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ACCURACY OF BIS(METHYLTIO)GLIOTOXIN IN DIAGNOSIS OF INVASIVE PULMONARY ASPERGILLOSIS: A COMPARATIVE STUDY WITH GALACTOMANNAN

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Objective:

To evaluate the accuracy of bis(methyltio)gliotoxin (a secondary metabolite produced by *Aspergillus*) in the diagnosis of invasive pulmonary aspergillosis (IPA) in serum samples.

Methods:

An observational study of 100 patients with haematological or oncological malignancies, and transplant recipients in a period of 6 months has been performed in a tertiary hospital in Spain

The European Organization for Research and Treatment of Cancer/Micology Study Group (EORTC/MSG) accepts GMN assay as criteria for IPA probable and proven definition, so we established case definition based on clinical manifestation: neutropenic patient with clinical manifestations of respiratory infection and new characteristic infiltrates on computed tomography imaging (dense, well-circumscribed lesion(s) with or without a halo sign, air-crescent sign, or cavity) and without other opportunistic pathogens.

Bis(methyltio)gliotoxin (bmGT) and galactomanan (GMN) were detected and quantified in a total of 298 serum samples. bmGT quantification was performed by High Performance Thin Layer Chromatography (HPTLC) and GMN detection by commercially available ELISA (Platelia Aspergillus Ag-BioRad). A GMN index higher than 0.7 and a bmGT value higher than 1mcg/ml were considered positive. Receiver Operating Characteristics curves were performed for comparing two diagnostics methods; area under curve (AUC), sensitivity, specificity, positive and negative predictive values were calculated.

Results:

According to the case definition, 38 samples (13.6%) of patients with IPA were analyzed: GMN was positive in 10 serum, and negative in 28. bmGT was positive in 16 samples and negative in 22.

From the 283 samples of patients without IPA, GMN was positive in 15 samples and negative in 268. bmGT was positive in 9 samples and negative in 274.

Statistical analysis showed an AUC of 0.611 for GMN and 0.682 for bmGT as we can see in Graphic 1.

Sensitivity and specificity were 26.3% and 94.7% for GMN and 42.1% and 96.8% for bmGT respectively. Positive predictive value (PPV) was 40% for GMN and 64% for bmGT. Negative predictive value (NPV) was 90.6% for GMN and 92.6% for bmGT (see Table 1).

Graphic 1: ROC Curve for bmGT and GMN.

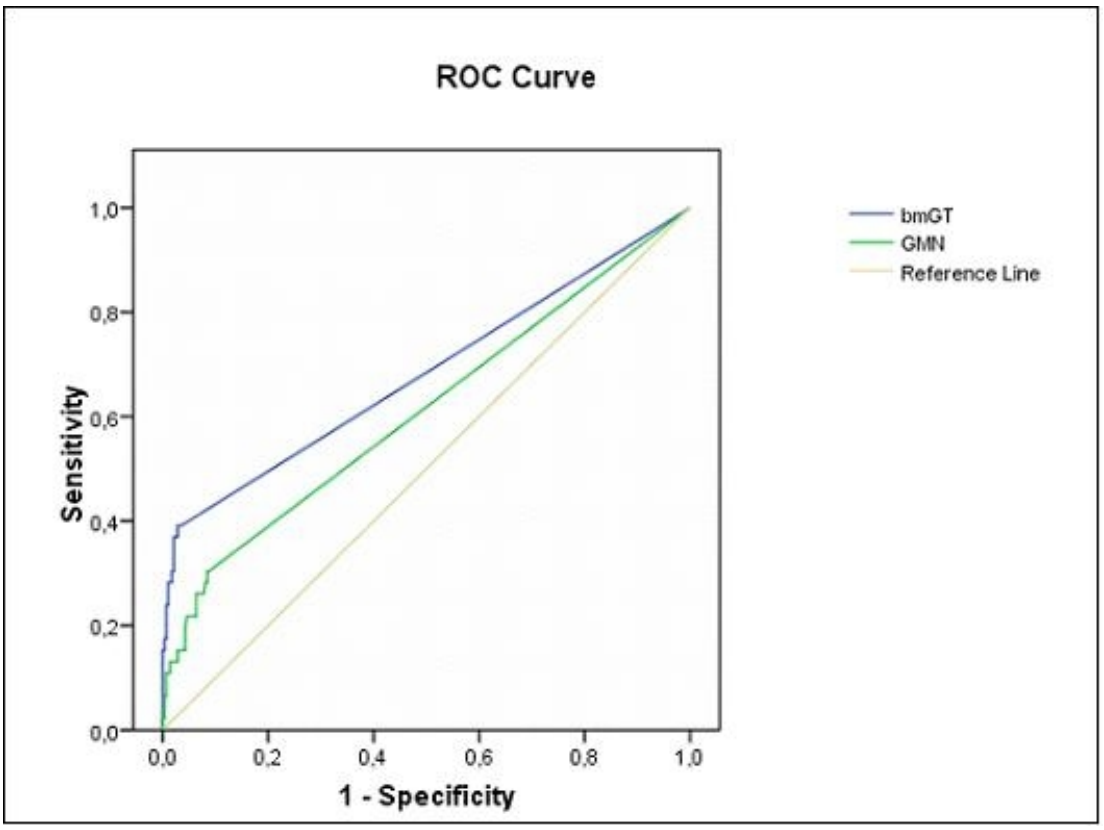

Table 1: AUC, sensitivity, specificity, PPV and NPV for GMN and bmGT.

	GMN	bmGT
AUC	0.611	0.682
Sensitivity (%)	26.3	42.1
Specificity (%)	94.7	96.8
Positive Predictive Value (%)	40	64
Negative Predictive Value (%)	90.6	92.6

Conclusions:
According to our data, bmGT is more sensitive and specific than GMN for IPA diagnosis in neutropenic patients with high risk of infection. Its PPV and NPV are also higher than those for GMN.

More clinical trials are being performed for validation of this technique. Accordingly bmGT could improve the diagnosis and consequently the treatment of patients suffering from IPA.