

# **Eventi emorragici potenzialmente fatali e/o gravemente invalidanti nel bambini con emofilia**

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# EMORRAGIA INTRACRANICA

- **Incidenza:** rischio maggiore nel 1°(24,4 per 1000) 2° anno di età (14,9 per 1000).
- **Durante il periodo neonatale:** 3,5– 4,0%, oltre 40–80 volte maggiore rispetto alla popolazione normale. **In seguito, 3-10%.**
- **Su 536 visite, effettuate in un periodo di 5aa in un reparto pediatrico di emergenza , a 84 emofilici, età mediana 4aa (range 0-21), è stata diagnosticata un'emorragia intracranica in 5 visite (0,93%).**

# EMORRAGIA INTRACRANICA

- ***Cause predisponenti***: gravità del difetto e presenza dell'inibitore fortemente associate all'evento : *grave vs. lieve*, **HR 3,96** (2,39-6,57); *inibitore vs. non-inibitore* **HR 2,52** (1,46-4,35)].
- ***Cause immediate e concause***: trauma da parto, trauma accidentale da caduta, trauma da contraccolpo, angiomi ed ectasie vascolari, febbre elevata, assunzione inappropriata di FANS.....

# ***Guideline on the management of haemophilia in the fetus and neonate. Chalmers E et al. BJH 2011***

## **Recommendations**

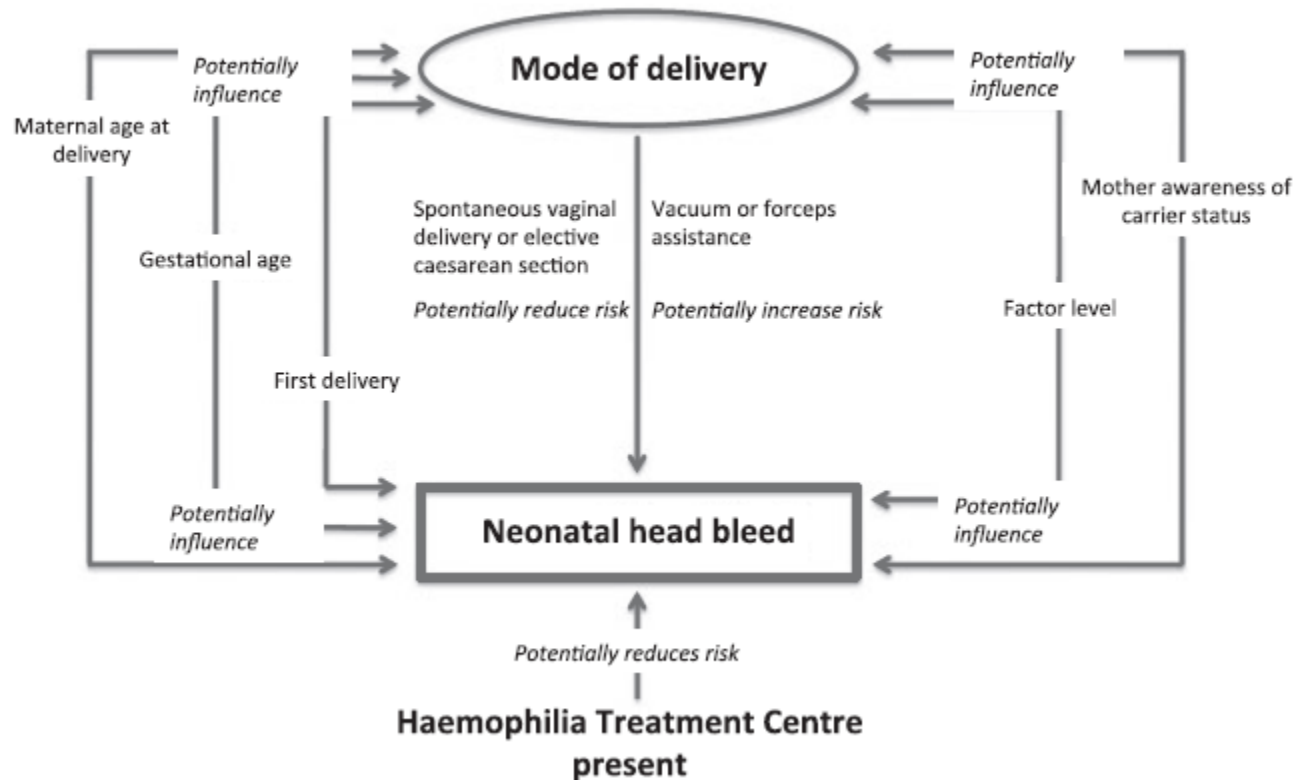
- Mode of delivery should be informed by both obstetric and haemostatic factors; haemophilia carrier status itself is not a contraindication to vaginal delivery (1C).
- The option of elective caesarean section in an attempt to reduce the risk of neonatal ICH may be considered on an individual basis, taking into account knowledge of the fetal haemophilia status and potential maternal morbidity (2C).
- Ventouse extraction, rotational and mid-cavity forceps are associated with an increased risk of bleeding and should be avoided (1A).
- Invasive monitoring procedures, such as placement of intrapartum scalp electrodes and fetal scalp blood sampling, should be avoided (1C).
- Decisions regarding the management of labour should always involve a consultant (1C).

***Neonatal bleeding in haemophilia: a European cohort study.  
Richards M et al. BJH 2012***

- 508 children with haemophilia A or B, born between 1990 and 2008.
- ***Head bleeds occurred in 18 (3.5%)*** within the first 28 d of life: **3** intraparenchymal bleeds, **1** subdural haematoma and **14** cephalohaematomas. Long-term **neurological sequelae in two (0.4%) cases**; no deaths occurred.
- ***Assisted delivery (forceps/vacuum) was the only risk factor for neonatal head bleeding (OR 8.84: 95% CI: 3.05–25.61).***
- ***Mild haemophilia and maternal awareness of her haemophilia carrier status seemed to be protective.***

# *Neonatal bleeding in haemophilia: a European cohort study.*

*Richards M et al. BJH 2012*



*Associations between intracranial haemorrhage and prescribed prophylaxis in a large cohort of haemophilia patients in the United States. Witmer C et al. BJH 2011*

***Prophylaxis*** was associated with a **significant risk reduction for ICH occurrence in patients with severe haemophilia** who were negative for human immunodeficiency virus or an inhibitor, with an **OR of 0.52 (0.34–0.81)** and **0.50 (0.32–0.77)**, respectively.

# EMORRAGIA INTRACRANICA

## *Diagnosi e trattamento*

- *Mai sottovalutare un trauma cranico, anche in assenza immediata di sintomi*
- *Dopo un trauma cranico, eseguire subito terapia sostitutiva ad alte dosi ed iniziare osservazione del piccolo paziente*
- *Eseguire esami diagnostici radiologici: TAC, RMN se del caso*



# EMORRAGIE GASTRO-INTESTINALI

- *Rare nei bambini in generale, accadono anche raramente nei bambini con emofilia*
- **Cause:** stati infettivi/inflammatori del tratto gastrointestinale, infezione da *Helicobacter pylori*, uso non appropriato di FANS, traumi, presenza di alterazioni locali.

# EMORRAGIE GASTRO-INTESTINALI

- *Upper gastrointestinal bleedings in patients with hereditary coagulation disorders in Northwest of Iran: prevalence of Helicobacter pylori infection* Dolatkhan R et al. Eur J Gastroenterol Hepatol 2011

**“H. pylori infection should be considered as an important cause of UGI bleeding in PWH”**

- *Upper gastrointestinal bleeding in children with haemophilia: a clinical significance of Helicobacter pylori infection* Choe BH et al. Haemophilia 2010

**“In children with haemophilia, H. pylori should also be considered as an important cause of GI bleeding. The recurrence of the infection and GI bleeding can be prevented with eradication of H. pylori. Screening test for H. pylori would be needed in children with haemophilia in endemic area”**

# EMORRAGIE GASTRO-INTESTINALI

- *Life-threatening haemorrhage from a gastric Dieulafoy lesion in a child with haemophilia.* Pitcher GJ et al. Haemophilia 2002

“A 5-year-old boy, diagnosed with haemophilia A at 3 months of age, experienced 3 episodes of massive haematemesis. A fiberoptic endoscopy was performed and then a laparotomy → diagnosis of Dieulafoy lesion (DL). DL, or calibre-persistent artery of the stomach, accounts for less than 2% of all acute upper GI bleeding episodes. The abnormal blood vessel is thought to be an anatomical variant, with persistence of the calibre of a subserosal vessel as it penetrates the muscularis propria”.

- *Solitary Rectal Ulcer: a rare cause of gastrointestinal bleeding in an adolescent with hemophilia A.* Bishop PR et al. J Clin Gastroenterol 2001

“An adolescent with hemophilia A who presented with a massive lower gastrointestinal bleed caused by a solitary rectal ulcer”.

# EMORRAGIE GASTRO-INTESTINALI

- *Endoscopic diagnosis of intramural hematoma in the colon sigmoideum in a child with high titer inhibitory hemophilia A.* Yankov IV et al. Folia Med (Plovdiv) 2014

- A 7-year-old child with diagnosed hemophilia A and high titer of factor VIII inhibitor.

The patient was admitted for rectorrhagia after falling onto his buttocks while playing.

Colonoscopy showed submucosal hematoma 25 cm from the anocutaneous line occluding the intestinal lumen with a lesion of the overlying mucosa as long as 20 mm.

# EMATOMA DEL M. ILEO-PSOAS

- *Ematomi muscolari* costituiscono il 10-25% degli episodi emorragici nell'emofilia grave.
- Una cross-sectional survey sul management degli ematomi muscolari condotta in 22 Centri, ha evidenziato *un'incidenza 492 ematomi muscolari/anno, in media 25/Centro*, prevalentemente associati a trauma.
- Sedi dei più gravi : ileopsoas 55%; polpaccio 18%; coscia 18%

# EMATOMA DEL M. ILEO-PSOAS

- *Iliopsoas haemorrhage in patients with haemophilia: results from one centre* Balkan C et al. Haemophilia 2005
- *Iliopsoas haematoma is a well-recognized complication of haemophilia, and is considered as potentially life threatening and significantly associated with morbidity. On 146 haemophiliacs (106 haemophilia A, (mean age  $14.9 \pm 7.5$  y, 40 haemophilia B, mean age  $12.3 \pm 6.1$  ), 14 iliopsoas bleeding episodes were identified in eight haemophiliacs (5.5%).*
- *No episodes in six patients receiving prophylaxis.*
- *Iliopsoas haematomas were confirmed by US in all patients.*
- *The most common symptoms: thigh, hip and groin pain, hip flexion contracture, abdominal tenderness and paraesthesia in the distribution of the femoral nerve.*

# EMATOMA DEL M. ILEO-PSOAS

- **Iliopsoas hematoma in patients with hemophilia: a single-center study**  
*Dauty M et al. Joint Bone Spine 2007*
- *Six cases of iliopsoas hematoma were diagnosed in 5 /410 patients (1.2%) with hemophilia over a 5 year-period : 4 had severe hemophilia A and 1 had moderate hemophilia A with a history of inhibitors to factor VIII ; age range: 13-33y.*
- *Hematoma was post-traumatic in 2 cases and spontaneous in 4 cases. Femoral nerve compression developed in 2 cases. There were four recurrences.*
- *An early diagnosis allows early Factor VIII therapy, which decreases the risk of femoral nerve involvement and recurrence.*
- *The use of prophylactic factor VIII therapy and compliance with recommendations about avoiding activities that put strain on the hip flexor muscles probably explain the low rate of iliopsoas muscle hematoma in patients with hemophilia in France.*

# ALTRI EMATOMI MUSCOLARI

- *Spontaneous obturator internus muscle haematoma: a new unpublished cause of iliopelvic pain in haemophilia.* Aouba A et al. Haemophilia 2011

Spontaneous obturator internus haematoma in two haemophilia children with inhibitor. Clinical feature was marked by an iliopelvic pain letting discussing hip haemarthrosis, appendicitis or iliopsoas haematoma. For both patients US failed to provide the diagnosis, which was possible by CT and MRI

- *Bilateral recurrent external obturator muscle hematoma: An unusual cause of pelvic pain in hemophilia.* Arpaci T et al. Molecular and clinical oncology 2016

Spontaneous bleeding of the bilateral external obturator muscles, which occurred three times within a period of 9 months in a hemophilia patient (22 y) with factor VIII inhibitors. Diagnosis : MRI