Increasing Awareness of Sex Chromosome Trisomies Among Healthcare Providers

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Abstract

Purpose: Sex chromosome trisomies are among the most common chromosomal abnormalities resulting in live birth (Gratton, et al., 2016). Despite their prevalence, there can be a delay in diagnosis due to not associating neurodevelopmental or learning problems with sex chromosome aneuploidy's (SCA's). (Visoostak et al., 2013). Increasing awareness of sex chromosome trisomies (SCT's) among healthcare providers (HCPs) is optimal in improving the care of these children. An educational activity to inform them on the various phenotypes of SCT's will help improve diagnosis and their care.

Review of Literature: PubMed and CINAHL Plus were used, eighteen articles were selected for review. Approximately 44% (8) Level II, 27% Level III (5) and IV (5), good quality articles. Screening and routine medical care should identify SCV's, but often HCPs don't know what to look for (Tartaglia, 2020). Being diagnosed with a SCA later in life continues to be a problem even though early diagnosis should help with learning, behavioral and health problems experienced throughout their life. (Berglund et. al, 2019)**.**

Methods: A one hour continuing education presentation on SCT's was implemented. It includes information regarding SCT's in general, each individually (XYY, XXY and XXX) as well as resources for additional information. The targeted population was 15 HCP's including Nurse Practitioners. Psychiatrists, Psychologists and Social Workers. A pretest was administered with a posttest immediately after and 4 weeks post activity to assess knowledge retention.

Implications for practice: HCP's can identify earlier a patient with and support their patients with these chromosome variations and make the necessary referrals for follow up. This earlier diagnosis will assist families with SCT's support and interventions. Families and children with SCT's will benefit receiving the necessary care and interventions early improving patient outcomes.

Keywords: Sex chromosome Trisomies (SCT's), Trisomy X, Klinefelter's Syndrome, 47, XYY, screening, early interventions

Background: Lack of knowledge and awareness regarding sex chromosome variations (SCV's) among healthcare providers often lead to a lag in diagnoses in children with these variations. Screening and routine medical care can identify SCVs, but often healthcare providers don't know what they are looking for (Tartaglia, et al., 2020). To receive an early diagnosis of a SCV practitioners need to be aware of the syndrome and knowledgeable about what to look for. Among SCV's, sex chromosome trisomies (SCTs) are among the most common trisomies resulting in live birth (Gratton, et al., 2016). About one in 650–1000 children are born with an extra X or Y chromosome (van Rijn, 2019). SCVs are not hereditary, caused by an error in cell division in utero. The most common cause is nondisjunction of the X or Y chromosome during early cell division, most often during meiosis (van Rijn, 2019).

Individuals with sex chromosome variations that are not diagnosed until later in life may not receive interventions that could be pivotal to their overall health and wellbeing. Early diagnosis may help with learning, behavioral and health problems experienced throughout their life (Berglund et. al, 2019). SCA's are associated with increased morbidity and mortality, learning and/or behavioral difficulties as well as reduced socioeconomic outcomes (Berglund et. al, 2019).

While individuals with SCTs can have a variety of presentations, being able to recognize certain clinical features of sex chromosome trisomies (SCTs) can enable children earlier treatment and interventions. For example, a child presenting to the office with low muscle tone and developmental delays, an SCT should be thought of. Or when a child with attentional difficulties and anxiety with a history of developmental delays, genetic testing for SCTs should

be considered. Parents of children diagnosed prenatally are often encouraged to monitor development and seek evaluations earlier due the known risks for delays (Thompson, et al. 2020).

Once diagnosed, many parents of children are dissatisfied with the ease of obtaining necessary services to support their child due their providers lack knowledge of the condition (Thompson, et al. 2020). Parents with concerns regarding their child's developmental delays or social difficulties often had difficulty convincing their providers that their children needed additional testing or follow up. Late diagnosis, as well as non-diagnosis have been a continuous concern and associated with increased morbidity and mortality (Berglund, et al. 2019). There has been found to be a delay of 4.8 years between parent concern and genetic testing (Visootsak, et al., 2013). Language difficulties are noted early in development. Language assessments showed high clinical significance emphasizing the importance of early detection and support (Urbanus et al., 2019).

As with many syndromes, children with SCT's can have varied symptoms, but SCT as a cause is often not thought of when children are presenting with developmental, medical, and psychiatric difficulties. According to Tartaglia, et al 2020, it is common among the trisomies for children to experience speech delays and hypotonia. Children with an extra X might have epicanthal folds, clinodactyly and smaller head circumference. These individuals are often a normal length and weight at birth but by school age are often taller stature with long legs. Symptoms of inattention and mood difficulties are also common among children with SCT's. Males with an extra X often do not experience spontaneous puberty and are often infertile as adults.

It is thought that many people with sex chromosome variations are not receiving optimal medical care and attention (Berglund et. al, 2020). When providers interact with children with certain features, they can discuss their concerns with the family and refer them for genetic counseling. Conversely if a family presents with their child experiencing these difficulties an educated provider would be able to think of SCTs and quickly recommend them for follow up. When assessing a child with multiple difficulties SCT as a cause should be considered. This diagnosis can then help the child obtain school support if needed as well as other interventions to help them succeed. If a SCT is suspected the only way to confirm a diagnosis is through cytogenic testing.

Methods: The project implemented a continuing education activity to healthcare providers in a local clinic to increase awareness of SCTs. This activity gave a brief overview of common clinical features of SCTs.

To develop the educational activity a literature search was performed, various papers were analyzed for information regarding the various syndromes. This information was then synthesized into a presentation. Once the educational activity was developed an eighteen-question test, including eleven questions specific to the activity was created to assess the knowledge of SCT's to be administered to the participants.

The CE activity was an hour long and the total time for participation was ninety minutes. This time included time for the pre and posttest administration and a brief Q&A after the activity concluded. The link for the test was placed in the chat on zoom for ease of access for the participants. Prior to administering, the link was tested by multiple people on a variety of electronics (phone, tablet, laptop) to confirm ease of use. The pretest was administered

immediately prior to the CE and the posttest was administered immediately after. Four weeks later an email was sent for with the same test to evaluate how the HCP retained the information. Each HCP had a unique identifier consisting of their street address and mother's date of birth.

In the activity the first slides focused on a background of sex chromosome variations, diagnosis, and an overview of commonalities between sex chromosome trisomies (SCTs). Next each of the three trisomies (XXX, XXY and XYY) were discussed in detail. The prevalence for each condition was discussed as well as the risks for medical, developmental, and psychiatric issues were discussed. Finally, a summary of the presentation and common features of the trisomies was given along with recommendations and resources.

Intervention: This project was presented as an online continuing education (CE) activity hosted via Zoom. The practice hosting the CE was a psychiatric practice, located in an urban setting. Flyers were sent out to outside providers including local pediatrician's office and various psychiatric providers in an attempt to have a variety of HCP's. The CE was held during the office's monthly staff education meeting. The population participating was a variety of psychiatric/mental health providers including Psychiatrists, Nurse Practitioners and Social Workers. All the participants had advanced education, post bachelor's degree with over half at the doctoral level.

The pre and posttest were administered via a link connected to a google form. The form then recorded response data that was immediately uploaded to the response section on the google form site. This data was then converted into a Microsoft Excel spreadsheet.

The tests were then paired by their unique identifier with the pretest score first then posttest. Two outliers were eliminated from the analysis due to incomplete data, only posttest results were

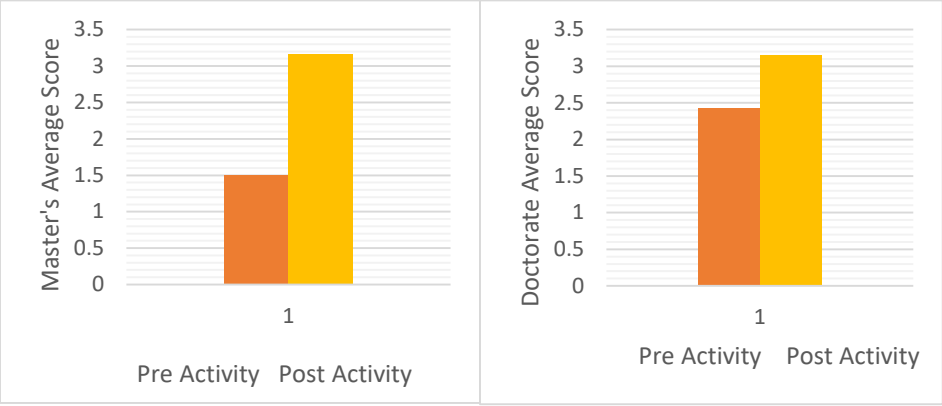
obtained. The data set had a total of twenty-six responses from thirteen participants. Descriptive statistics were used to summarize the results of the pre and posttest scores.

Results: Within the group of analyzed data seven participants, (54%) had a doctoral degree and six, (46%) were at the master's level. Of the thirteen participants included only two responded to the four week follow up to determine how the knowledge was retained over time. These additional two results from the four week follow up were not included in the analyses.

One question asked about their level of knowledge of SCTs, scoring from a 1 "little/no knowledge" to a 5 "proficient/expert". The results of the participants were compared by level of education, Figure 1. The 6 master's prepared participants on average rated their level of knowledge of SCT's a 1.5% prior to the activity. After the activity the average increased to 3.2%. The 7 participants that had a doctoral level of education had an average pre activity knowledge score of 2.4%. After the activity their score average increased to 3.1%. Showing an improvement in provider knowledge due to the activity.

Figure 1. Pre/Posttest Score by Level of Education

Average score of participants by level of education



Note: Average scores were calculated by participants response to their "level of education"

Each of the answer sheets were downloaded into a spreadsheet in Microsoft Excel. There was a total of eleven questions pertaining to sex chromosome trisomies and seven pertaining to demographics and other subjective information. Each of the questions regarding SCT's were multiple choice. To analyze the data the answers were converted to "0" for incorrect and "1" for correct in Excel. The pre and posttest answers were distinguished by the time they were submitted. The questions submitted prior to the start of the presentation around 12:00pm were pretest results. Those submitted after the end of the activity around 1:00pm were grouped as posttest results.

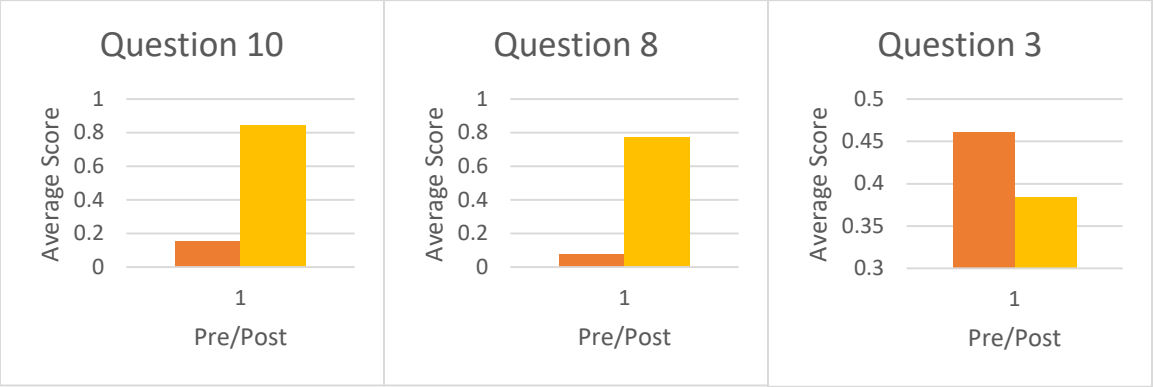
The pretest ~~the~~ question with the most correct responses was "which is the most common SCT" (Question 7) at 54%. There were two questions that were answered incorrectly at 8%. These questions were pertaining to which SCTs were related to short stature (Question #1) and how a SCT is diagnosed (Question #8). Being able to assess which questions had the greatest and least amount of improvement is critical in redesigning the activity for future education among providers. In the posttest the question answered incorrectly the most frequently was "which SCT(s) are associated with unique physical features that leads to an early diagnosis in children?" (Question 2) at 31%. The question "which SCT(s) has an increased risk for language delays?" (Question 4) was correctly answered the most at 92%.

The results of the study were promising. Overall, the results showed improvement in the knowledge of the participants. When comparing the pretest scores and posttest scores two questions showed the greatest improvement overall (69%), Figure 2. These questions were "which of the following SCT's is associated with an increased risk of violent crime?" (Question 10) and "which SCT(s) can be diagnosed solely by clinical assessments?" (Question 8). One

question was answered incorrectly more (-8%) after the learning activity compared to the first and this was "individuals in which SCT(s) often experience a delay in pubertal development?" (Question 3). Further investigation as to why the decrease in correct responses post activity would be needed to help improve this score as well.

Figure 2. Pretest/Posttest Most and Least Improved Questions

Average score of the most and least improved questions



Note: These are the average scores of the two most improved questions when comparing the pre and posttest and the lowest scoring from the CE activity from February.

For this quality improvement project, the costs for were minimal. There were not any fees associated with renting out space because it was completed virtually. The practice provided the zoom account and the CE credits. An increase in knowledge after an educational activity was the anticipated outcome and this was achieved. After completing the educational activity the participants knowledge of SCT's increased. No unintended consequences of the project have been identified.

Discussion: Studies show that many if not most individuals with sex chromosome abnormalities are diagnosed late or never (Berglund, et al. 2020). One cause can be related to the

lack of provider awareness of the characteristics associated with these syndromes. The aim of this project was to provide an educational activity to increase the knowledge of SCTs among healthcare providers. The CE activity provided this education to HCPs and ultimately could increase the post-natal diagnosis of SCT's due to increased awareness.

Overall, the data showed this activity provided an increase of knowledge among the participants. This was observed in both the qualitative and quantitative measures used to obtain results. The participants rated their overall level of knowledge had improved post activity. The master's prepared participants increased by 1.7% and the doctoral prepared participants knowledge increased by 0.7%. The doctoral prepared participants rated their knowledge prior to the activity higher than the master's prepared participants. Having a higher confidence with the syndromes among the doctoral prepared could be attributed to the additional number of years of education they have received.

When evaluating the questions individually all the questions except one, question 3, regarding delays in pubertal development was answered correctly more post activity. On the pretest six participants answered this question correctly while posttest only five answered correctly. When analyzing the results, this participant originally answered the question correctly, but post activity answered incorrectly as "all the above". Further analysis into why the question was answered incorrectly (participant accidentally pressed wrong answer, information in the activity was difficult to understand etc.) would be necessary to ensure the participants are receiving the correct information.

Originally the project was designed as a lesson presented to multiple practices during their lunch hour. This would have allowed for a more diverse group of providers and potentially a higher number of participants. Due to COVID-19 restrictions many of the offices were hesitant

to have the provider come into their practice for a presentation. One practice volunteered to present via zoom during the practice's monthly meeting. The practice had over 30 providers, but this was not a mandatory activity and unfortunately yielded a low number of providers (15). Due to incomplete tests only 13 of those attending were able to be analyzed.

Another limitation was not being able to get many responses at the 4 week follow up. Many attempts were made to obtain this posttest, but only two participants responded. Part of the project was to assess how the activity helped with providers ability to retain the information learned. Being unable to compare this data with the posttest immediately following the activity was disappointing as there was no opportunity to assess if the providers remembered the information.

The educational activity was sent out to a variety of practices the owner associated with including primary care, but the group attending were all psychiatric providers. While there were a variety of psychiatric providers having other types of healthcare practitioners would have been ideal. Other comparisons regarding the type of provider and knowledge base would have been able to be analyzed. Due to the low number and homogeneity of providers specialty the results may not be representative of healthcare providers in general.

Despite the small number of participants, the results did show an increase in knowledge. Being able to provider short educational activities to providers will continue to improve their awareness. Even among providers that rated their knowledge as high there was an improvement in their scores after the activity. Next steps would be to continue to record presentations like this one and disseminate among providers. Having various practices require their employees to obtain this CE would continue to increase awareness. Being able to distinguish the symptoms in

children with SCT's earlier can help lead to an earlier diagnosis and receiving necessary interventions to help improve their quality of living.

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