70.0)	1 (100.0)	1 (50.0)		
	Tertiary Specialized Hospital	4 (21.0)	0	0	0		
	Private Hospital	6 (31.6)	1 (10.0)	0	1 (50.0)		
Total		19	10	1	2		

Statistical significance was analyzed by chi-square test. $P\!<.01$ was considered as significant. * Statistical significance was analyzed by Fisher precise test.

Table 6

The regimen of atend	olol treatment.						
		Once/d	Twice/d	Three times/d	Other	$\chi^{\rm 2}/{\rm Fisher}$	Р
Gender						1.776*	.734
	Female	2 (16.7)	5 (35.7)	1 (20.0)	0		
	Male	10 (83.3)	9 (64.3)	4 (80.0)	1 (100.0)		
Age (year)						10.671 [*]	.261
	<30	2 (16.7)	0	0	0		
	30-39	2 (16.7)	5 (35.7)	3 (60.0)	0		
	40-49	3 (25.0)	6 (42.9)	2 (40.0)	0		
	≥50	5 (41.6)	3 (21.4)	0	1 (100.0)		
Title						16.426*	.155
	Chief/Professor	3 (25.0)	7 (50.0)	0	0		
	Assistant Chief/Assistant Professor	2 (16.7)	3 (21.4)	4 (80.0)	0		
	Attending	5 (41.7)	4 (28.6)	1 (20.0)	1 (100.0)		
	Resident	1 (8.3)	0	0	0		
	Other	1 (8.3)	0	0	0		
Length of practice (year)						7.656*	.641
	<10	2 (16.7)	4 (28.6)	1 (20.0)	0		
	10–19	2 (16.7)	4 (28.6)	3 (60.0)	0		
	20-29	5 (41.6)	3 (21.4)	1 (20.0)	0		
	≥30	3 (25.0)	3 (21.4)	0	1 (100.0)		
Classification of hospital						11.960*	.146
	Other	2 (16.7)	1 (7.1)	0	0		
	Tertiary General Hospital	4 (33.3)	10 (71.4)	3 (60.0)	0		
	Tertiary Specialized Hospital	1 (8.3)	1 (7.1)	2 (40.0)	0		
	Private Hospital	5 (41.7)	2 (14.3)	0	1 (100.0)		
Total		12	14	5	1		

P < .01 was considered as significant.

* Statistical significance was analyzed by Fisher precise test.

The results showed no difference between doctors chose dose escalation or not in propranolol treatment with different characteristics (Table 7).

There was a significant difference between doctors with atenolol experience or not from different classification of hospitals. Most doctors favored the acceptability of atenolol from tertiary general hospitals (53.1%) (Table 8).

4. Discussion

The main goal of IH treatment is to control its rapid proliferation or eliminate its impairment of vital organs. Oral B-blockers play an important role in the management of IH. Propranolol has been increasingly used for the treatment of severe IHs since 2008. Several consensus guidelines on oral propranolol have been published mainly as suggestions, with regimen adjustments at the mercy of the prescriber.^[7,9] As more doctors have begun using oral propranolol as the first-line therapy for IH, side effects from the drug have been reported with increasing frequency. Atenolol, a hydrophilic, second generation selective beta-1 blocker, could be an alternative and associated with fewer side effects in the treatment of IH.^[10] There are no current published guidelines for the use of atenolol in the management of IH, although its use is becoming increasingly common attributing to its confirmed efficacy, accessibility, and favorable side-effect profile.[3,10,11] In a survey conducted in 2015, IHs were mainly treated by oral and maxillofacial surgeons and plastic and reconstructive surgerons in mainland China.^[12] In this survey, most respondents belonged to board-certified doctors of stomatology (25.93%), vascular surgery (17.28%) and plastic surgery (16.05%). In an AHRQ review, a multidisciplinary, multi-institutional expert panel and a European expert consensus group recommend an initial dose of 1 mg/kg/d and a maintenance dose of 2 to 3 mg/kg/d.^[13] In this survey, 55 (67.90%) of the respondents following medication guidelines of propranolol titrated the dosage up to the target dose according to the patients' age, weight, and response.

Although propranolol treatment in IH patients has been used for over 10 years, the dosage varies from doctor to doctor. A British guideline supports 2 mg/kg/d as the maintenance dose and a maximum of 3 mg/kg/d if necessary.^[8] The latest medication guideline in the USA suggests that clinicians should dose propranolol between 2 and 3 mg/kg/d unless there are comorbidities or side effects that necessitate a lower dose.^[7] Currently, the recommended dosage of oral propranolol in the guideline from mainland China is 1.5 to 2 mg/kg/d.^[14] Our previous practice showed oral propranolol in the dose of 2 mg/kg/d was effective in 90% IH cases.^[15] In this study, the dosage of oral propranolol in mainland China was not uniform either and this inconsistency showed significant differences among different levels of healthcare institutions.

Similarly, available data do not permit evidence-based recommendations on the dosing frequency of oral propranolol, but officially approved drug both European Union and USA regulators labeling is for twice-daily dosing. A study on propranolol pharmacokinetics in patients treated for IH supported the use of twice-daily dosing preferably to 3-times-daily dosing^[16]. In our survey, most doctors from tertiary hospitals choose 2 mg/kg/d twice daily, while most of those in private practice choose 1 mg/kg/d once daily. These results may implicate that most of the doctors from tertiary hospitals in mainland China are on the upper level of knowledge hierarchy and have more experience and better ability in the treatment of IH. Meanwhile, it is worth noting that only doctors from tertiary hospitals used the dose of 3 mg/kg/d, and that there is significant

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	 1-1	

The differences between doctors	chose dose escalation	or not in atenolol treatment with	different characteristics.

		No Dose Escalation	Dose Escalation	χ^{2} /Fisher	Р
Gender Age (year) Title Length of practice (year) Classification of hospital				0.042*	.838
	Female	5 (29.4)	3 (20.0)		
	Male	12 (70.6)	12 (80.0)		
Gender Age (year) Title				1.261 [†]	.825
	<30	1 (5.9)	1 (6.7)		
	30–39	5 (29.4)	5 (33.3)		
	40–49	5 (29.4)	6 (40.0)		
	≥50	6 (35.3)	3 (20.0)		
Title			х <i>У</i>	2.082 [†]	1.000
	Chief/Professor	5 (29.4)	5 (33.3)		
	Assistant Chief/Assistant Professor	5 (29.4)	4 (26.7)		
	Attending	6 (35.3)	5 (33.3)		
	Resident	1 (5.9)	0		
	Other	0	1 (6.7)		
Length of practice (year)				3.385*	.336
0 1 0 /	<10	3 (17.6)	4 (26.7)		
	10–19	6 (35.4)	3 (20.0)		
	20–29	3 (17.6)	6 (40.0)		
	≥30	5 (29.4)	2 (13.3)		
Classification of hospital			х <i>У</i>	2.299*	.513
	Other	1 (5.9)	2 (13.3)		
	Tertiary General Hospital	10 (58.8)	7 (46.7)		
	Tertiary Specialized Hospital	1 (5.9)	3 (20.0)		
	Private Hospital	5 (29.4)	3 (20.0)		
Total	·	17	15		

 $P{<}.01$ was considered as significant. * Statistical significance was analyzed by chi-square test.

⁺ Statistical significance was analyzed by Fisher precise test.

Table 8

The differences between doctors have atenolol experience or not with different characteristics.

		No Atenolol experience	Atenolol experience	χ^2 /Fisher	Р
Gender				2.686*	.101
	Female	21 (42.9)	8 (25.0)		
	Male	28 (57.1)	24 (75.0)		
Age (year)				0.974*	.807
	<30	1 (2.0)	2 (6.3)		
	30-39	15 (30.6)	10 (31.3)		
	40-49	18 (36.8)	11 (34.3)		
	>50	15 (30.6)	9 (28.1)		
Title		× ,	× 7	2.983 [†]	.607
	Chief/Professor	21 (42.9)	10 (31.3)		
	Assistant Chief/Assistant Professor	12 (24.5)	9 (28.1)		
	Attending	13 (26.5)	11 (34.4)		
	Resident	3 (6.1)	1 (3.1)		
	Other	0	1 (3.1)		
Length of practice (year)				1.798 [*]	.615
0 1 0 /	<10	6 (12.2)	7 (21.9)		
	10–19	18 (36.7)	9 (28.1)		
	20-29	16 (32.7)	9 (28.1)		
	>30	9 (18.4)	7 (21.9)		
Classification of hospital				16.546 [*]	.001 [‡]
	Other	0	3 (9.4)		
	Tertiary General Hospital	23 (46.9)	17 (53.1)		
	Tertiary Specialized Hospital	22 (44.9)	4 (12.5)		
	Private Hospital	4 (8.2)	8 (25.0)		
Total	,	49	32		

 $^{\ast}\mbox{Statistical significance was analyzed by chi-square test.}$

[†] Statistical significance was analyzed by Fisher precise test.

 ^{+}P <.01 was considered as significant.

difference in whether atenolol was used by doctors from different levels of healthcare institutions in mainland China. The above results indicate that doctors from higher-level hospitals are more aggressive and experienced than those in private practice. Although the lower dose seems to be helpful to reduce drug-induced risks, the lower dose may cause less effectiveness which could lead to longer duration of treatment or being hard to make the rapid proliferation of IH resolve rapidly.

There are still no consensus guidelines on oral atenolol in the management of IH. Small cohort studies of oral atenolol showed comparative effectiveness versus propranolol and positive effects on IH resolution with few side effects. In a reliable RCT, investigators randomized 23 patients from 1 to 15 months old with problematic IH to receive oral atenolol (1 mg/kg/d once daily) or oral propranolol (2 mg/kg/d 3 times daily) for 6 months. Seven of 13 patients randomized to atenolol had complete response (53.8%) compared with 6 of 10 children randomized to propranolol (60%) (P=.68). Upon withdrawal of treatment, 4 (40%) children treated with propranolol and two (15.4%) treated with atenolol had rebound growth^[16]. In our survey, we notice that 81 respondents (100%) stated that they chose oral propranolol for the treatment of IHs and 32 respondents (39.51%) stated that they used atenolol for the management of IH in mainland China, which meant that the acceptability of atenolol was much less than that of propranolol among prescribers. Currently, oral atenolol has not been recommended as first-line therapy for the management of IH in guidelines. However, oral atenolol with seemingly fewer side effects has demonstrated similar safety and effectiveness to oral propranolol. Oral atenolol may serve as another first-line treatment for IH to give doctors and patients more choices.

The major limitation of this study is the small sample size. Moreover, although our study revealed that oral atenolol may serve as another first-line treatment for IH in order to give doctors and patients more choices, further investigation regarding the effectiveness and outcomes of oral atenolol therapy for IH is imperative.

5. Conclusions

In conclusion, oral atenolol will become another first-line therapy for IH in mainland China, which can give doctors and patients more choices. This survey is helpful to standardize and develop a guideline for oral atenolol therapy.

Author contributions

Conceptualization: Jia-Wei Zheng. Data Curation: Ze-Liang Zhao, Chao Liu, Qi-Zhang Wang. Formal Analysis: Ze-Liang Zhao, Chao Liu. Funding Acquisition: Chao Liu, Jia-Wei Zheng. Investigation: Ze-Liang Zhao, Chao Liu, Qi-Zhang Wang. Methodology: Ze-Liang Zhao, Chao Liu, Qi-Zhang Wang.

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- Visualization: Ze-Liang Zhao, Chao Liu.
- Writing original draft preparation: Ze-Liang Zhao, Chao Liu.
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