A Successful 9 year Journey by a China-Canada Professional Group to Transfer Current Hemophilia Assessment Tools from Canada to Advance Pediatric Hemophilia Care in China.

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INTRODUCTION

Hemophilia Treatment Centers (HTC) Development, China: A great leap forward since WFH launched priority project in China in 2000.

2 Landmark Developments

(1) 2004: Inauguration Hemophilia Treatment Center Collaborative Network China (HTCCNC) with 6 core centers, laying the corner stone for development

(2) 2015: Landmark achievement of 50 HTCs established across China **creating an urgent demand in professional training.** (Figure 1).

Figure 1. Map of 50 HTCs

Cost constraints

- A major road block in treatment
- Estimate 40,000 – 50,000 hemophilia boys at risk for early joint disease by school age. **Urgent need for lower cost effective replacement treatment intervention.**

China/Canada Collaborative Working group

Hemophilia care professionals with specific interest and experiences in China, from Beijing and Guangzhou, China, Toronto, Ottawa, and Calgary, Canada formed a collaborative Working Group to implement teaching and training and transfer current hemophilia assessment tools from Canada to China thus enhancing care for boys with hemophilia and research within China. (Table 1)

Table 1. China/Canada Collaborative Working Group

CHINA	CANADA
Beijing Children Hospital Beijing Dr R Wu, Chair, Pediatric Group (HTCCNC)	**Hospital for Sick Children Toronto** Dr V Blanchette, Chair, Collaborative Group Chair, International Prophylaxis Study Group
Nanfang Hospital Guangzhou Dr J Sun, Chair, Nursing and Prophylaxis group	**Children's Hospital of Eastern Ontario** Dr K H Luke, WFH Consultant, China
Peking Union Medical College Hospital, Beijing Dr L Chen chair Physiotherapy Group	**Foot Hills Hospital Calgary** Dr M C Poon, WFH Consultant, China

METHODS

The cross cultural adaptation of each tool required four steps:

A. Translate the methods and procedures into Simplified Chinese.
B. Conduct focus group meetings with patients/parents and healthcare professionals to resolve culturally sensitive language and practical issues.
C. Train local professionals to utilize the tools.
D. Conduct a validation study for use in China.

RESULTS

The schedule to transfer the assessment tools were prioritized in accordance with the progress of development in China

ADAPTATION AND RELIABILITY – HEMOPHILIA JOINT HEALTH SCORE (HJHS) V2.1

2008 - 2009
Forward/Backward translation - HJHS V2.1

2009 August
Train the Trainer Workshop on Hemophilia Physiotherapy- 6 Trainees completed training. [1]

2009 November
Reliability study, Guangzhou. 4 Trainees as assessors.
Inter-rater r = 0.9; Intra-rater r = 0.91 Reliability confirmed. [2]

ADAPTATION AND VALIDATION OF CANADIAN HEMOPHILIA OUTCOMES - KIDS LIFE ASSESSMENT TOOL (CHO-KLAT) V 2.0

2008 - 2009 Forward/backward translation into simple Chinese.

2009 – 2010 Focus group meetings by patients/parents from rural and urban.

- **All 35 question relevant.**
- 9 additional questions elicited addressing social economical difference in China. **These are grouped separately as a module for Socioeconomic conditions (SEC).**

2010 – 2011 Cognitive debriefing session to test wording and interpretation.
2011 A consensus meeting at BCH to adapt the Chinese CHO-KLAT version 2.0
2012 Validation Study: 4 HTCs across China. BCH (Northern), Nanfang (Southern), Hefei (Eastern), Chengdu(Western) . Child and parent each completed the PedsQL and CHO-KLAT twice, 1 - 2 weeks apart.
Validity compared to PedsQL r = 0.65 for boys r = 0.66 for parents.
Intra-rater (test retest) r = 0.88 for boys r = 0.90 for parents Validity confirmed [3,4]

IMAGING STUDY BY MRI and ULTRASOUND

2011 Dr NN Zhang: 6 month training at HSC Toronto under Dr A Doria.
2015 Image training workshop at BCH and Nanfang Hospital by Dr A Doria and BCH team Patient Acquisition study comparing MRI and U/S findings on 6 index joints on 36 severe hemophilia boys. **Manuscript and guidelines, and U/S scoring to be completed in Aug 2016.** 1 MRI and 1U/S radiologist trained at Nanfang Hospital.

PHARMACOKINETIC STUDIES - 2015

2015 Dr N Chen: Coagulation training on FVIII, Inhibitor Assays and Quality control practices in Canada: Kingston and Toronto, with visit to Winnipeg and Calgary. **Preliminary PK studies began on Chinese hemophilia boys at BCH.**

SUCCESSFUL OUTCOMES

PEDIATRIC HEMOPHILIA CARE DEVELOPMENT

BCH team completed training and leads as Chair for Pediatric Forum, 2008 – 2010, Annual WFH Pediatric Workshop and **Dr. Wu established Pediatric Hemophilia Working Group, 2014. Recognized by MOH as a model centre for comprehensive pediatric hemophilia care in China.**

CLINICAL TRIALS

- 3 pilot low dose prophylaxis studies [5,6,7]

Pilot study	Analyzable # of Patients	Prophylaxis Duration (10 u / kg)	Mean ABR on Prophylaxis	% Reduction
SHORT TERM Single Centre BCH	34	BIW for 3 months	12	80
SHORT TERM Multicentre	66	BIW for 6 weeks to 3 months	9	79
LONG TERM Single Centre BCH	6	BIW for 18 months	11.3	75
		TIW for 12 months	4.8	93

- 3 Quality of Life studies

Time	Study	# of patients/ parents	CHO-KLAT	
			Boys	Parents
2012	Validation Study (4 centers: BCH, Chengdu, Anhui, Nanfang)	60	63	58
2012	PAC Study 5 Centers: BCH, PUMC, Tianjin, Wuhan, Nanfang	30	60	53
2014	Pediatric Working Group Survey 13 Centres Canada	310	57 74	55 73

PROFESSIONAL TRAINING

May 2015: Multidisciplinary team building training on coagulation, HJHS, image MRI/ultrasound and CHO-KLAT at Chengdu to enhance comprehensive care and capacity for clinical research.

CHIP study China, to be launched 2016

A multicentre, long term, 1-year perspective, secondary escalating dose, prophylaxis study on Chinese severe hemophilia A boys using four low dose FVIII regimens.

DISCUSSIONS

The challenge to close the gap in Pediatric hemophilia care in China is daunting. 40,000 – 50,000 hemophilia boys are at risk. With the record growth in economy in China, social medical support for the PWH has improved in many developed regions. However, poor support and insurance in rural and poorer regions will remain very suboptimal.

A high priority is to develop lower cost effective treatment for urgent interim intervention. Two proposed clinical trials are ready for grant submission:

1. A randomized controlled 2 years long term individualized prophylaxis study comparing PK dosing and low dose regimens in CHINESE hemophilia A boys.
2. A two year long term Radiogenomic study on Chinese hemophilia boys .

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