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Ingestible Sensor Capsule with Extended Battery Capacity Allows Early Diagnosis of GI Malignancy in Comorbid Patients with Occult Bleeding and Anemia

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PE, KS, WU, WES, CTR do not have any relevant potential conflict of interest

Abstract:

HemoPill is a commercially available ingestible electronic capsule that detects hematin and blood through photometric measurements. An examination with HemoPill requires no special preparation and can be done bedside. Its major advantage is the non-invasive luminal blood detection, requiring only small amount of blood or hematin (> 20 ml) for a positive result, making it especially suitable in multimorbid and/or geriatric patients not primarily fit for endoscopic diagnostic allowing rapid and uncomplicated bleeding detection.

Recent clinical reports showed that HemoPill is useful in stratifying patients with anemia and bleeding in the setting of an emergency department. The second generation with an extended battery capacity of nine hours opens the possibility to detect blood in the middle and lower gastrointestinal (GI) tract.

Herein we report another advantage of the extended battery capacity allowing non-invasive bleeding detection in the middle and lower GI tract, leading to early endoscopic diagnosis of GI-malignancies with occult bleeding in comorbid patients with severe anemia.

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[...]



Introduction:

HemoPill is a swallowable electronic capsule (Fig. 1a) that detects hematin and blood through photometric measurements, which are wirelessly transmitted every 4 seconds to a proprietary receiver (Fig. 1b), which is put in a single-use bag that is worn by the patient during the examination. The photometric measurements are plotted over time and displayed as the “HemoPill Indicator” (HI) with a HI reaching the red marked zone on the receiver display indicating the detection of intraluminal blood or hematin (Fig 1b and Fig.2a). Preclinical studies showed that it diagnoses bleeding in the gastric lumen with high sensitivity and specificity [1], with measurements being robust to the effects of gastric content [1, 2]. Aside of an intact deglutition, an examination with HemoPill requires no special preparations other than a glass of water and can be done bedside. Its major advantage is the non-invasive luminal blood detection in multimorbid and/or geriatric patients not primarily fit for endoscopic diagnostic allowing rapid and uncomplicated bleeding detection. It is commercially available in Germany since 2019.

Recent clinical reports showed that it is useful in stratifying patients with anemia and bleeding in setting of an emergency department [3]. This study utilized the first capsule generation with a battery capacity of 2-3h allowing blood detection only in the upper GI tract. A recent update brought an increased battery capacity of nine hours opening the possibility to detect blood in the middle and lower GI tract, as shown by Brunk et al [4].

Herein we report another advantage of the extended battery capacity allowing a non-invasive bleeding detection in the middle and lower GI tract, leading to early and expedited endoscopic diagnosis of GI-malignancies in two patients with chronic bleeding leading to severe anemia.

First case:

A 56-year-old female patient was referred due to recurrent anemia and melena with a hemoglobin (Hb) concentration of 5 g/dl. A month before presenting to our unit she was admitted to another hospital, also due to severe anemia with a Hb of 3 g/dl. There, a colonoscopy was performed and revealed no sign of bleeding but a sigmoid tubular adenoma, which was thought to be the potential bleeding source and thus resected without complication. After the transfusion of three packs of red blood cells (pRBC) she was discharged with stable Hb and no further signs of bleeding. An upper GI study (EGD) was not performed for unknown reasons. Her medication was notable for apixaban as stroke prophylaxis due to atrial fibrillation.

In our unit an EGD was performed after transfusing 2 units of pRBC, revealing no intraluminal blood or other bleeding sign. She was scheduled for a repeat colonoscopy followed by standard capsule endoscopy but did not tolerate the bowel preparation due to stark nausea and recurrent vomiting. Thus, only sigmoidoscopy after an enema was performed revealing no signs of bleeding or abnormality at the site of the previous polypectomy. At this point no further clinical signs of bleeding or melena occurred and the Hb remained stable. She stayed inpatient for observation during which she suffered a syncope due to profuse melena. An urgent EGD again revealed no blood or bleeding in the upper GI tract. Since previous bowel preparation was not tolerated and deemed impossible after a syncope, HemoPill was utilized and placed directly into the duodenum using a snare during the urgent EGD. After one hour the receiver indicated a positive signal (Video 1). Since the receiver has no position indicator or

other geographical function, plain abdominal x-ray image was taken shortly afterwards, to approximate the location of the capsule and thus the source of bleeding. It was identified to be in the proximity of the Treitz ligament, suggesting a bleeding in the proximal jejunum. Urgent push enteroscopy was performed and revealed a sponge-like dark solid lesions with a large blood clot and active diffuse bleeding upon contact at ca. 90 cm from the incisors. The lesion was tattooed and hemoclips were placed for markings. Urgent computer tomography (CT) failed to identify the tumor in the jejunum and only the clips were seen. Surgical consult was requested, and a jejunum resection was performed. Intraoperatively a tumor was confirmed, which was shown to be an angiosarcoma in the pathology (Video 1).

Second case:

A 77-year-old female patient was referred due to severe anemia with a Hb of 5 g/dl without any clinical sign of bleeding. Due to obesity with a BMI of 37 kg/m² and her advanced age, we opted to postpone the endoscopic diagnostic and utilize HemoPill after previously transfusing 2 pRBC. After ca. 5 hours a positive signal was recorded (Fig. 2a). Plain abdominal X-ray shortly afterwards revealed the capsule to be in the projection of the coecum. Consequently, the patient was scheduled for a timely colonoscopy and bowel preparation was initiated (Fig. 2b). The colonoscopy showed a stenosis in the ascending colon (Fig. 2c), which proven to be malignant in the histology and a malignant polyp in the sigmoid, which was resected curatively during a second colonoscopy. No further tumor manifestation was seen in her staging allowing her to proceed to surgery confirming the diagnosis of a colon carcinoma.

Discussion:

These two cases showcased HemoPill's potential as a useful novel adjunct in our arsenal of non-invasive bleeding diagnostic tool in the upper, middle and lower GI tract. Due to its ease of use, not requiring any preparation other than intact swallowing and a glass of water, it is strongly suitable for use in geriatric or comorbid patients not primarily suitable for endoscopic examinations. In patients without intact swallowing and without any bleeding sign in EGD, HemoPill can be placed directly in duodenum allowing rapid blood detection in the middle and lower GI-Tract without the necessity of a bowel preparation. In contrast to a radiological study, such as CT or magnetic resonance imaging (MRI), it is immediately available, requires no contrast agent, which is beneficial in patients with chronic kidney failure. Due to its small size (approximately half the thickness of a standard capsule endoscopy) the chance of a retained capsule is widely reduced.

A major drawback of HemoPill compared to a contrast enhanced CT angiography, is the lack of an exact bleeding localization. Furthermore, the photometric results are only sent to a local receiver within a limited range of 50 cm which necessitates the patient to wear the receiver during the examination. Thus, multiple manual checks are needed to see if results turn positive and to schedule a timely plain abdomen study, which is currently necessary to estimate the HemoPill location (and hence the bleeding). In our cases the plain abdomen studies were taken approx. 30-60 min after the positive result. Had they been taken at a later time, it could have been more difficult to identify the site of the hemorrhage. Nevertheless, the X-ray results would still have been helpful, because the "hemorrhage search area" would be narrowed down to the capsule site and the area proximal thereof. Performing a CT-scan is an alternative to a plain abdomen study, which could provide an exact location of the capsule but can be

logistically challenging in a lot of units due to acute availability, especially on weekend and night. Furthermore, patients would also experience higher radiation exposure. In the first patient the actively bleeding tumor was not visible in the urgent CT scan despite the use of contrast agent.

The multiple manual checks represent an enormous challenge for the staff, especially if the patient is not able to check the result independently. In our experience these challenges can only be tackled with a strong nursing staff motivation along with patient and family empowerment to understand the importance of multiple receiver checks during the 9 hours study period and a timely performed abdomen imaging to estimate the capsule's location and with it, the bleeding source. Future technical improvements are needed to improve and facilitate capsule localization. A longer transmitting distance to the receiver or another alerting system for the nursing staff in case of a positive HI could also improve practicability, avoiding the need of multiple direct checking by the patients.

Compared to conventional pan-enteric video capsule endoscopy (PCE), a HemoPill is smaller at 7x26.3 mm (vs. PillCam Colon or Pillcam Crohn at 11.6x31.5 mm), offering a more comfortable swallowing experience and theoretically reduce the risk of capsule retention. Its biggest disadvantage is that it cannot offer any image from the GI tract, but it is also more practical, as it requires no fasting or any bowel preparation. While PCE's results can be unreliable if the view is obscured by bowel contents, HemoPill measurements are principally unaffected by recent meals or other intestinal or gastric content. Additionally, PCE recordings are typically reviewed a day after the capsule is swallowed, causing a delay in diagnosis, albeit not clinically significant in most patients. While some PCE devices offer a live feed on the receiver or through an external device connected to the receiver, this also demands high staff involvement for monitoring similar to Hemopill, if the patient could not do this independently. In contrast, HemoPill provides real-time results plotted directly on the receiver without needing an extra device. Moreover, HemoPill is less expensive than standard PCE in Germany. Just recently a study with another commercially available blood-detecting swallowable capsule has been published, showing promising results to detect active bleeding in the upper GI-tract [5]. The availability of this second blood-detecting capsule heralds a new dawn of non-invasive bleeding detection in clinical practice.

In summary HemoPill showed the potential to serve as a non-invasive diagnostic adjunct tool to detect GI bleeding especially in those primarily not suitable for extensive endoscopic diagnostic (e.g., comorbid or geriatric patients). Further studies (i.e., the "Rabbit"-Study, Study-ID: DRKS00026103) aim to clarify the potential of HemoPill as an alternative to video-capsule endoscopy in diagnosing bleeding in the middle GI tract. We believe the role of non-invasive diagnostics to detect upper, middle and lower GI bleeding would further increase in the future.

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Figure legends:

Figure 1: a) The swallowable bleeding sensor capsule, HemoPill, is measuring 26.3 mm x 7 mm with a measuring gap for the photometric measurements. b) Proprietary HemoPill receiver, which plots the photometric measurement results over time. This figure displays an example of a positive blood detection, showed by a HI within the red zone.
Source for both figures: Ovesco Endoscopy AG, Tübingen, Germany

Figure 2: a) positive HI indicating that blood has been detected five hours after swallowing the capsule with a maximum HI reached after 8 hours. b) Plain abdominal X-ray shortly after the positive HI: the Hemopill was approximately located in projection of the coecum. c) Colonoscopy revealed a non-traverseable stenosis, proven to be cancer in the histology.

Video legend:

The video showed the direct placement of the capsule to the duodenum during the urgent egd to expedite the diagnostic pathway and bypass the gastric passage. After ca. 1h the HI was positive indicating a positive blood detection. Soon after a plain abdominal x-ray was performed showing the capsule to be approximately at the level of the ligament of Treitz. Urgent push enteroscopy revealed a bleeding tumor in the jejunum, histologically confirmed as an angiosarcoma.

