Quick Finger-prick Test Reliably Monitors Clozapine Levels

SCOTTSDALE, Arizona — A quick, inexpensive test that uses a drop of blood from a finger prick can be used to reliably detect and monitor therapeutic plasma levels of clozapine (multiple brands), new research shows.

"Therapeutic drug monitoring during clozapine treatment is very important, both to assess compliance and efficacy," Dan Cohen, MD, from the Mental Health Organization North-Holland North and the University of Groningen, the Netherlands, told Medscape Medical News.

"[Clozapine] is the only evidence-based drug in therapy-resistant schizophrenia, and resistance to it should be avoided whenever possible," Dr Cohen said.

"Moreover, fixed doses of clozapine can produce up to 45-fold interindividual variability in serum levels in patients with treatment-resistant schizophrenia. This could easily result in a false clozapine nonresponse in some patients, and this is why reliable therapeutic monitoring is so important."

Results of the test's accuracy were presented at the American Society of Clinical Psychopharmacology (ASCP) 2016 Annual Meeting.

Meeting a Need

In many countries, both developed and developing, therapeutic drug monitoring is not available.

"The challenge was to develop a technique that enables clozapine therapeutic drug monitoring to be made available in countries such as Russia, Israel, and Serbia, and also in African countries," Dr Cohen said.

The dried blood spot (DBS) technique has been used and validated in the screening of newborns for inborn errors of metabolism and also to monitor drug treatment of tuberculosis and epilepsy, he said.

The technique involves taking a drop of capillary blood from a finger prick, collecting it on filter paper, and letting the drop dry for 3 hours or longer.

The filter paper is then sent by mail to a laboratory that is equipped to determine the levels of drug that are contained in the dried blood sample.

The investigators assessed the DBS technique in 15 patients (mean age, 44 years) whose conditions were stable with clozapine treatment.

Blood sampling took place at 2, 4, 6, and 8 hours after clozapine intake. Blood samples were obtained from regular venous samples, and DBS samples were obtained from both venously sampled blood and capillary blood.

There was good coorelation between the results from venous samples and capillary DBS, Dr Cohen said.

"The dried blood spot analysis showed good linearity over the concentration time curve measured, and the accuracy and between- and within-day precision variation values, which we validated three times, were within accepted ranges, and bioequivalence was shown between all the different blood samples," he said.

The DBS samples were stable at 20° C (room temperature) for 2 weeks and at 5° C for 3 days.

"You can collect the blood wherever you are, and the only requirement is a postal service. You can send the filter paper to a laboratory in the Netherlands, or the US, or wherever they have the technique to punch the dried blood spot out of the filter paper and do some technical measurements to determine the drug level. The laboratory equipment costs about $350,000,
while the filter paper costs only $10.00," Dr Cohen said.

Results can be obtained in 2 weeks at the most, he said. "And for countries where there is no therapeutic drug monitoring available, 2 weeks is not very long, because for the first time, you get the results."

Reassuring Results

"Dr Cohen's group has introduced a very effective program to increase the comfort, knowledge, and awareness of clinicians in using clozapine, and the audience found his talk interesting and exciting," said Stanley N. Caroff, MD, professor, Perelman School of Medicine, University of Pennsylvania, in Philadelphia, when asked by Medscape Medical News to comment on the study.

"Clozapine is one of the few drugs in which the doctor can rely on plasma levels to determine if the drug is at a therapeutic level or at a toxic level, and so plasma levels can be very helpful in facilitating effective treatment. This new way of testing by using capillary blood is very cost-effective and much more convenient for both the patient and the physician. The hope is that this dried blood spot testing will help clinicians be more comfortable and more precise in using clozapine in treatment resistant schizophrenic patients," Dr Caroff said.

Dr Cohen and Dr Caroff have disclosed no relevant financial relationships.