ICT-Schisto

Prospective study on a rapid diagnostic test for schistosomiasis

performed on blood from fingerprick

Study protocol ed 2

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Introduction

Schistosomiasis is a parasitic infection caused by fluke worms of the genus *Schistosoma*. According to estimates, 200 million infected people are affected, in particular in sub-Saharan Africa. In Europe, the prevalence in African immigrants has been estimated to range from 6 to 25%.

Most infections are clinically mild or even asymptomatic for a long time. However, chronic infections can lead to severe complications, mainly involving the urinary (haematuria, hydronephrosis, squamous bladder cancer) and the gastrointestinal tract (mucosal granulomatous inflammation, pseudopolyposis, microulceration, bleeding, hepatosplenomegaly, portal hypertension).

The detection of the eggs of the parasite in stool and urine through microscopic examination is the gold standard for diagnosis. However, its sensitivity is unsatisfactory. Hence, numerous indirect, immunological tests have been implemented. According to the results of a diagnostic study (Beltrame et al, submitted), the immunochromatographic (rapid) test (ICT) demonstrated a high sensitivity (96%), with a negative predictive value of 97%. The specificity was about 80%. Therefore, it could be the ideal tool for screening purpose in non-endemic settings. Moreover, the execution of the test does not require highly-skilled staff nor highly-equipped laboratories: the blood sample is centrifuged, 30 µL of serum are added with a pipette to a cassette, followed by two drops of eluent (supplied with the kit). After 20 minutes, a positive test is defined by the appearance of a colored band (similarly to a pregnancy test).

Such a test could permit to implement screening programs for schistosomiasis also outside the (few) referral centres for tropical diseases in Italy, even in primary health care centers for immigrants. Particularly in the last setting, the use of the test on blood collected by fingerprick could make the screening more feasible. The use of a fingerprick instead of venipuncture would

minimize the biological risk for the staff. Moreover, it would not require even a minimal lab equipment (a centrifuge and pipettes). Globally, the execution of the test would be more rapid and of easier in settings dealing with the current high burden of migration flow.

Study objective

Aim of this study is to compare the results of the ICT performed on a blood drop obtained from fingerprick to the results of the same test executed according to current indications (on serum from venipuncture).

Methods

The study design is prospective.

Eligible participants will be selected among African immigrants admitted for any cause to the ward of the Centre for Tropical Diseases (CTD), Negrar.

Inclusion criteria:

- Age ≥18 years
- Females and males
- Exposure to epidemiological risk of infection (living in endemic areas, bathing in fresh water)
- Written consent to the study

Exclusion criteria:

- Impossibility of execution of one of the two study methods, for any reason

Study procedures

Preliminarily to the study onset, the nurses will receive a short training about the use of ICT by the lab staff.

During the study, the Investigators will seek written informed consent from all consecutive eligible patients admitted to the CTD ward.

A nurse will collect both blood samples from each patient, through two methods:

1. Venipuncture: blood collected in an EDTA tube, labeled with the patient's code
2. Fingerprick: blood drop directly added to the device

1. The sample in EDTA tube will be centrifuged and processed for ICT execution by the lab staff of CTD. The result will be read by two lab technicians. In case of discordant results, a third technician will read the test. The results will be registered in an electronic database.
2. The fingerprick will be performed by the same nurse for immediate execution of ICT in the ward. An investigator will be the second reader. In case of discordant results, a second investigator will be involved in reading. The nurse will write the patient's code in the CRF, checking that it matches with the code reported in the label of the corresponding EDTA tube. The nurse and the investigator(s) will independently report their the results in the CRF. The investigator will fill in remaining information required by the CRF (date, such as country of origin, sex).

In case two independent readers would report a result as indeterminate (essentially given by a very weak positive band), the result will be registered as such.

The Principal Investigator or a previously-identified Investigator will collect all CRFs, will match the information with the results obtained by the lab staff and will enter all required data, anonymously, in the study database (Excel file).

Primary outcome

Degree of concordance of the ICT performed after fingerprick with ICT performed on serum.

Statistical analysis

The concordance will be assessed using Cohen's Kappa coefficient.

The results of Cohen's kappa will be interpreted as follows:

Poor agreement = Less than 0.20

Fair agreement = 0.20 to 0.40

Moderate agreement = 0.40 to 0.60

Good agreement = 0.60 to 0.80

Very good agreement = 0.80 to 1.00

The use of ICT on blood spot will be recommended as a possible alternative to its use on serum only in case of kappa ≥ 0.8.

Sample size:

Expected prevalence of schistosomiasis in the study population is around 38%, according to a recent study (Beltrame et al, submitted). The sample size was calculated using the "R Studio" software (Open source Ed), considering alpha≤ 0.05, study power≥ 80%, one-sided test.

The number of patients to be included in the study resulted 69.

Ethical issues:

Ethical clearance from the competent Ethics Committee will be sought prior to the study onset. Written informed consent will be obtained from all included subjects.

Study-specific risks for patients enrolled are negligible, as finger prick is the only procedure that is not routinely executed on patients with schistosomiasis. Hence, there will not be a study-specific insurance coverage.